INFANT FEEDING IN HIV IN CANADA: PROVIDER PERSPECTIVES

INFANT FEEDING IN HIV IN CANADA:
An exploration of Healthcare Provider Perspectives: Knowledge, Attitudes and Practices Survey and Clinical and Research Priority Setting Meeting

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LAY ABSTRACT

Infant Feeding in HIV in Canada is an increasingly challenging aspect of clinical care. Information on breastmilk transmission comes from studies completed in lower income countries, and this may not be applicable to the Canadian HIV setting. Previous literature has not explored provider perspectives on this issue, especially in high-income countries like Canada. In this knowledge, attitudes and practices survey of HIV care providers in Canada, the main findings were that formula feeding should remain the recommendation due to the potential risk of HIV infection occurring in the baby, however women should be supported to access formula and resources to overcome barriers to formula feeding. Providers do not feel that breastfeeding is a criminal matter, but in some circumstances may consider involving child protection services. We performed community consultation using focus groups to understand some of the issues women face with infant feeding, some of the clinical solutions they would support, and research questions and knowledge translation they would want undertaken. A provider meeting to discuss the challenges pertaining to infant feeding in Canada demonstrated that although populations differ, the need for knowledge translational resources to convey information to women living with HIV on infant feeding was universal. Furthermore, the need for evidence based consensus clinical management guidelines would improve the quality of care provided.

ABSTRACT

Infant Feeding in HIV in Canada is an increasingly challenging and confusing aspect of clinical care for providers and patients due to differences in recommendations in Canada compared to low income countries. The frequency of breastfeeding occurring in Canada is not documented or known, and is shrouded in stigma because of fear of criminalization or child apprehension in the midst of a culture where 'breast is best' messaging dominates. Breastmilk transmission data comes from observational and randomized controlled trials completed in low resource settings, which may not be generalizable to Canadian clinical settings. Previous literature has not explored provider perspectives on this issue, especially in high resource settings. We developed a survey to explore the knowledge, attitudes and practices of adult and pediatric HIV care providers in Canada. This survey explores the provider knowledge levels, risk tolerance and perceived stigma pertaining to infant feeding in HIV. Using exploratory analysis including descriptive statistics and regression modelling, we developed scales on the above listed three subject areas. The overall opinions of providers were that formula feeding should remain the recommendation due to the potential risk to the infant; and that women should be supported to access formula and resources to overcome barriers to formula feeding. Providers varied in their risk tolerance and the degree of stigma they perceived associated with infant feeding for their patients. Providers did not feel that breastfeeding is a criminal matter, but in some circumstances they would consider involving child protection services. Focus group consultation with women living with HIV, provided insight into the experiences, and clinical and research priorities for women living with HIV on infant feeding. A provider meeting was organized to discuss the challenges and

resources pertaining to infant feeding in Canada across the provinces. Providers described diverse patient populations with differing needs. Using a World Café model for discussion, priority needs were decided through consensus including the need for knowledge translational resources to convey information to women living with HIV on infant feeding, and the need for evidence based consensus clinical management guidelines was evident. Quantifying the frequency of breastfeeding occurring in Canada by women living with HIV will help to understand how often this issue is encountered. A preliminary qualitative approach to understanding infant feeding issues for women living with HIV using focus groups is described. However, further exploration in a community based approached is needed to explore the needs and challenges faced by families affected by HIV around infant feeding.

Keywords: HIV, infant feeding, breastfeeding, HIV stigma, risk tolerance, knowledge translation

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LIST OF ALL ABBREVIATIONS AND SYMBOLS

ACB - African Caribbean Black

Adjusted Odds Ratio - AOR

AFASS – Acceptable, Feasible, Affordable, Safe and Sustainable

AIDS – Acquired Immunodeficiency Syndrome

AMMI - Association Medical Microbiologists and Infectious Diseases

ANOVA – Analysis of Variance

ART – Antiretroviral Therapy

ASO – AIDS Service Organization

BHIVA – British HIV Association

Brfdg – Breastfeeding

CANAC - Canadian Association of Nurses in HIV/AIDS Care

CAS – Children's Aid Society

CATIE – Canadian AIDS Treatment Information Exchange

CD-4 T cell – cluster of differentiation-4 thymus lymphocyte cell

CHABAC – Canadian HIV/AIDS Black, African and Caribbean Network

CHAP - Canadian HIV/AIDS Pharmacists Network

CI – Confidence Interval

CIFHN – Canadian Infant Feeding in HIV Network

CIHR - Canadian Institutes of Health Research

CMPA – Canadian Medical Protection Agency

CPARG – Canadian Pediatric and Perinatal AIDS Research Group

Ctty hosp – Community Hospital

Ctty practice – Community Practice

DC-SIGN – Dendritic Cell-Specific Intercellular Adhesion Molecule-3-Grabbing Non-Integrin protein

DNA – Deoxyribonucleic Acid

GP – General Pediatrician

HEU - HIV Exposed Uninfected infant

HIV – Human Immunodeficiency Virus

HIV+ - HIV positive

HIVP – Human Immunodeficiency Virus Provider

HR – Hazard Ratio

I^2 – I-square statistic

ICAN – Interagency Coalition on AIDS and Development

ID – Infectious Diseases Specialist

IDU – Intravenous Drug User

i.e. – id est

IHPREG – Interdisciplinary HIV Pregnancy Research Group

KT – Knowledge Translation

MCQ – Multiple Choice Questions

MD – Medical Doctor

MM – Medical Microbiologist

NRTI – Nucleoside Reverse Transcriptase Inhibitors

NNRTI – Non-Nucleoside Reverse Transcriptase Inhibitors

OB - Obstetrician

OR – Odds Ratio

OT – Occupational Therapist

Peds – Pediatricians

Peds ID – Pediatric Infectious Diseases Specialist

PH – Public Health

PHAC – Public Health Agency fo Canada

Pharm. - Pharmacist

PRA – Peer Research Associate

PI – Prediction Interval

P/T – part-time

PT - Physiotherapist

RCT - Randomized Controlled Trial

RD – Registered Dietician

REDCap – Research Electronic Data Capture

Repro – Reproductive specialist

RN – Registered Nurse

RRRF – Relative Risk of Replacement Feeding

SD – Standard Deviation

SOGC - Society of Obstetricians and Gynecologist of Canada

SPSS – Statistical Package for the Social Sciences

SW – Social Worker

Transitioned – Transitions from pediatric to adult are

uL - microliter

VT – vertical transmission

WHO – World Health Organization

DECLARATION OF ACADEMIC ACHIEVEMENT

S. Khan and M. Smieja developed the components of this thesis with feedback from supervisory committee members M. McConnell, and L. Thabane. S. Khan wrote and researched the findings. Input was provided throughout the course of this work from S.A. Bitnun, S. Read, VL Kennedy, and M Loutfy.

CHAPTER 1: Introduction

Vertical transmission (VT) is the cause of 90% of pediatric HIV infections worldwide(1). Without any intervention, the risk of VT ranges from 15-25% in high resource settings and between 25-45% in low resources settings(1,2). Vertical transmission can occur in utero, at the time of delivery, and postpartum through breastfeeding(3).

Prevention of VT of HIV using antiretroviral interventions has significantly reduced this risk. The global standard of care for VT now includes combination antiretroviral therapy to suppress viral load during pregnancy, antiretroviral interventions at the time of delivery, and antiretroviral prophylaxis for the infant after birth(3,4). The main difference in VT recommendations globally relate to infant feeding; in high resource settings, the recommendation is exclusive formula feeding to reduce the potential risk of postnatal VT. The estimated additional risk of breastfeeding that occurs in low resource settings among women with established HIV infection was previously considered to be 15% without maternal antiretrovirals (95% confidence interval [CI] 7-22%)(1,6), but more recent evidence now estimates this risk now with antiretroviral intervention to be 2-5% (7,8). In Canada, and other high resource settings with optimal antiretroviral interventions and exclusive formula feeding occurs, the risk of vertical transmission has been reduced from approximately 20% in 1980s to <1% in 2000s.

The question of infant feeding in HIV is a complex issue, bio medically, ethically, and clinically. Our understanding of HIV transmission through breastmilk has evolved over time and many aspects are still not completely answered. From the first documented cases of breastmilk transmission, the guidelines on infant feeding have swung on a

pendulum between exclusive formula feeding in all contexts, to the current state of exclusive breastfeeding in low middle-income countries and exclusive formula feeding in high resource contexts. Research on breastmilk and breastfeeding populations include in-vitro analysis of breastmilk, observational cohort studies, and meta-analyses of large randomized controlled trials (RCTs). This growing body of evidence suggests a low risk of breastfeeding-related HIV transmission (2-5%). This has resulted in debate as to whether breastfeeding with antiretroviral interventions could be an option in Canadian recommendations.

This debate occurs because of multiple reasons including patient factors, provider factors and knowledge gaps. Patient and provider factors include the fact that patients and providers often have either had children or cared for patients living with HIV in low-middle income contexts and understand the sociocultural complexities of infant feeding decisions in society; however, risk tolerance among providers and women can vary significantly. Knowledge gaps persist such as the actual quantifiable risk of transmission in virologically suppressed women living with HIV in a high resource setting. With these remaining questions, clinical recommendations on infant feeding end up being based on expert opinion, which can lead to a patriarchal or medico legal approach to clinical recommendations, sometimes lacking input from all stakeholders including the woman, the child, the clinician, the family, and the community.

These issues are complex and require an in-depth assessment of both the provider and the patient knowledge, attitudes and experiences on infant feeding in the HIV context.

This thesis will begin in Chapter Two with a narrative review of the literature on breastfeeding transmission as it evolved over time, and summarize the changes to the

guidelines on infant feeding. We will start with a discussion on the first cases of breastmilk transmission, and early evidence of HIV in breastmilk. This is followed by observational and RCT data that identified important risk factors for breastmilk transmission including maternal immunologic status, duration of breastfeeding, rapid weaning, and mixed feeding. These findings resulted in the major changes in guidelines, which initially supported formula feeding to mitigate this risk. However, as increased morbidity and mortality occurred due to resource constraints affecting the safety and feasibility of formula feeding, recommendations were again revised to be more context specific. As antiretrovirals became more available, guidelines were again revised to consider the variability in access to consistent antiretroviral interventions. As the debate continued, meta-analyses focused on quantifying the risk of breastmilk transmission were published. These findings now quantify the risk of breastmilk transmission as much lower than initially described, from 15% to 2-5% in the context of antiretroviral therapy virologic suppression(7). These findings have framed the most recent 2016 WHO guidelines, which have shifted to breastfeeding being more widely recommended, for more flexible durations in the context of antiretroviral interventions.

Although the risk is better quantified, the actual mechanisms and biology behind breastmilk transmission remains unclearly elucidated. Risk factors that likely contribute to the degree of risk based on in vitro breastmilk analyses, and clinical studies are summarized in a discussion on the maternal, infant and feeding related factors, which have been described in basic science and clinical research.

Understanding the global evolution of this issue is essential to frame the Canadian conversation on infant feeding in HIV. The discussion will then shift to summarize

changes in guidelines over time, and the gaps in knowledge which remain due to the reality that the primary studies have all been done in low-middle income contexts where breastfeeding occurs making it not entirely generalizable to the Canadian context. Chapter Two will conclude with a summary of the issues surrounding infant feeding in HIV in Canada, including the known prevalence of breastfeeding in Canada, and the legal implications of it.

The focus of Chapter Three is the data gathered from a Knowledge, Attitudes and Practices Survey for HIV Care providers in Canada. As discussed in Chapter One, providers are a key stakeholder in the infant feeding discussion, generation of research questions, and revisions of guidelines based on evidence. The development of the survey by measurement and content experts, followed by the piloting process using the online REDCap format is described. The method of sampling, dissemination, and data collection will be summarized. The results including the development of quantitative knowledge scales on key concepts, perceived stigma scale, and a risk tolerance scale were developed to summarize the data. Provider characteristics, general patient characteristics, and previous provider experience are used to find associations with scores on the three main scales. Overall, common attitudes and practices of Canadian clinical HIV care providers are also summarized in order to provide widely agreed upon aspects of care. Key findings from this survey will highlight areas of consensus among providers, and areas which remain contentious. Limitations of the survey are also described for future efforts to be taken on provider engagement on this subject.

Chapter Four will summarize the qualitative findings of community consultation focus groups held before and after a National HIV Care Provider Research and Clinical

Consensus meeting. Women living with HIV who had recent experience with pregnancy and infant feeding participated in a focus group to explore their experience, challenges, and potential research and clinical solutions. Directed content analysis of transcripts elicited three key areas for discussion, which parallel the findings from the provider meeting. The provider meeting summary will include participant characteristics, and method of recruitment for this meeting. At this meeting providers were asked to summarize key elements of infant feeding related care provided and ongoing challenges encountered. A summary table of HIV clinics across Canada and their patient demographics, available resources, and services, and specific needs is provided. Experts from basic science, legal, social science, and clinical epidemiology offered high-level summaries of the main issues surrounding infant feeding in Canada is described. A consensus building World Café Discussion allowed for determination of priority areas and next steps as it pertains to the infant feeding in HIV discussion in Canada is included.

We will conclude in Chapter Five by summarizing the previous chapters, further discussion on the work completed thus far which has mainly focused on provider perspectives. We will take the discussion from the past, the present, and what is needed in the future to improve the care for families affected by HIV in Canada as it pertains to infant feeding.

CHAPTER 2: Background on Issues surrounding infant feeding in HIV

2.1 HIV in breastmilk causes vertical transmission

To understand the current recommendations on infant feeding in HIV the history of breastfeeding transmission must first be reviewed. The first reported case of HIV transmission through breastfeeding was in 1985(9,10). This case involved a previously healthy mother and infant who was breastfed for 6 weeks(11,12). The woman had delivered by caesarean section, and required a blood transfusion postpartum. One unit of blood donated from a man who developed Acquired Immunodeficiency Syndrome (AIDS) 1 year later. After the blood donor was diagnosed with AIDS, the mother and child were tested and found to be HIV-seropositive. Since the father was seronegative and the mother received the transfusion after delivery, breastmilk was presumed to be the source of infection of the infant. Similar case series were reported of infants born to parents with no known risk factors for HIV infection, presumed to be HIV negative at birth. Most cases involved transfusion related HIV infection of the mother after delivery, and postpartum infection of the infant after birth. One case involved a wet nurse who later died of AIDS-related complications when the infant was 17 months old. The presumed mechanism of transmission in these cases was breastfeeding(13). This hypothesis was later corroborated through laboratory analysis of breastmilk confirming the presence of HIV-1 by culture and polymerase chain reaction techniques(6). HIV was also found in both cellular and cell-free breastmilk components.

After HIV breastfeeding transmission was confirmed in small case series, observational data began to be collected to understand this risk further. During the early

1990's researchers begin to quantify this risk and identify potential factors that may increase the risk of HIV breastfeeding transmission.

2.2 Studies on breastmilk transmission

2.2.1 Observational studies of duration of breastfeeding and maternal viral load

Due to the ethical challenges of randomizing infants born to women living with HIV to breastfeeding versus bottle feeding, most of the data came from observational studies(14). In 1991, a cohort of infants born to women living with HIV in Zaire were followed in 3 arms: exclusive breastfeeding, exclusive formula-feeding and mixed-feeding. The risk of transmission was 21% in the 28 breastfed infants, 0% in the 10 formula-fed infants, and 19% in the 68 mixed-fed infants(15). The first cohort study to demonstrate a dose-response relationship with duration of breast-feeding was conducted in Italy, and involved 168 breast-fed infants compared to 793 formula-fed controls. Infants were breastfed for a median duration of 2 months (range 0.1 - 18.2 months)(16). As the duration of breastfeeding increased from a range of less than 20 days compared to greater than 92 days the odds ratio of HIV transmission increased from 2.16 (95% CI: 1.17, 4.0) to 6.41 (95% CI: 2.98, 13.79).

Duration of breastfeeding as a risk factor was assessed with a meta-analysis of individual patient data from 9 observational studies. Of the 4085 children included, 993 (24%) became infected(17). Of the 539 infants with a known timing of infection, 42% (n=225) had late postnatal transmission throughout breast-feeding with a constant hazard function over time. The cumulative probability at 18 months of age was 9.3%, or 8.9 transmissions per 100 child years of breastfeeding (95% CI: 7.8, 10.2). Specific

covariates assessed to understand risk factors included maternal and infant variables. Risk was noted to be higher with a lower maternal CD4-positive T-lymphocyte count. The hazard ratio for CD4<200cells/uL was 8.0 (95% CI: 4.8, 13.3) compared to CD4>500cells/uL (HR 3.7 (95% CI: 2.4, 5.6). This was an interesting finding as CD4 counts tend to fall in later stages of chronic HIV infection.

Timing of maternal infection was explored in another meta-analysis. Specifically, postnatal versus prenatal HIV infection of the mother and the risk of MTCT was assessed by Dunn et al. in a meta-analysis of 4 studies(6). Breast-feeding by women with postnatal infection resulted in a risk of transmission of 29% (95 CI: 16%, 42%), whereas breast-feeding by those with prenatal infections resulted in a risk of transmission of 14% (95% CI: 7%, 22%). The authors hypothesized that the increased risk of transmission found with postnatal infection related to the higher levels of viremia in acute infection.

Further risk factors explored in cohort studies, include acute HIV infection, breast disease, and duration of breastfeeding. A case series of 104 women infected from blood transfusions post-partum who exclusively breastfed their infants in China from January 2000 to June 2008, documented a transmission rate of 35.8%, with an average duration of breastfeeding of 16.5 months (range, 1-28 months)(18). In this retrospective review, the presence of breast disease (cracked nipples, mastitis) while breastfeeding increased the risk from 31.1% (95% CI: 21.5, 40.7%) to 62.5% (95% CI: 35.4, 84.9%) among those with and without breast disease during lactation (p=0.016). No significant difference in transmission beyond 6 months of breast-feeding, indicated that much of the transmission occurred early, related to a high viral load in the acute infection period. These

observational data informed randomized clinical trials (RCTs) in the era preceding widespread anti-retroviral availability.

2.2.2 Randomized controlled trials: risk vs. benefit of formula feeding

In the early 2000's, due to clinical equipoise around the true risk versus benefit of breastfeeding in low resource contexts where formula may not be readily available, randomized clinical trials (RCT) were conducted(19). From 1992 to 1998 an RCT among four antenatal clinics in Nairobi Kenya was conducted to compare morbidity, mortality and nutrition among formula fed versus breastfed infants(20). Mothers were randomized to formula feed (n=186) or breastfeed (n=185) conditions however, compliance with feeding arm was lower in the formula feeding arm (70% vs. 96%, $p<0.001$). The cumulative proportion of HIV infection at 2 year follow-up was significantly lower in the formula feeding arm (21% vs 37%, $p=0.001$). Mortality at 12 and 24 months did not significantly differ between the two groups (20.0% vs 24.4%; hazard ratio [HR], 0.8; 95% confidence interval [CI]: 0.5, 1.3), even after adjusting for infant HIV infection status (HR, 1.1; 95% CI: 0.7, 1.7). Infection with HIV was associated with a nine fold increased mortality risk (95% CI 5.3 15.3, $p<0.001$). The incidence of diarrhea during the 2 years of follow-up was similar in formula and breastfeeding arms (155 vs 149 per 100 person-years, respectively). The incidence of pneumonia was identical in the two groups (62 per 100 person-years), and there were no significant differences in incidence of other recorded illnesses. Infants in the breastfeeding arm tended to have better nutritional status, significantly so during the first 6 months of life ($p=0.003$). This study went on to state that formula provided a 28% protective effect from an adverse outcome (HIV infection or death). However, this study defined breastfeeding as 'any use of breastmilk', whereas

formula compliance was defined as complete avoidance of breastmilk. Therefore, this study was comparing mixed feeding to exclusive formula feeding, which was later recognized as the highest risk strategy for infant feeding. Additionally, we know the comparison of outcomes in the real world can be significantly different from outcomes obtained in the context of a RCT in a low resources setting. This study was not necessarily generalizable, as all women participating in the trial had access to potable water, extensive health education on safe formula preparation, reliable formula access, and medical care for their infants. This study contributed support for the WHO guidelines at the time which advocated for "context specific counselling for pregnant women living with HIV, allowing each woman to select the feeding method that maximized benefits and minimized risk given her individual situation"(21). This type of vague open-ended recommendation--albeit less patriarchal--resulted in variable practice, confusion among health care providers, and unclear messaging to patients.

2.2.3 Testing the risk in pragmatic studies

Although the strong association between breastmilk exposure and transmission was demonstrated, what was not apparent was the potential adverse effect of making general recommendations given the context specific implications of infant feeding. Several pragmatic research studies were conducted. For example, the Rakai Community Cohort Study in rural Uganda was a seminal study illustrating the challenges of formula feeding in low resource settings. In this study, women were counselled and allowed to either formula-feed (n=75) or breastfeed (n=107). It demonstrated a cumulative 12-month probability of infant mortality of 18% (95% CI: 11%, 29%) among the formula-fed compared to 3% (95% CI: 1%, 9%) among the breast-fed infants (unadjusted HR = 6.1,

95% CI: 1.7, 21.4, p=0.01)(22). There was no significant difference in HIV-free survival by feeding choice in the formula-fed (86%) compared to the breast-fed group (96%) (Adjusted HR = 2.8 [95% CI: 0.67, 11.7, p=0.16]. In this study, the six-fold excess mortality in non-breastfed infants noted by investigators actually led to discontinuation of formula provision for newly delivered babies, and encouragement of exclusive breast-feeding. The study's household hygiene survey revealed multiple concerns related to formula feeding in a low resource context: 59% of mothers (n=17) admitted to re-use of feeding utensils without washing, 86.7% of mothers (n=25) admitted to using infant feeding bottles which were contraindicated by the program due to the difficulty with cleaning, 17.2% (n=5) of women stored leftover feeds for later, 31.1% (n=9) of women reported difficulty maintaining clean utensils and 65.5% (n=19) reported difficulty measuring the correct amount of formula powder. Twenty-three homes (79.3%) had a toilet facility, but only 11 of the 23 (47.8%) of these had hand washing facilities. The risk of mortality with formula-feeding was much greater in rural populations with limited access to clean water and medical care even among infants not infected with HIV despite antiretroviral therapy to mom or newborn prophylaxis during breastfeeding. These studies spoke to the practicalities of providing clean and safe formula in low resource settings where water and clean utensils may be tenuous in supply.

The potential for mixed feeding to occur when both breast and formula feeding are options also needed further study. In an observational study from South Africa in 2001, 551 HIV-infected pregnant women with no access to antiretroviral medications were counselled to practice exclusive breastfeeding for at least 3 months. Their infants were followed for HIV transmission and HIV-free survival based on if they were never breastfed

(n=157, 28.5%), exclusively breastfed (n=103, 18.7%) and mixed fed (n=291, 52.8%)(23). Exclusive breastfeeding defined as a time-dependent variable in a Cox model, had significantly lower risk of HIV infection (HR 0.56, 95% CI: 0.32, 0.98, p=0.04) than mixed breastfeeding, and had a similar risk to never breastfeeding (HR 1.19, 95% CI: 0.63, 2.22, p=0.59).

Feeding solid foods or nonhuman milks in addition to breastmilk during the first 3–6 months of life to infants born to women living with HIV is associated with a 4 to 10-fold greater risk of postnatal transmission, compared with exclusive breast-feeding (21, 68, 36, 69, 70). In one study from Zimbabwe (ZVITAMBO), rates of postnatal transmission were 5.1, 6.7, and 10.5 infections per 100 child-years of breast-feeding for infants who were exclusively breastfed, predominantly breast-fed (feeding breastmilk and other non-milk liquids), and mixed fed, respectively. This further suggests that even water and other non-milk liquids increase postnatal risk, compared with strict exclusive breastfeeding(27). Mixed feeding is hypothesized to increase the risk of transmission through a few mechanisms. The main mechanism described is the increased intestinal permeability to HIV from inflammation due to multiple antigen exposures from breastmilk and formula or, increased diarrheal illness (due to contaminated formula or bottle feeding equipment) allows for HIV bowel lumen translocation(28). A secondary mechanism described is increased mammary gland inflammation when infants partially satiated by non-breastmilk food, suckle less vigorously, causing milk stasis in the breast, engorgement and mastitis. This mammary gland inflammation increases breastmilk viral load(27). Increased HIV transmission was one concern, but morbidity from formula feeding was somewhat unexpected.

2.2.4 Morbidity in formula versus breast-fed infants

The MASHI study in Botswana was a large RCT designed to answer the question of increased morbidity due to formula feeding compared to breastfeeding with extended infant zidovudine prophylaxis(29) . The 1200 mothers received zidovudine 300 mg orally twice daily from 34 weeks' gestation and during labor. Infants were randomized to 6 months of breastfeeding plus prophylactic infant zidovudine, or formula feeding plus 1 month of infant zidovudine. Although the 7-month HIV infection rates were lower in the formula fed group compared to the infant group (5.6% vs. 9.0%, p=0.04; 95% CI: -6.4%, -0.4%), the cumulative mortality at 7 months was higher for the formula fed group than for the breastfed group (9.3% vs 4.9%, p=0.003). The rate of hospitalizations was significantly higher in the formula fed group 20.8% vs. 15.6%, p=0.04). Overall cumulative mortality or HIV infection rates at 18 months were similar: 13.9% versus 15.1% in the formula fed versus breastfed group respectively, (p=0.6, 95% CI for difference -5.3% to 2.9%). The authors concluded that higher rates of morbidity and mortality were associated with formula feeding. This merited a careful assessment of the local management of childhood illnesses (diarrheal and respiratory) before the implementation of a formula feeding strategy for PMTCT in low resource settings.

An alternative approach was taken in the Kesho Bora trial, where antiretroviral prophylaxis to the infant was studied to see if it could mitigate the risks of breastfeeding. This was a multi-center RCT examining the difference between triple antiretroviral therapy versus then-standard monotherapy prophylaxis in 751 HIV-exposed African infants. This study in fact demonstrated the morbidity which occurs even in HIV uninfected children because of feeding status(30). Non-breastfed infants tended toward a greater morbidity risk than breastfed infants from 0-6months (OR: 1.22; 95% CI: 0.99, 1.50, p=0.058).

Analysis of morbidity for HIV uninfected infants between 0 and 2.9 months of age was higher in the never-breastfed infants compared to exclusively breastfed (OR 1.49, 95% CI: 1.01, 2.2, p=0.042). Similarly, the risk of serious infectious events (gastroenteritis, and lower respiratory tract infections) increased using a regression model with breastfeeding as a time-dependent variable adjusting for study site, maternal education, economic level, and co-trimoxazole prophylaxis. Between 0 and 6 months, the odd's ratio for non-breastfeeding infants was 5.3 (95% CI: 2.42, 11.8; P<0.001), and no other variables were independently associated with serious infectious events. Morbidity was higher in formula fed infants even if they were not HIV infected. This led to a hypothesis that nonspecific immunologic benefits of breastmilk were protecting against infections, and led to an improved nutritional and hydration status.

2.2.5 Does brief breastfeeding and rapid wean reduce the risk?

Based on the concern that the greatest risk period for morbidity of infants was early, an attempt at assessing the benefit of a brief breastfeeding period in early infancy was tested in a Zambian RCT. This study enrolled 958 women living with HIV and their infants who intended to exclusively breastfeed for 4 months; 481 women were randomized to a counselling program that encouraged abrupt weaning at 4 months, and 477 to a program that encouraged breastfeeding for as long as the women chose(31). In the intervention arm, 69.0% of women stopped breastfeeding at 5 months or earlier, and 68.8% of women reported completing the wean in less than 2 days. There was no significant difference between the groups in the rate of HIV-free survival at 24 months (68.4% and 64%, p=0.13). Children who were infected with HIV by 4 months had a higher mortality by 24 months if they had been assigned to the intervention group (73.6% versus

54.8%, p=0.007). Therefore, early cessation of breast-feeding by women living with HIV in a low-resource setting did not improve HIV-free survival and was harmful to HIV-infected infants. Practically speaking, abrupt stopping of breastfeeding resulted in adverse events for mothers (engorgement) and babies (crying, refusing to feed).

The risks associated with a general recommendation against breastfeeding in all contexts was seen through studies described above, but analysis of socioeconomic and systemic factors faced when living in low resource settings provided more substantial data. In 2005 in Botswana, unusually heavy rains and flooding led to an outbreak of infant diarrhea(32). A CDC outbreak investigation concluded that the most significant risk factor for diarrhea was lack of breastfeeding (adjusted odds ratio [AOR]: 50; 95% CI=4.5 -100) (32). The practicalities of implementation of PMTCT feeding programs in low and middle-income settings became apparent.

Challenges in implementation of infant feeding PMTCT interventions included: poor quality counseling done by health workers on infant feeding, suboptimal formula preparation and bottle cleaning, inadequate dietary nutritional content for children after 6 months, and spillover of formula to HIV-negative women after the introduction of formula had significant negative effects to non-HIV exposed infants. Maintaining adequate supply and distribution of powdered formula to women monthly through clinics and hospitals nationwide was a major challenge resulting in mixed feeding. These factors necessitated a change in recommendations due to the practical challenges of exclusive formula feeding in low resource contexts.

2.2.6 Maternal, Infant and Feeding related risk factors

There are other factors aside from duration and quantity of breastmilk known to increase the risk of breastmilk transmission, mainly from basic science studies. These factors include infant, maternal and feeding related factors, summarized in Table 1.

Table 1: Factors associated with breastmilk transmission of HIV

Maternal	**Infant**	**Milk/Feeding**
• Stage of HIV disease o Viral load o Antiretroviral use • Nutritional status (vitamin A deficiency) • Mastitis / Cracked nipples/ Breast abscess	• Intestinal and mucosal integrity due to infection or malnutrition or gut immaturity • Antiretroviral use	• Mixed feeding • Rapidity of wean • Cell free vs. Cell Associated virus • Other viruses (CMV, EBV in breastmilk)

Maternal Factors:

HIV infection status

Maternal factors include timing of maternal infection, as seen in the case series of women who were acutely infected post-partum due to blood transfusion(6). Acute HIV infection is the first 4-5 weeks in which the virus disseminates into tissues and organs, establishing a proviral reservoir within days, as viremia rapidly increases to a peak of 10^7 to 10^8 HIV RNA copies/mL. Thereafter the viral load decreases, and reaches a plateau set point, that persists chronically(33). A viral load of <400 copies/mL has a transmission risk of <1%, and a viral load of >100,000 copies/mL has a 32% risk of transmission overall.

Low maternal CD4 count (<200 cells/uL) has also been an observed risk factor in some studies, with a 5-fold increased risk of transmission compared to CD4 counts >500cells/uL in the normal range(25). This is hypothesized to be due to more advanced progression of HIV disease and lower immunological protective factors in breastmilk.

Nutritional Status

Early observational studies showed a potential link between vitamin A deficiency and increased risk of vertical transmission theorized to be related to compromised epithelial integrity of tissues in the vaginal mucosa and mammary glands(34). However, a Cochrane review of RCTs comparing vitamin A supplementation with placebo in HIV-infected pregnant or breastfeeding women showed vitamin A supplementation had no effect on the risk of MTCT (4 trials, 6517 women: RR 1.04, 95% CI 0.87 to 1.24; I^2=68%). These trials were conducted between 1995 and 2005 in Africa in women living with HIV on variable dose and duration of supplementation(35). Important criticisms of this meta-analysis were that participants either had no anti-retroviral therapy (ART), or the study design did not clarify whether ART was available or not.

Breast or Nipple inflammation

Breast related factors also play a role, as seen in a cohort of breastfeeding women living with HIV in Zimbabwe in which 30.8% had nipple disease (eczema 22.1%, cracked and sore nipples 10.6%)(36). Nipple inflammation has also been considered a factor, as one small observational study in Brazil showed bleeding cracked nipples to have a higher association with transmission, not seen with a history of cracked nipples alone(37).

Breastmilk contains cell-associated and cell-free HIV virus. Cell-free viral load is related to passive leakage of virus through mammary epithelial tight junctions. It is also important to note that breastmilk viral load does not correlate directly with plasma viral load due to other interacting factors(38). Mastitis or local breast inflammation itself has been associated with increased breastmilk viral load. Clinical and subclinical mastitis as indicated by elevated breastmilk sodium/potassium ratio or lactoferrin concentration is associated with higher breastmilk HIV load and breast-feeding–associated HIV transmission rates. The ratio of extracellular ions (sodium) to intracellular ions (potassium) becomes elevated when cell membranes are disrupted, which may also facilitate greater leakage of HIV from plasma to breastmilk(27). Although clinical mastitis is a relatively rare condition(16), as much as 50% of all breastfeeding associated transmission may be attributable to subclinical mastitis, with a reported 11-fold greater odds of transmission in women with subclinical mastitis(39).

Infant factors:

Mucosal permeability

In young infants, the mucosal and intestinal barrier is immature, and the tight junctions between enterocytes remain open. Oral candidiasis in the breastfed child has been associated with vertical transmission, without clear causality understood(40). This mucosal inflammatory condition causes disruption of oral endothelium that may also allow for a portal of entry while breastfeeding(40-42). Animal models of simian and feline immunodeficiency viruses have shown that applying cell-free virus on to mucosa can result in transmission of infection(42)(43). The HIV virus also can survive the harsh

environments of enzymes and acidity of the oral and gastric mucosa, as HIV RNA has been isolated from oropharyngeal gastric aspirates of infants born to women living with HIV(44)(45).

Gastrointestinal infections and malnutrition disrupt maturation of gut mucosa, and increase intestinal permeability. Among the epithelial cells in the Peyer's patches of the intestine, M-cells appear to play a role in transporting the virus across the intestinal barrier and presenting it to macrophages in the serosa as has been seen in rabbit models(46). Intestinal permeability as measured by differential absorption of carbohydrates (lactulose-mannitol assays) has been proven to be multifold higher in African infants at 3 and 12 months of life when compared to European infants(47). Similarly lipopolysaccharides (endotoxins of Gram-negative bacteria normally found in the intestinal lumen) can be measured in the bloodstream and can be a surrogate marker for disrupted intestinal integrity(48). Lipopolysaccharides are a stimulator of immune cells, and inflammatory mediators. These lipopolysaccharides are hypothesized to increase the risk of acquisition of HIV infection. Plasma lipopolysaccharide levels were lower during exclusive breastfeeding in comparison to during weaning period, and when compared to formula fed infants, suggesting breastfeeding protects against disruption of the intestinal barrier. Lactoferrin and transforming growth factor B are found in breastmilk and likely promote growth and integrity of the epithelial barrier. In the BAN study, which followed infants who were breastfed, including those who became infected, it did appear that prior to infection a rise in lipopolysaccharide was seen. In the CHER trial, the lipopolysaccharide levels decreased to almost undetectable by a year of age, indicating a higher risk period in the

first year of life due to immature intestinal mucosa predisposing to greater risk of transmission(49).

Milk factors

Both cell-free and cell-associated HIV virus are present in both colostrum and mature breastmilk of women living with HIV. Studies assessing colostrum, and mature milk at multiple time points post-partum have found higher cell associated virus in colostrum due to the higher cell content of colostrum compared to mature milk (48, 49). Among samples examined in one study, the proportion of infected cells ranged from less than 1 in 10,000 to 1 in 3 cells.

Cell free virus in breastmilk supernatants also varies widely, and it remains unclear if virus is higher in colostrum versus mature milk(52). The composition of colostrum varies in types of cells and immune modulators (including vitamin A, immunoglobulins, and lactoferrin), however infants have much greater volume of exposure to mature milk than they do to colostrum. The infant's immune system is also maturing over time, while also having reduction in circulating maternal antibodies(53). In one study avoidance of colostrum did not appear to lower the risk of transmission comparing 29 children who only ingested colostrum, 26 who ingested breastmilk with no colostrum, and 93 who received both(37). There are many questions, which are not yet answered about breastmilk and the mechanisms of transmission.

The concept of 'treating' breastmilk through heat or pasteurization methods have been attempted in the past, however the effect this has on the nutritional or immunologic properties of breastmilk is not fully understood(54). Donor milk banks such as in Neonatal

intensive care units typically pasteurize all milk received from donors screened for known pathogens including HIV(55). This recommendation of temporary use of heat-treated breastmilk remains in the most recent 2016 WHO guideline update. This is suggested as an interim feeding strategy for specific short term situations, such as if antiretrovirals become temporarily unavailable, or to assist mothers in stopping breastfeeding(56).

2.2.7 Antiretroviral interventions

As antiretrovirals became available in low-resource/high HIV burden settings, the question of optimal prophylaxis to prevent breastfeeding transmission, as well as the consequences of prolonged antiretroviral exposure through breastmilk arose. The ability to suppress plasma and potentially breastmilk viral load is likely the most important intervention to minimize the risk of breastmilk transmission.

Multiple studies have assessed antiretroviral interventions to mom or baby while breastfeeding. A 2014 Cochrane review aimed to determine which antiretroviral regimens are efficacious and safe for reducing vertical transmission of HIV through breastfeeding to avert child morbidity and mortality(57). Seven RCTs were included in the meta-analysis, all of which used different regimens; 2 were maternal prophylaxis only (Kesho Bora 2011, and Shapiro 2010), 4 were infant prophylaxis-only studies (Gray 2005, SWEN 2008, Kumwenda 2008, and Coovadia 2012), and 1 study used both maternal and infant prophylaxis (Chasela 2010) (59-65). This systematic review concluded that antiretroviral prophylaxis during breastfeeding to either mother or infant reduces the risk of infant HIV infection and of infant HIV infection or death. Prophylaxis should be continued for the duration of breastfeeding; however, infants who receive nevirapine prophylaxis and later become HIV-infected are more likely to have nevirapine resistance. This review was

unable to determine if maternal or infant antiretroviral prophylaxis was superior, however virologic suppression or compliance with medications in mothers plays a role in effectiveness of prophylaxis. The potential for maternal or infant resistance and response to subsequent ART after prophylaxis requires more evidence. Of note, WHO Option B+, which encourages lifelong ART among postpartum women with HIV, is being adopted increasingly in low middle-income countries. In breastfeeding postpartum women, this may result in a greater antiretroviral toxicity to infants, as well as a higher risk of potential antiviral resistance in those infants who become infected.

Stopping ART in breastfeeding women can lead to a rebound in plasma viral load and increase the risk of late transmissions. A recent study published in 2016 was a further analysis of the Breastfeeding, Antiretrovirals and Nutrition Study (BAN) which randomized to 28 weeks of either maternal triple antiretrovirals, infant nevirapine (NVP), or no further drugs post-partum. This analysis intended to assess the association between adherence, breastmilk RNA, and transmission. Thirty-one transmission events occurring between 2 and 28 weeks postpartum were included in this analysis, all with more than one plasma or breastmilk sample available. As a comparison 15% (due to sample availability) of the mothers randomized to the two treatment arms who did not transmit to their infant by 28 weeks postpartum (n=232) were also included. Maternal adherence was calculated by pill counts and categorized as poor (0-80%), partial (81-98%), and near perfect (>98%). In this analysis plasma viral load did not meaningfully differ between transmitting and non-transmitting mothers in the infant NVP arm, nor between transmitting mothers in either antiretroviral arm. However, among mothers randomized to maternal antiretrovirals, the median plasma viral load was two logs higher among transmitting mothers compared non-

transmitting mothers. Adherence was associated with a relative reduction in the odds of having detectable breastmilk viral load in partial adherence (76%, 95% CI: 28, 92%) and near perfect adherence (62% 95% CI: 14, 83%) compared to poor adherence, even when adjusted for nutritional randomization, baseline maternal characteristics. Mothers with detectable breastmilk viral load, and a paired plasma sample typically had a detectable plasma viral load. Two (<1%) mothers had a detectable breastmilk viral load (56 and 77 copies/mL) and undetectable plasma viral load at 6 weeks postpartum. Mothers with a detectable viral load had 59 times (95% CI: 21 to 169) the odds of having a detectable breastmilk viral load, compared to mothers with an undetectable plasma viral load. Adjusting for study arm, baseline maternal CD4 count, and baseline maternal plasma viral load results in slightly attenuated association between detectable plasma and breastmilk viral load (OR 40, 95% CI: 15 to 107). Among the 27 transmissions with plasma viral load available, only one transmission occurred in a woman with an undetectable viral load, and this occurred at 24 weeks postpartum after three viral load measures ranging from 8000 to 108,000 copies/mL. The remaining 26 transmissions occurred in mothers with baseline plasma viral loads >3500 copies/mL. No mother who consistently maintained a plasma viral load <100 copies/mL transmitted. A model was created to predict the number of transmissions based on adherence. If all 848 mothers randomized to maternal antiretroviral therapy were 100% adherent the model predicted 20.4 transmissions (95% prediction interval (PI) 12, 30%). If all mothers had been 0% adherent the model predicted 42.3 transmission (95% PI: 30, 56%). This indicates the importance of maternal antiretroviral adherence in reducing plasma and breastmilk viral load to minimize transmission. Antiretrovirals are likely the most important prevention intervention

available; however, they are not entirely benign when offered to mom or baby during breastfeeding.

2.2.8 Pharmacologic implications of women on cART during breastfeeding

The recommendation for women living with HIV to remain on ART while breastfeeding to reduce viral load, and improve maternal health is of clear benefit. However, the pharmacokinetics of antiretrovirals passing into breastmilk to breastfed infants, and the potential for low-level exposure resulting in resistance if an infant is infected, or potential toxicity to the infant receiving medication through breastmilk is not fully known. From a systematic review published in 2015 which included 24 studies, NRTIs accumulate in breastmilk at a breastmilk to maternal plasma ratio of 0.89 to 1.21, NNRTIs from 0.71 to 0.94, and PIs from 0.17 to 0.21(59). From the infant's plasma measurements, this was equivalent to ingesting 8.4, 12.5, and 1.1% of lamivudine, nevirapine, and efavirenz of pediatric dosing of these medications. Increasing multi-drug resistance has been seen to be emerging in infants who are breastfed by mothers on combination antiretroviral prophylaxis(66,67).

2.2.9 How evidence results in changes to guidelines

In summary, as knowledge advanced in our understanding of HIV transmission through breastmilk, recommendations evolved over time. Initially the recommendation to exclusively formula feed was implemented, which resulted in an increased rate of other infectious complications (diarrheal illness, pneumonia) due to risk of contaminated or unsafe formula being used. When the increased risk of transmission with mixed feeding was demonstrated, this led to a trend of short initial exclusive breastfeeding phase of (6

months) and a rapid wean off breastmilk. However, because complementary food supplies were unreliable or inadequate to meet the nutritional needs of young infants the WHO recommendations again changed.

As evidence mounted that in low resource settings mixed feeding, or formula feeding alone actually led to worse outcomes, the WHO responded by creating the AFASS criteria (Affordable, Feasible, Accessible, Safe, and Secure) in 2003 that were slightly revised with a similar premise in 2010(69,70). These criteria clarified the contexts in which exclusive breastfeeding would be safer for infants of mothers living with HIV, both reducing the risk of HIV transmission and of infant mortality to "support the greatest likelihood of HIV-free survival"(63,64). If AFASS criteria were not met, a minimum of 6 months of exclusive breastfeeding until a sustainable complementary food supply is attained was recommended.

The 2010 WHO guidelines also took a more public health approach, stating that national authorities should decide on infant feeding recommendations and implement the necessary programming to support this type of infant feeding policy, rather than individual based counselling at clinics. Another more explicit recommendation in the 2010 guidelines was exclusive breastfeeding for 6 months, followed by introduction of complementary foods and continued breastfeeding until 12 months of age when a nutritionally adequate and safe diet without breastmilk can be provided. This duration is different from the WHO infant feeding recommendations for HIV uninfected women, where breastfeeding is recommended until two years of age and later if issues related to food insecurity persist. The reason to differentiate the duration of breastfeeding in women living with HIV was due to the risk of mortality among children younger than 12 months

being higher and outweighing the risk of transmission in the first 12 months. It is also much more possible to provide a diet based on family foods that excludes breastmilk but is still nutritionally adequate for the growing child. The concern about retention in care for mothers living with HIV and antiretroviral adherence after 12 months was another reason to consider stopping ongoing infant HIV exposure through breastmilk at this age. The concern about affecting health outcomes of infants through long-term exposure to antiretroviral drugs through breastmilk was a consideration as to limiting the duration of breastfeeding.

The other major shift in the 2010 guidelines was for the first time recommending antiretroviral drug interventions to prevent postnatal transmission of HIV, ideally with lifelong ART to mom or infant prophylaxis for the duration of breastfeeding. Due to the significant reduction in risk of transmission with consistent antiretroviral use, mothers were encouraged again to exclusively breastfeed for the first 6 months of life, but also to continue breastfeeding alongside complementary foods until 12 months of life. Breastfeeding should only stop once a nutritionally adequate and safe diet without breastmilk can be provided.

2.3 Current recommendations for infant feeding

2.3.1 The WHO 2016 Infant Feeding Update

The 2016 WHO update attempted to address practical issues surrounding the duration of breastfeeding, and mixed feeding in an era where antiretroviral therapy is significantly more available after aggressive scale-up measures. There were three major revisions to the recommendations, which are outlined below, followed by a review of the evidence used to justify these changes.

The first revision to the 2016 recommendations focused on duration of breastfeeding. Mothers living with HIV should breastfeed for at least 12 months (low quality of evidence), and may continue for up to 24 months or longer (similar to the general population) (very low quality of evidence) while being fully supported for antiretroviral adherence. The recommendation that breastfeeding should only stop once a nutritionally adequate and safe diet without breastmilk is feasible was reaffirmed.

The second revision provided more clarity to the issue of weaning from breastfeeding. According to this revision, when a mother decides to stop breastfeeding at any time, weaning should occur gradually within 1 month. Abruptly stopping breastfeeding is not advisable.

Lastly, this revision reassures mothers living with HIV and health-care workers that antiretroviral therapy reduces the risk of postnatal transmission in the context of mixed feeding. Although exclusive breastfeeding is recommended, practicing mixed feeding is not a reason to stop breastfeeding in the presence of antiretroviral drugs. Similarly, when mothers do not plan to breastfeed for 12 months, shorter durations of breastfeeding of less than 12 months are better than never initiating breastfeeding at all.

2.3.2 The evidence for the 2016 update

The WHO based these revisions on four new sources of evidence, three of which were commissioned for the update. Two systematic reviews commissioned for this update were by Chikhungu et al.(7), another systematic review by Zunza et al.(65) and lastly a modelling exercise commissioned for the guidelines examining the effect of ART among mothers living with HIV on infant survival based on different background risk assessments of diarrheal mortality.

The first systematic review focused on the difference in HIV-free survival of the infant at 12, 18, or 24 months in infants born to women who were on antiretrovirals by type of feeding. The meta-analysis identified 18 cohort studies, 7 of which were nested within RCTs. The majority of studies did not provide details regarding type of feeding, and assumed most mothers exclusively breastfed up to 5 or 6 months as recommended. Ten studies provided estimates of 12-month HIV-free survival for breastfed infants whose mothers were on antiretrovirals up to 6 months postnatally. The pooled estimate of HIV-free survival at 12 months was 89.8% (95% CI: 86.5%, 93.2%) with considerable heterogeneity (I^2=83%). The pooled estimate in the 3 studies where mothers were on lifelong ART was slightly higher at 91.4% (95% CI: 87.5%, 95.4%) with similarly high heterogeneity. Eight studies provided estimates for 18-month HIV-free survival. Five studies included women who were on antiretrovirals up to 6 months postnatally, with an HIV-free survival at 18 months of 89.2% (95% CI: 83.9%, 94.6%) again with substantial heterogeneity (I^2=91.4%). The pooled estimate from the three studies where women were on lifelong antiretroviral therapy was higher at 95.9% (95% CI: 92.8%, 99.3%) with an I^2=82.1%. At 24 months HIV-free survival estimates from three studies, two of which were in mothers on 6 months of antiretroviral therapy was 89.1% (95%CI: 79.3, 98.9%) with extensive heterogeneity (I^2=96.6%). Of note, an important finding in the three studies, which provided estimates at 12, 18 and 24 months was that there was no statistically significant difference in HIV-free survival at the three time points. The main sources of heterogeneity in the analyses related to differences in the indication, timing of initiation and duration of maternal antiretrovirals, and variability in breastfeeding practices. Although a random effects model was appropriately used in the analysis, due to the small

number of studies for each transmission time point the estimated transmission risks may not be a reliable estimate.

Four studies compared infant feeding modality in women receiving antiretroviral therapy for 6 months or for the duration of breastfeeding. Cournil et al. was the largest study conducted in 824 infants (women were excluded if were clinical stage 4 or with a CD4<200 cells/mm^3)(66). This study showed HIV-free survival at 18 months was highest in formula fed (97.6%), versus breastfed for less than 3 months (87.0%), versus breastfed for more than 3 months (95.0%). Eighteen-month HIV-free survival did not significantly differ in formula fed versus breastfed for more than 3 months. The study by Alvarez-Uria et al. which reported HIV-free survival at 18 months (HIV transmission occurred after 8 weeks, and was measured at 12 months) at 18 months in 318 infant with mothers on lifelong antiretrovirals showed a significantly higher survival in breastfed infants compared to formula fed (96% vs. 86%). In Peltier et al., which studied 532 infants born to mothers on antiretroviral therapy for at least 7 months and reported HIV-free survival at 9 months, also showed significantly higher survival in breastfed infants (95% vs. 94%). Whereas in Homsy et al.'s study of 118 infants born to mothers on antiretrovirals for at least 6 months found 12 month HIV-free survival was not significantly higher in breastfed infants compared to formula fed infants (82% vs. 67%). This study however only had 9 children who were formula fed, of whom 3 died, 2 of which were mixed fed.

Overall quality of studies was assessed using the Newcastle-Ottawa scale for non-randomized trials. Pooled analysis using GRADE Evidence profiles determined the quality of all recommendations was very low due to inconsistency, lack of detail, or risk of bias.

The second systematic review focused on HIV transmission between birth and 6 months, postnatal transmission between 6 weeks and 6 months, and overall transmission rates at 12, 18 and 24 months based on type of feeding (exclusive breastfeeding, mixed feeding) in women on antiretroviral for at least 6 months post-partum. Eleven studies were selected, four of which were cohorts nested within RCTs. In all studies, mothers were on antiretrovirals before or during pregnancy, and continued for at least 6 months postnatally. In eight studies, women stopped antiretrovirals at 6 months or upon breastfeeding cessation, 2 studies continued lifelong antiretrovirals in mothers, 1 study (Giuliano et al.) provided lifelong ART only for treatment eligible mothers with very low CD4 counts. Six studies reported overall transmission rates at 6 months (which include peripartum transmissions). The pooled estimate of overall transmission at 6 months was 3.54% (95% CI: 1.15, 5.93%), with considerable heterogeneity (I^2=94%). A more accurate reflection of breastfeeding transmission at 6 months would be to exclude peripartum infections diagnosed before 6 weeks of age, which was reported in six studies. The pooled transmission rate was 1.08% (95% CI: 0.32%, 1.85%) with heterogeneity of I^2=66.4%. Overall transmissions at 12 months (including peripartum) was available for five studies, and was 4.23% (95% CI =2.79%, 5.49%) with I^2=71.2%, whereas the two studies which reported postnatal transmission rates had a pooled estimate of 2.93% (95% CI: 0.68%, 5.18%) with I^2 = 39.9%. Ngoma et al was the only study to report overall estimates of transmission at 18 months in the 219 infants, with lifelong antiretrovirals to mothers with a transmission rate of 4.1% (95% CI: 2.2%, 7.6%). In all the studies, women were recommended and assumed to have exclusively breastfed their infants for a total of 6 months, with no method to confirm this practice. Only two studies reported the total

duration of breastfeeding of 12 months. No studies provided a transmission rate according to feeding modality (exclusive vs. mixed feeding). Alvarez-Uria et al. noted that one of the infected children was mix-fed, but did not provide that rate of transmission by feeding modality.

Studies had variability in frequency, and location of counselling, types of support and methods of data collection regarding infant feeding. The studies were all observational, and downgraded for indirectness, in the pooled analysis further downgrading for inconsistency, and heterogeneity in transmission rates resulting in a very low level of evidence for transmission rates at 6 and 12 months and low level of evidence for 18-month transmission data.

The third commissioned work for the 2016 WHO guidelines was a Cost-Effectiveness of Preventing AIDS Complications-infant model to simulate HIV exposed uninfected infants through the first 24 months of life. The model projected HIV-free survival at 24 months when three key parameters were varied: breastfeeding duration, maternal antiretroviral duration during breastfeeding, and the Relative Risk of infant and child mortality associated with Replacement Feeding (RRRF). The RRRF is a score that varies from 1.0 to 6.0, where if RRRF=1 there is no difference in mortality from formula feeding when compared to breastfeeding, and RRRF=6 this indicates a 6 fold increase in mortality such as in extreme water sanitation crises. RRRF is a critical component of the analysis, and was derived from existing studies; sub-Saharan African would be considered to have a RRRF between 2 and 3. Urban sites with good quality water or rural sites with healthcare services for infants who develop illnesses may have a RRRF close to 1.

The key findings were that as mortality risks from replacement feeding or RRRF increase, the optimal duration of breastfeeding increases. The baseline RRRF must be greater than 4, in order for the optimal breastfeeding duration to exceed 6 months. This indicates that in settings with high RRRF values, where contaminated water supplies or diarrhea outbreaks occur, the optimal breastfeeding duration exceeds the previously recommended 12 month duration. Extending beyond the 12 month duration of breastfeeding increases 24 month HIV-free survival by a small amount (<1%). This is an interesting finding because one of the challenges for low middle-income contexts was having a different breastfeeding duration recommended for women living with and without HIV. These data indicate that recommending 12 versus 24 months of breastfeeding should not be based on factors related to HIV free survival, but rather broader systemic issues such as harmonizing recommendation for HIV-uninfected women or local acceptability.

The other key finding from this work demonstrated that cessation of maternal antiretroviral therapy during breastfeeding markedly reduces HIV free survival. If antiretrovirals are discontinued during breastfeeding, this decreases HIV free survival independent of the RRRF. This finding reinforces the critical nature of concomitant antiretrovirals for the duration of breastfeeding. Although this was a modelling exercise, which uses overall mortality rates not HIV specific mortality, and is limited by some assumptions such as equating antiretroviral interruption with having never been on antiretrovirals, there is some merit to this exercise in understanding that the incremental risk of breastfeeding beyond 12 months while on antiretrovirals likely is not significant at a population level.

The last systematic review included in the WHO 2016 update focused on understanding the effect of interventions to reduce MTCT and infant growth outcomes, and non-HIV infections (respiratory tract infections, and gastrointestinal infections). Fourteen reports from seven RCTs and three cohort studies were included. The intervention of breastfeeding versus formula feeding was assessed in one RCT and three prospective cohort studies assessing outcomes of growth and non-HIV infections. Kindra et al. found no difference in z-scores between breastfed vs. formula fed infants at 9 months of age. Mbori-Ngacha et al. and Becquet et al. defined malnutrition differently, but neither found a statistically significant difference in risk between breast or formula fed infants. The pooled estimate from two observational studies that defined respiratory infections differently suggested a lower incidence in breast than formula fed infants (HR=0.65; 95% CI: 0.41, 1.00). After adjusting for HIV status, breast-fed infants were 40% less likely to developed respiratory infections (HR=0.60; 95% CI: 0.36, 0.98). Two studies found that breastfed infants were at lower risk for diarrhea (RR=0.31; 95% CI: 0.13 to 0.74), and significantly lower for breast-fed infants after adjusting for HIV status in the infant (HR=0.74; 95% CI = 0.57, 0.97).

When comparing the intervention for extended antiretroviral prophylaxis versus short-course (peripartum) antiretroviral prophylaxis during breastfeeding, 5 studies compared the incidence of severe adverse events. Some of these antiretrovirals were given directly to the infants, and some were given to the mothers and the infant was exposed through drugs, which pass into breastmilk. The risk of growth faltering was 12% higher in infants on extended antiretroviral prophylaxis than short-courses (RR=1.12; 95% CI: 0.83, 1.50). The incidence of pneumonia in the extended antiretroviral group was -

0.01 (95% CI: -0.02, -0.00). There was no difference in meningitis, gastroenteritis, or sepsis between the intervention groups.

Early breastfeeding cessation (4 months) versus patient preference (median 16.2 months) was another intervention in one RCT. Weight for age z scores at 2 years of age was similar between the two groups (mean difference 0.12; 95% CI -0.10, 0.34). Prolonged diarrhea (lasting at least seven days) during the period of 7-24 months of age was two times as likely if breastfeeding was stopped early (OR 1.70; 95% CI: 1.28, 2.26). Overall, the meta-analysis found that breastfeeding may reduce the risk of diarrheal morbidity, respiratory tract infections and malnutrition compared to formula feeding in HIV-exposed infants.

Although these recent publications have been helpful in clarifying duration of breastfeeding, weaning and antiretroviral interventions for the WHO guidelines, these studies are all done in low to middle-income countries. The WHO 2016 update states that these guidelines are intended mainly for countries with high HIV prevalence and settings in which diarrhea, pneumonia and undernutrition are common causes of infant and child mortality. The update also states that “it may also be relevant to settings with a low prevalence of HIV depending on the background rates and causes of infant and child mortality”(56). All infant feeding recommendations stem from a common goal of supporting the greatest likelihood of HIV-free survival of children born to mothers living with HIV, with a secondary aim of not harming the health of the mothers.

2.3.3 Risk of breastfeeding transmission with concomitant antiretroviral therapy

A major criticism in generalizing these data from low resource countries to high resource countries is due to the variable antiretroviral use in many of these settings. The best quantification of the risk of transmission in women on antiretroviral therapy in low-income countries comes from two systematic reviews, one discussed above commissioned by the WHO(7), and the second not yet published but presented as an abstract at the International AIDS Society Meeting in 2015.

The first systematic review of both RCTs and observational cohorts(7) included mothers on antiretroviral therapy from before or early pregnancy until at least 6 months post-partum and their breastfed children. In this review, the authors included data from studies that reported the cumulative risk of transmission and separately reported out the risk of transmission from studies, which documented postnatal transmission. The second systematic review by Loutfy et al. included mothers on antiretroviral therapy, with a documented negative viral load who breastfed for any duration of time(67). This review reported the risk of in utero transmission based on the studies, which had data from 1-month post-partum. They then subtracted the in utero transmission risk from the post-partum transmission risks to provide a summary estimate at subsequent time points to report out a breastfeeding risk of transmission. They also provide a cumulative risk, which includes the baseline risk of in utero transmission (See Table 2). This analysis included three RCTs, and seven observational studies all from low-middle income settings. The transmission risk at 1 month was 2.9% (95% CI 2.2,3.8), at 3 months was 3.6% (95% CI 2.7, 4.0), at 6 months was 4.0% (95% CI 3.1, 5.2), and at 12 months was 5.1% (95% CI 4.0, 6.5).

Table 2: Transmission risk from systematic reviews

	Chikhungu Transmission Rates (95% CI)		Loutfy Transmission Rates (95% CI)	
	Cumulative	Breastfeeding	Cumulative	Breastfeeding
1 month (in utero)			2.9% (2.2 – 3.9%)	n/a
3 months			3.6% (2.7-4.7%)	3.6-2.9 = 0.7%
6 months	3.54% (1.15 - 5.93%)	1.08 (0.32-1.85%)	4.0% (3.1-5.2%)	4.0-2.9 = 1.1%
12 months	4.23 (2.97-5.49%)	2.93% (0.68-5.18%)	5.1% (4.0-6.5%)	5.1-2.9 = 2.2%
18 months			5.1% (4.0 -6.4%)	5.1-2.9 = 2.2%
Studies included	Ngoma 2015 Sagay 2015 Thalwalakwa 2014 Guiliano 2013 Coovadia 2012 Jamieson 2012 Alvares-Uria 2012 Thomas 2011 Marazzi 2009 Kilewo 2009 Peltier 2009		Alvares-Uria 2012 Kesho Bora 2010 Kesho Bora 2011 Kilewo 2009 Marazzi 2009 Palombi 2012 Shapiro 2010 Shapiro 2013 Taha 2009 Thior 2006 Thomas 2011	

These two systematic reviews provide evidence that the overall risk of breastfeeding transmission is 1-3% up to 18 months in women on antiretroviral therapy through pregnancy and until at least 6 months postpartum. Although these data are from a research context in low to middle resource settings with different medication use than that used in a Canadian context, and undetectable viral loads confirmed at variable and limited time points during follow-up this is the closest estimate of transmission risk we can expect to find.

2.3.4 Guidelines in high resource countries

In high resource settings the recommendations from major bodies including The United States Department of Health and Human Services (DHHS)(68), Canadian Pediatric and Perinatal AIDS Research Group(69), and the British HIV Association (BHIVA)(70) continue to recommend formula feeding for all infants born to mothers with HIV. However, they all allude to the various pressures that many women face regarding breastfeeding, from cultural, family, or personal factors. The Canadian recommendation states to address possible barriers to formula feeding during pregnancy and postnatally. The Canadian and British guidelines explicitly state that if a woman discloses she is breastfeeding that is not an indication for automatic referral to child protection services.

The WHO guidelines create a divide between high-resource countries, where exclusive formula feeding is recommended for mothers living with HIV, and the rest of the world, where exclusive breastfeeding while the mother is receiving ART is recommended. However, there are locations within the wealthiest nations where safe drinking water is not available, and where the cost and availability of formula is prohibitive. For example, in Canada, some Aboriginal, First Nations and rural communities lack sustainable access to clean drinking water(71). Similarly, comprehensive programs to provide subsidized formula are lacking in many high resource settings, including 3 territories and 5 provinces in Canada(72).

This recommendation also by default led to the reality that all research to understand the biological risk of transmission, antiretroviral breastmilk pharmacokinetic and dynamic studies, and antiretroviral HIV resistance from breastmilk must occur in a context where breastfeeding is happening(73). Therefore, all large randomized controlled trials done to understand these highly technical research questions needed to occur in

low and middle income settings. This not only leads to ethical dilemmas of studying disadvantaged communities for the benefit of a different population, but also the reality that application of these findings cannot be generalized to other contexts with greater resources for monitoring and treatment.

The 2016 WHO Infant Feeding update has taken a more overarching approach. Although intended mainly for countries of high HIV prevalence where diarrhea, pneumonia, and undernutrition are the common causes of child mortality, they state that it may also be relevant to settings with low HIV prevalence, such as mothers living with HIV who choose to breastfeed even if this is not the primary recommendation of their national and local health authority.

2.4 Canadian Context and Infant Feeding

2.4.1 Does breastfeeding occur in high resource countries despite guidelines?

Infant feeding in HIV is an issue affecting women and children living with HIV, and by extension their families and communities. This is significant given one of the fastest growing HIV-positive populations in Canada is women, with increasing pregnancy rates among this group (75,76). This population has grown because of (1) increased uptake of prenatal HIV testing(76), (2) significant numbers of newcomers to Canada coming from HIV-endemic countries(77), (3) commendable advances in antiretroviral therapy (ART) improving survival(78), (4) improved strategies for reduction of perinatal HIV transmission(69) and (5) normalization of pregnancy for women living with HIV(79).

In light of these trends, this issue of infant feeding in an HIV context in Canada needs further examination to ensure recommendations are grounded in good evidence and best practices. Although the guidelines are clear and suggest women living with HIV

should formula feed to reduce the risk of vertical transmission, published cases of breastfeeding in high resource countries continue to occur. A case which illustrates the psychosocial issues which affects feeding choices for women living with HIV includes a 29 year old married women from sub-Saharan Africa living in Alberta who reported consistent adherence to antiretrovirals(80). Her viral load was undetectable, and she was counselled to not breastfeed and offered free formula. She regularly attended high-risk pregnancy clinic visits, and received post-partum home visits. The infant was tested for HIV and resulted negative at birth, 3, and 8 months; however, the 13-month test was positive. Upon review of pharmacy records, a discrepancy between the amounts of antiretrovirals prescribed and dispensed was noted. Also stored samples showed undetectable nelfinavir levels in her bloodwork. Formula dispensary records showed the patient had declined formula saying she had been given formula by family, but later admitted that due to fear of disclosure, she breastfed. When asked, the patient cited lack of support from her husband in taking antiretroviral therapy and fear of stigma from not being able to breastfeed. For some if they do not breastfeed, their community equates this to HIV positive status, which is highly stigmatizing, and women may feel compelled to breastfeed to prevent involuntary disclosure. Further, this can be difficult to explain to care providers who may not understand the cultural stigma associated with HIV, leading to women breastfeeding without disclosing to their providers out of fear of criminalization, child protection involvement of simply fear of disappointing care providers. This can often be at a challenging time for women who are postpartum, with many new stressors, and antiretroviral compliance has also been shown to wane during this time when compared

to compliance levels in pregnancy both in African studies, but also data from the United States(83-85).

A recent review of available surveillance, and program monitoring data from 1988 to 2008 in New York State (n=8972 infants born to women living with HIV) revealed that 1.8% of infants had confirmed breastfeeding (15.5% were unknown). Among confirmed breastfed cases 11.8% had concomitant mother-to-child transmission resulting in an odds ratio of 4.42 (95% CI: 2.68, 7.29) compared to non-breastfed infants(83). A similar review from 2005 to 2008 of the Enhanced Perinatal Surveillance system from 15 US jurisdictions (n=8054 infants born to women living with HIV), found that 80 infants were breastfed (<1%), (n=400 had unknown breastfeeding status). Of these 80 infants confirmed to have breastfed, 23.8% became HIV infected. The adjusted odds ratio in breastfed infants was 4.6 (95% CI: 2.2, 9.8%). It would be important to note that antiretroviral use was not ideal, during pregnancy 85.2% in uninfected infants, and 45.3% in infected infants(84).

At multiple events with women living with HIV including a community forum in Canada attended by more than 50 women, and in the USA attended by more than 100 women on infant feeding, and in focus groups with women the reality that breastfeeding is occurring and providers are not being informed is increasingly being recognized(83, 84). However, the extent or frequency remains unclear. A sentiment described is that women do not feel comfortable disclosing this to their providers for fear of potential legal or child protection service involvement. An exception to this was two cases in 2016 where two women living with HIV in Toronto decided to breastfeed their infants, and involved their HIV care providers in this decision to optimize the management of the infant given

the inherent risks they were counselled about(8). Breastfeeding is happening in Canada, and potentially now with more involvement of care providers due to gradually reduced stigma based on evolving guidelines and recommendations.

2.4.2 HIV Transmission and legal and child protection implications in the Canadian context

There is one legal precedent of a woman being criminally charged for failing to provide the necessities of life for her child by actively denying her HIV status at the time of delivery, thereby delaying preventive antiretroviral medication being administered to the child. The infant subsequently became HIV infected. Under Canadian criminal principles, no charges can be laid for not taking steps to prevent HIV infection during pregnancy. However, a woman could potentially face charges if she fails to state her HIV status at delivery, refuses preventative medication to the infant, or breastfeeds her child. Similarly, child protection agency involvement also could occur based on concerns of not being able to provide the necessary care an infant needs. In fact, only recent changes to guidelines made an explicit statement that 'automatic' involvement of child protection is not warranted if a woman discloses she is breastfeeding. This highly controversial aspect was first broached in the 2010 British HIV Association Statement on Infant feeding(70), and echoed by The Canadian Pediatric AIDS Research Group Statement. The Canadian statement recommends that if a mother living with HIV is found to be breastfeeding her infant, then her personal and/or cultural beliefs about breastfeeding should be explored, barriers to formula feeding identified, and that an automatic referral to child protection services is not warranted(69). These confusing legal aspects inflict further stigma upon women, making them feel uncomfortable to ask about breastfeeding and risks. In turn,

they may breastfeed in secrecy without informing their care providers out of fear of legal consequences.

2.4.3 Provider counselling of patients

Counselling conversations by providers with patients focus on the risks of breastfeeding, the use of bottle-feeding, and ensuring formula is accessible for women living with HIV. Guidelines in high resource countries endorse the safest and most conservative route, recommending exclusive formula feeding. However, gaps in our understanding of the 'true' risk in a Canadian context remain. The potential for variability in providers' knowledge, attitudes and practices pertaining to infant feeding is becoming an increasingly relevant question.

A recent viewpoint published in Clinical Infectious Disease in 2014 describes the reality that women in the United States are choosing to breastfeed. The National Perinatal HIV Hotline receives at least two calls per year from clinicians with questions about counselling HIV-infected pregnant women who are considering breastfeeding. Two cases are described in which providers had frank discussions with their patients, in case 1, the woman opted to breastfeed for 6 weeks mainly to avoid involuntary disclosure of her HIV status, and in case 2 the woman opted for banked human breastmilk for 1 year due to concerns of optimal nutrition and immune support. The authors describe essential elements to the counselling: validating the desire to breastfeed, understanding her motivation to breastfeed, and exploring alternatives (formula, banked breastmilk, flash-heat treatment, lactation surrogates, and breastfeeding with antiretroviral interventions to mom and/or baby). They also provide harm reduction strategies if a woman living with HIV opts to breastfeed. These strategies include: discussion on timing and methods of

weaning, avoidance of mixed feeding, ensuring viral suppression in mom and consideration of prolonged infant antiretroviral prophylaxis if mother is not suppressed or there are concerns of adherence, monthly monitoring or maternal viral load, PCR testing in the infant monthly, and at 1, 3 and 6 months after weaning, monitoring for antiretroviral toxicity in the infant, education on mastitis signs and treatment for mastitis to minimize shedding in the breastmilk compartment. Harm reduction approaches are often criticized on moral grounds, and in the context of HIV transmission the fact that the infant is not a consenting adult in the decision of infant feeding and risk of transmission is debated(87). This further highlights the need to ensure that all care providers are involved in a shared-decision making model conversations with the family, from the obstetric, infectious diseases, and pediatric provider(96-97). Another concern raised regarding harm reduction approaches is that they can lead women who may otherwise not have considered breastfeeding to do so, leading to higher rates of transmission. Or if misunderstood, breastfeeding advocates may begin to misinterpret the approach and begin inappropriately promoting breastfeeding as a preferred option for all mothers living with HIV(89). This further delineates the need for better understanding of both provider and patient knowledge, attitudes and perspectives in order to create informed counselling on the issue to optimize outcomes.

The specific domains of infant feeding counselling are not standardized, and providers understanding of evolving guidelines and the evidence available to support them is likely highly variable. The attitudes providers have and their risk tolerance are likely influenced by multiple factors including the types of patients they care for (pregnant women living with HIV versus infant born to a mother living with HIV), years in practice,

and experience in HIV endemic countries or not. Practices likely also vary based on the 'frequency' with which these patients are cared for, the threshold required to consider child protection referral, and the region practiced in.

2.5 Conclusions

The questions that addressed in the following two chapters include understanding the current knowledge, attitudes and practices related to infant feeding in HIV of providers who provide care for families affected by HIV in Canada. Specifically, to understand the knowledge gaps based on current evidence that persist, and among which providers targeted interventions of knowledge translation resources are needed. Similarly, in order to advance counselling and guideline development it is important to understand the attitudes and practices providers have related to infant feeding, including involvement of other services, legal issues and factors which affect stigma for families affected by HIV. Chapter Three will focus on a knowledge, attitudes and practices survey developed for diverse care providers in a Canadian context. Chapter Four will advance the discussion further by summarizing the key findings from a research and clinical priority-setting meeting on infant feeding in HIV in Canada. Upon the conclusion of the thesis, I hope to have summarized the main issues related to infant feeding in HIV in Canada, elucidate the current clinical gaps and set priorities for discussion in future guidelines and knowledge translation resources for both providers and patients.

CHAPTER 3: Knowledge, Attitudes and Practices of Canadian HIV Care Providers on infant feeding in HIV

3.1 Abstract

Knowledge, attitudes and practices of Canadian HIV Care providers on infant feeding in HIV have not been previously studied.

Methods: We developed a survey to examine differences in provider perspectives on infant feeding in HIV, and understand factors associated with these differences, including: gender, years in practice, and prior experience caring for people living with HIV. The knowledge questions consisted of 26 items (range of potential score was 0 to 26, higher scores indicating greater knowledge). These questions were on content knowledge of guidelines, infant feeding terminology, and breastmilk transmission. The attitudes and practices questions focused on two main areas: the degree of risk tolerance a provider has towards HIV transmission from feeding, and the degree of stigma/barrier a provider perceives women face related to infant feeding decisions. The risk tolerance of transmission score consisted of 23 items, resulting in a possible minimum and maximum score of 0 to 37, respectively, with higher scores indicating increased tolerance to risk of transmission by feeding. The perceived stigma/barrier scale consisted of 15 items, resulting in a minimum and maximum score of 15 to 73, respectively based mainly on the 14 questions asked on a 5-point Likert scale, and 1 multiple choice question. A higher score indicates an increased perceived stigma/barrier. The survey developed by content and measurement experts, utilized questions including Likert scales, multiple choice, and scenario-based questions. The survey was distributed through local and national care provider networks to a variety of healthcare providers, including pediatricians, infectious diseases specialists, obstetricians, and nurses. Exploratory analysis including descriptive statistics, frequencies, and percentages were used to summarize the data. Linear

regression was used to identify factors associated with knowledge, attitudes and practices. If type of provider group was a significant predictor, mean scores were compares using ANOVA to determine which group was different.

Results: The survey received 151 responses: 103 from Canadian HIV providers (response rate 17%), 21 from Canadian Infectious Diseases/Medical Microbiologists (response rate 4%), and 27 from Toronto-based Community Pediatricians (response rate 16%). The mean age across all surveys was 44.5 years (SD = 13.1). Overall 68.9 % of respondents care for patients living with HIV. The gender distribution was 72.2% female. The range of the 26 point knowledge score was 20 (minimum score 5 and maximum score was 25) across all groups. The range of the 37 point risk tolerance scores was 29, (minimum score 6 to a maximum of 35). The range of the 73 point perceived stigma/barrier scores was 40, (minimum score was 33, maximum 73).

Conclusions: Overall, providers are still reticent to recommend breastfeeding due to the potential risk of transmission. Providers do not believe that breastfeeding should be considered a criminal activity in the HIV context. Supporting formula feeding is a greater priority among providers given the lack of clear quantification of the risk of breastfeeding. This is the first survey to determine the knowledge, attitudes and practices of HIV providers in a high resource setting pertaining to infant feeding. Future guidelines and Knowledge Translation (KT) resources are needed for both providers and patients to standardize the counselling, and improve the understanding of this complex issue.

3.2 Knowledge, Attitudes and Practices Survey

3.2.1 Introduction

There is a paucity of data on HIV practitioners' knowledge, attitude and practices regarding infant feeding in the HIV context in high resource countries. In low and middle income countries, there has been qualitative and quantitative research on doctors, nurses, midwives and lay community health care workers knowledge of guidelines, counselling practices, and attitudes towards breastfeeding and transmission risks(90–97). These papers focus on knowledge of WHO guidelines encouraging breastfeeding, and implementation of recommended counselling practices. Gaps identified include discussion on heat treatment as an option, and need for provider training in non-directive counselling.

In high resource settings, infant feeding in HIV recommendations, health care provider training and health care delivery differs significantly than in low-income countries. There are likely differences in knowledge, attitudes and practices related to infant feeding amongst different types of HIV care providers in Canada. These differences may be due to the variability in guidelines, provider practice experience in different resource settings, and differences in priorities of pediatric versus adult providers in the mother infant dyad. Characterizing these differences, and understanding factors associated with these differences was the main objective of the Knowledge, Attitudes and Practices Survey.

3.2.2 Hypotheses

This study examines whether

1. Knowledge of infant feeding in HIV is higher among HIV care providers compared to Infectious Disease providers or General Pediatricians;

2. Attitudes are similar across provider types (i.e.: similar risk tolerance in pediatricians compared to adult care providers); and
3. Insight into perceived stigma on the challenges women face on infant feeding and HIV is higher among HIV care providers relative to other provider types.

3.2.3 Exploratory analysis

Exploratory analysis was used to examine which demographic factors (gender, age, years in practice, clinical experience in lower resource settings) are associated with knowledge, risk tolerance, and perceived stigma/barrier scales. I also examined clinical scenarios related to infant feeding and HIV in which other services are involved (Public Health, Children's Aid Society, and Pediatric Infectious Diseases)

3.2.4 Methods

Population and Sampling

The population of interest for this survey was the range of providers who care for mothers living with HIV and their infants, which included three groups: infectious diseases physicians, pediatricians, and multidisciplinary HIV care providers. The sampling framework consisted of using existing networks with email distribution lists. The infectious disease and HIV care providers surveys were accessible on a national scale. Following an unsuccessful attempt to reach the National Canadian Pediatric group, a pediatrician survey was undertaken utilizing an existing regional Community Pediatricians Network in Toronto (n=165). The Infectious Diseases/Medical Microbiologist group was targeted using the national network, the Association of Medical Microbiologists and Infectious Diseases Physicians (n=547). The HIV Care Providers were reached through

multidisciplinary HIV networks (n=607) including; Canadian HIV/AIDS Pharmacist Network (n=131), Canadian Perinatal/Pediatric AIDS Research Group (n=45), CIHR HIV Clinical Trials Network (n=215), Canadian Association of Nurses in HIV/AIDS Care (n=209), and the Society of Obstetricians and Gynecologists Infectious Diseases Subsection (n=7).

The study had approval from the research ethics board at The Hospital for Sick Children, Toronto, Canada.

Survey Development

A literature search conducted prior to the development of the survey found no relevant publications or existing surveys for healthcare workers on infant feeding in HIV from a high resource context. A survey was developed by a group of content experts including adult and pediatric HIV physicians, an obstetrician with an ID/HIV interest, HIV clinic nurses and a social worker to include areas of content knowledge from Canadian and WHO guidelines, as well as to address areas of clinical care that may be more subjective. These areas included involvement of child protection services, public health, criminalization of HIV transmission, government subsidization of formula for women living with HIV, tolerance to vertical risk of transmission, prioritization of a mother's right to choose infant feeding strategy, understanding of HIV related stigma as it pertains to infant feeding and counselling practices on infant feeding.

The development of the survey was an iterative process, requiring multiple revisions to ensure content and face validity. Initial domains of questions were discussed with 3 main content experts in multiple face to face meetings, leading to a table of specifications (Table 7). Drafts were electronically circulated to a larger group of HIV care

providers (2 nurses, 1 social worker, 1 adult and 4 pediatric infectious disease physicians) for initial review. Initial group meetings were held to discuss each question systematically for content, language, and measurement issues, allowing for specific revisions. These meetings were followed by one-on-one meetings with content and measurement experts (MM, MS), for further targeted revisions. Group members completed revisions of the final draft electronically.

The questions were divided into 4 main domains: demographic questions (e.g. age, gender, type of practice), knowledge questions, attitude questions, and practice questions. There were 26 knowledge questions consisting of 14 multiple-choice questions (MCQs), and 12 true or false questions. Regardless of format of the question for the purposes of the score all knowledge questions were dichotomized to correct or incorrect (0 or 1 point). For creation of the score the main areas of knowledge were factors related to transmission (9 items), feeding awareness (3 items), WHO guideline questions (7 items), and Canadian guideline questions (7 items), leading to a maximum correct knowledge score of 26.

There were 19 attitude questions; 5 were in a multiple choice format, and 14 were in a Likert format. Four items from the attitude questions contributed to the risk tolerance score (a maximum of 8 points), and 15 of the attitude questions contributed to the perceived barrier/stigma score (a maximum of 73 points).

The practice section included 3 multiple choice questions, and 4 scenarios each with the same 4 questions. The multiple choice questions contributed to the risk tolerance scale (a maximum of 13 points), and the scenarios contributed to the risk tolerance scale (a maximum of 16 points).

The majority of the survey was identical across the three groups, however the HIV care provider survey contained an additional 11 questions, with more detail given their relative expertise in the area; however these were excluded from the comparative analyses between groups.

The survey questions for knowledge were summarized into an overall knowledge scale (with a maximum possible score of 26). The score was based on accurate understanding of aspects of infant feeding or guidelines including: risk of HIV transmission from feeding (1 item), risk factors associated with transmission (8 items), definitions of exclusive versus mixed feeding (2 items), awareness of WHO (7 items), and Canadian guidelines on infant feeding (7 items), and formula provision policies in Canada (1 item).

The attitudes and practices questions were summarized into two main areas. The first assessed the degree of risk tolerance a provider has towards HIV transmission from feeding. This scale had a maximum possible score of 37, with a higher number indicating a greater degree of risk tolerance. The second pertained to the degree of stigma/barrier a provider perceives women face related to infant feeding decisions. This had a maximum possible score of 73 points, with a higher score indicating a greater perception of stigma/barriers faced by women.

Piloting and Survey Distribution

The survey was piloted amongst a subset (2-14 participants) of each of the three groups to determine any technical or readability issues. After final revisions were completed, the survey was distributed via email to the three groups via their email-lists using the Research Electronic Data Capture (REDCap) survey platform. A modified Dillman technique was utilized which included reminder emails at week 3, 5, 7, and 8 to

try to optimize response rate(98,99). Unfortunately, the surveying period was over August and September, when people may have been away due to summer holidays. In addition, we used a draw for gift cards to try to incentivize potential participants to complete the survey.

Analysis

Exploratory analysis including descriptive statistics, frequencies, and percentages to summarize the data. Linear regression identified factors associated with knowledge, attitudes and practices scales. All analyses were conducted at the 5% significance level ($p<0.05$) using IBM SPSS v.20. If survey group was a significant predictor, mean scores were compared using ANOVA to determine which group was different. Thereafter, t-tests were performed between groups to determine which provider group differed. Linear regression was performed with relevant predictors, where dummy variables were used to separate groups.

3.2.5 Results

The survey received 151 responses: 103 from the HIV providers group (response rate 17%), 21 from Infectious Diseases group (response rate 4%), and 27 from the Community Pediatrics group (response rate 16%). The demographics are summarized in Table 1. The mean age across all surveys was 45.4 years (SD = 11.6). Overall 69.1% of respondents cared for patients living with HIV. The gender distribution was 72.2% female. Fourteen (13.7%) of the HIV providers had provided HIV care abroad.

Table 3: Demographic characteristics of the three survey groups

	HIV Providers N (%)	Infectious Diseases N (%)	Pediatricians N (%)	P
Number of respondents	103 (17%)	21 (4%)	27 (16%)	
Age (Mean, and SD)	44.5 (11.0)	37.2 (6.0)	54.5 (10.8)	0.01
Female	80.8%	66.7%	59.3%	0.06
Province (n, % total) Maritimes Quebec Ontario Manitoba Alberta Saskatchewan British Columbia Yukon Territory No data	 3 (2.9) 12 (11.5) 36 (34.6) 7 (6.7) 8 (7.7) 10 (9.6) 23 (22.1) 1 (1.0) 3 (2.9)	 3 (14.3) 2 (9.5) 12 (57.1) 3 (14.3) 2 (9.5) 1 (4.8) 1 (4.8) 0 0	 All Ontario	
Type of practice (n, % total)	Academic 67 (64.4) Ctty hosp 21 (20.2) Ctty practice 27 (26.0) Research 3 (2.9)	Academic 19 (90.5) Ctty hosp 4 (19.0) Ctty practice 1 (4.8) Other 2 (9.5)	Inpatient 3 (11.1) Outpatient 16 (59.3) Both 8 (29.6)	
Years in practice (n, % total) 1-5 6-10 11-20 >20	 31 (32.0) 25 (25.8) 19 (19.6) 22 (22.7)	 n/a	 1 (3.7) 2 (7.4/0 5 (18.5) 18 (66.7)	

Provider type (n, % total)	RN 48 (46.6) MD 26 (25.2) Pharm 22 (21.4) SW 4 (3.9) Other 3 (2.9) Midwife 0	Adult ID 5 (23.8) Ped ID 9 (4.3) MM 1 (4.7) Trainee 6 (28.6)	n/a	
Care for HIV + women or exposed infants	No 31 (29.8) Yes 73 (70.2) (women)	No 15 (71.4) Yes 6 (28.6) (women/infants)	No 10 (37.0) Yes 17 (63.0) (infants)	
# patients/ yr	0: 23 (22.3) 1-5: 31 (30.1) 6-15: 23 (22.3) 16-30: 13 (12.6) 31-50: 8 (7.8) >50: 5 (4.9)	n/a	0: 10 (37.0) 1-2: 11 (40.7) 3-5: 1 (3.7) 6-10: 2 (7.4) >10: 3 (11.1)	

Ctty hosp =Community hospital, Ctty practice=community practice, RN=registered nurse, MD=medical doctor, Pharm=pharmacist, SW=social worker, ID=infectious diseases, MM=medical microbiologist

Survey questions were designed to measure different concepts, and due to variance in the style and format of questions, it required a thoughtful process to answer. This was done to minimize participant bias towards selecting a similar answer without thought. Knowledge questions were weighted equally, be being valued as either correct for 1 point or incorrect for 0 points regardless of the format of the question (multiple choice or true/false).

Attitude and practice questions on perceived stigma or risk tolerance were often asked on a Likert scale to allow for greater nuance. Therefore, if a response was on a 5-point Likert scale, it may weigh more heavily on the overall score compared to another

question asked in a 4-point multiple-choice format. Although this may lead to some issues weighing more heavily in the overall scale, this was required in order to display the breadth of range in responses. Further descriptions on the types of questions and the range of these attitude scores are described later.

3.2.5.1 Knowledge

The knowledge section consisted of 26 items, allowing for a range of potential scores between 0 and 26, with higher scores indicating greater knowledge. The range of participant scores was 23 (minimum score 2, maximum score 25) across all groups.

Using an ANOVA to compare the mean values of the knowledge, risk tolerance and perceived barrier/stigma scale, the only scale which had a significant difference between groups was the knowledge scale ($p=0.006$). Thereafter independent t-tests between the different survey groups showed that the Pediatric group had a significantly lower score when compared to both the HIV providers and the infectious diseases group ($p<0.01$ and $p<0.01$, respectively). This was also confirmed using regression analysis with dummy variable coding, where the Pediatric group was associated with a lower knowledge score ($B=-0.23$, $p=0.01$)

Using linear regression as independent variables, age, gender, and treating HIV patients in current practice were not associated with a greater knowledge score. Having been in practice for more than 5 years was a question asked of the Pediatric and HIV providers only and it was not associated with a higher knowledge score. Among the HIV providers and infectious diseases group, the type of practice was not significantly associated with the knowledge score; however being in an academic practice was positively associated with increased knowledge (Standardized $B = 0.35$, $p<.01$), and

being involved in research was negatively associated with knowledge (Standardized B=-0.30, p<0.01). Among the HIV providers group, having international experience in HIV care was not associated with increased knowledge. Using regression with a dummy variable (nurse being held as a constant), physicians and pharmacists were significantly associated with a higher knowledge scores (B=0.42, p<0.01, and B=0.20, p=0.02 respectively).

Table 4: Factors associated with knowledge by profession

Variable	**Summary Statistics**
Providers Group: Knowledge Score	Mean (SD)
All providers	17.2 (4.6)
HIV Providers (HIVP)	17.6 (4.8)
Infectious Diseases (ID)	18.5 (2.6)
Pediatricians (Peds)	14.6 (3.9)
Significant Predictors ANOVA	Statistical test coefficient, p value
Survey type and knowledge score (F, p)	**5.93 (0.03**)
T Tests comparing ID to HIVP (t, p)	1.27 (0.21)
T Tests comparing HIVP to Peds (t, p)	**3.33 (<0.01)**
T Tests comparing ID to Peds (t, p)	**4.13 (<0.01)**
Predictors (HIV constant B=17.57)	Standardized Beta coefficient, p value
Survey type (ID)	0.07 (0.37)
Survey type (Peds)	**-0.25 (<0.01)**
Age (year)	0.047 (0.57)
Female Gender	-0.06 (0.49)
Having HIV + patients	0.14 (0.08)
Risk tolerance score	-0.04 (0.63)
Stigma/barrier score	-0.08 (0.31)
Questions asked on 2 of 3 surveys: ID and HIVP	

Type of practice	Standardized Beta coefficient, p value
Academic	**0.35 (<0.01)**
Community hospital	-0.07 (0.42)
Community practice	-0.36 (0.72)
Research	**-0.30 (<0.01)**
HIVP and Peds	
Years in practice (0=<5, 1=>5 years)	0.17 (0.05)
HIVP Group only	
International experience (y=1, n=0)	0.17 (0.08)
Profession (nurse=constant **B= 15.66)**	
Social worker	-0.10 (0.23)
Physician	**0.42 (<0.01)**
Pharmacist	**0.20 (0.02)**

HIVP= HIV Providers, ID = Infectious Disease and Medical Microbiologists, Peds= Pediatricians, SD = standard deviation, F= F-test, t = t-test, HIV+ = HIV positive

3.2.5.2 Risk Tolerance

The risk tolerance of transmission score consisted of 23 items, resulting in a maximum score of 37, with higher scores indicating increased tolerance to risk of transmission by feeding. The range of all participant scores was 29, (minimum score 6, maximum 35).

Using ANOVA, there was no significant difference in risk tolerance between provider groups ($F_{2, 149} = 0.57$, p=0.57). Using linear regression, age and gender were not associated with risk tolerance (p=0.36, and 0.48 respectively). However, treating HIV patients was associated with a lower risk tolerance (B=-0.21, p=0.01). Among the infectious disease and HIV providers groups the type of practice was not significantly associated with risk tolerance. Among the HIV and the Pediatric provider groups years

in practice more than 5 years was not associated with risk tolerance. Among the HIVP group, international experience was not associated with risk tolerance. Using regression holding nurse as a constant, type of profession was not associated with risk tolerance.

Table 5: Factors associated with risk tolerance of vertical transmission score

Variable	**Summary Statistics**
Providers Group: Risk Tolerance Score	Mean (SD)
All providers	18.0 (5.1)
HIV Providers (HIVP)	18.2 (4.9)
Infectious Diseases (ID)	17.1 (3.2)
Pediatricians (Peds)	17.5 (6.7)
Predictors	Standardized Beta coefficient, p value
Age (yr)	0.07 (0.36)
Female gender	0.06 (0.48)
Care for HIV	**-0.21 (0.01)**
Knowledge score	-0.04 (0.63)
Stigma/barrier score	0.11 (0.18)
ID and HIV	Standardized Beta coefficient, p value
Type of practice	
Academic	-0.09 (0.34)
Community hospital	0.16 (0.08)
Community practice	0.10 (0.25)
Research	0.03 (0.78)
HIVP and Peds	Standardized Beta coefficient, p value
Years in practice (0=<5, 1=>5 years)	-0.04 (0.69)
HIVP Group only	Standardized Beta coefficient, p value
International experience (y=1, n=0)	-0.11 (0.29)

Profession (nurse constant, B=18.42)	
Social worker	-0.07 (0.47)
Physician	-0.90 (0.36)
Pharmacist	0.01 (0.96)

HIVP= HIV Providers, ID = Infectious Disease and Medical Microbiologists, Peds= Pediatricians, SD = standard deviation

3.2.5.3 Perceived Stigma/Barrier Scale

The perceived stigma/barrier scale consisted of 15 items, resulting in a possible minimum and maximum score of 15 to 73. A higher score indicates an increased perceived stigma/barrier. The range of all participant scores was 40, (minimum score 33, maximum 73).

The HIV provider group differed significantly from both the pediatric and infectious diseases group in the stigma/barrier scale ($t(127) = 3.61$, $p<0.01$, and $t(121) = 2.88$ ($p<0.01$) respectively). Both the Pediatric group and the infectious diseases groups were associated with a lower barrier and stigma score ($B=-0.30$, $p<0.01$, and $B=-0.21$, $p<0.01$ respectively). Age or having HIV positive patients were not associated with the stigma/barrier score. However gender was associated, being of the female gender was associated with a higher stigma barrier score ($B=0.194$, $p=0.02$). Knowledge and risk tolerance scores were not associated with the stigma/barrier score.

Among the Infectious Diseases and HIV provider groups, all of the provider work settings were significantly associated with the stigma/barrier score. Interestingly being in an academic or research practice was associated with a lower stigma/barrier score ($B=-0.18$, $p=0.05$, and $B=-0.25$, $p=0.01$ respectively). Whereas being in a community hospital

or community practice was associated with a higher stigma/barrier score (B=0.2, p=0.03, and B=0.18, p=0.05 respectively).

Among the HIV and the Pediatric provider groups years in practice was not associated with stigma/barrier score. Among the HIVP group, neither international experience nor profession were associated with the stigma/barrier score.

Table 6: Factors associated with perceived stigma/barriers for women related to infant feeding score

Variable	**Summary Statistics**
Providers Group: Stigma/Barrier Scale	Mean (SD)
All providers	59.1 (7.4)
HIVP	59.0 (6.7)
ID/MM	55.2 (5.9)
CP	55.1 (8.4)
Significant Predictors ANOVA	Statistical test coefficient, p value
Survey type and knowledge score (F, p)	**8.97 (<0.01**)
T Tests comparing ID to HIVP (t, p)	**2.88 (<0.01)**
T Tests comparing HIVP to Peds (t, p)	**3.61 (<0.01)**
T Tests comparing ID to Peds (t, p)	0.53 (0.60)
Predictors (HIV constant B=60.74)	Standardized Beta coefficient, p value
Survey type (ID)	-0.21 (<0.01)
Survey type (Peds)	**-0.30 (<0.01)**
Age (year)	-0.12 (0.14)
Female Gender	**0.19 (0.02)**
Having HIV + patients	-0.067 (0.41)
Risk tolerance score	0.11 (0.18)
Knowledge score	-0.08 (0.31)
ID and HIVP	Standardized Beta coefficient, p value
Type of practice	

Academic	**-0.18 (0.05)**
Community hospital	**0.20 (0.03)**
Community practice	**0.18 (0.05**)
Research	**-0.25 (0.01)**
HIVP and Peds	Standardized Beta coefficient, p value
Years in practice (<5 years or >5 years)	0.03 (0.71)
HIVP Group only	Standardized Beta coefficient, p value
International experience	-0.07 (0.52)
Profession (nurse constant, B=60.41)	
Social worker	-0.03 (0.77)
Physician	-0.10 (0.32)
Pharmacist	-0.10 (0.30)

HIVP= HIV Providers, ID = Infectious Disease and Medical Microbiologists, Peds= Pediatricians, SD = standard deviation, HIV+ = HIV positive

3.2.5.4 Cultural considerations

HIV care providers were asked which populations of pregnant women living with HIV are seen in their practice. Most providers selected 1-3 ethnic populations for their clinic (n=33, 30, and 31 respectively). Sixty-five providers (62.5%) selected African born, 50 (48.1%) selected Caucasian, 49 (47.1%) selected indigenous Canadians, 19 (18.3%) selected black Caribbean, 3 (2.9%) selected South Asian, 2 (1.9%) selected south east Asian, 2 (1.9%), 2 (1.9%) providers selected substance users, 2 selected black American born, and 1 (1.0%) selected Latin American. Interestingly despite the spread of ethnicities, 99 out of 104 respondents felt that ethnicity/culture influences the wish to breastfeed.

An attitude question asked of providers was if community cultural traditions influences stigma for women living with HIV who are not breastfeeding. Eighty-five providers (56.0%) strongly agreed, 48 (31.6%) agreed, and 4 (2.6%) disagreed, and 6 (3.9%) strongly disagreed, 7 (4%) didn't answer. This is an important consideration when developing resources or support for women regarding infant feeding and the important role culture plays.

3.2.5.5 Risk factors for transmission:

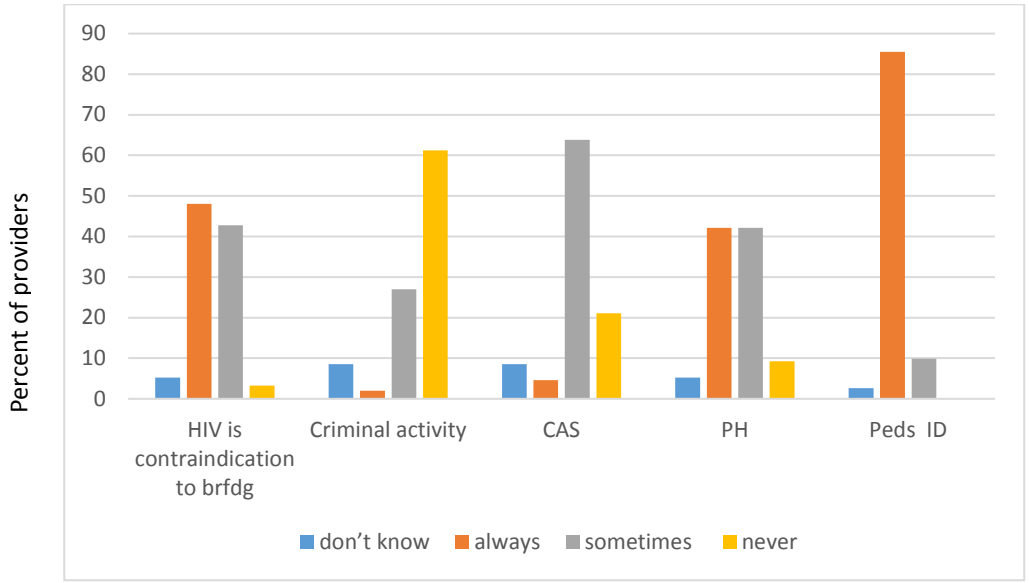
The relative importance of risk factors on HIV transmission were appropriately selected by the majority of respondents. Risk factors rated as moderately to very important by providers included: viral load (n=145, 95.4%), use of maternal antiretrovirals during breastfeeding (n=140, 92.1%), nipple/skin integrity was (n=136, 89.5%), exclusive breastfeeding (n=133, 87.5%), infant antiretroviral use during breastfeeding (n=111, 73.0%), and duration of breastfeeding (n=99, 65%). The actual significance of the duration of wean was endorsed by 75 respondents (49.3%) which has been debated in the literature, this received the most "I don't know" responses at 48 (31.6%). Risk factors which are known to be less relevant, such as maternal CD4 and antiviral class of medication, were rated as less important but still endorsed by 90 respondents (59.2%), and antiviral class by 89 (58.5%). Overall, Pediatric providers selected "I don't know" as a response on average 9.5%, HIVP 13.0%, and infectious diseases 19.7%.

3.2.5.6 Practice around breastfeeding

Respondents stated that they would always involve: pediatric infectious disease consultants (130 respondents, 85.5%), public health personnel (64 respondents, 42.1%),

or the Children's Aid Society (7 respondents, 4.6%) (Figure 1). These questions were followed by scenarios, which described various risks of transmission. Thereafter when asked about actual practices, the majority of people would consider calling the Children's Aid Society (105, 69.1%), or public health in certain situations (114, (75.0%).

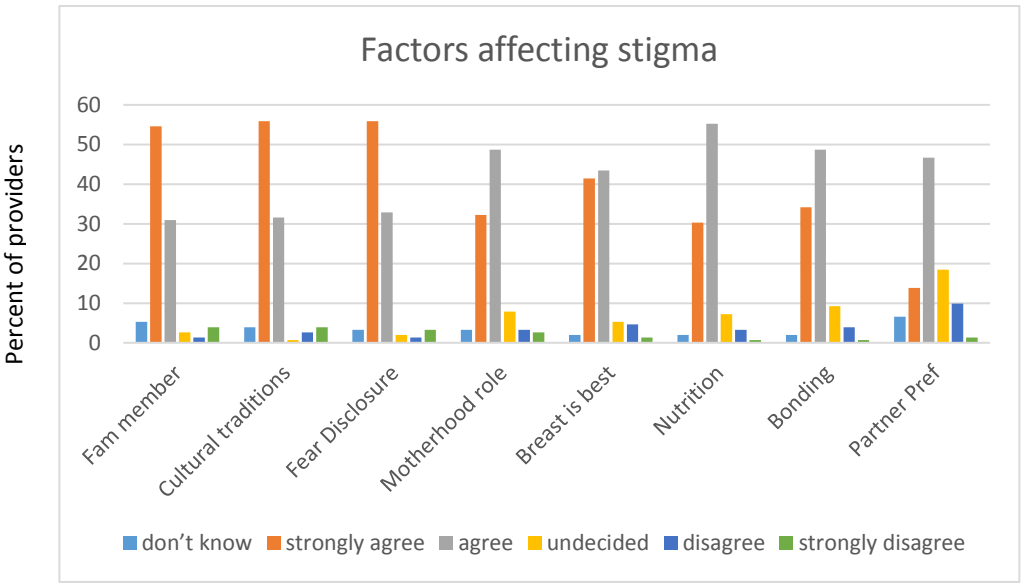
Figure 1: Percent of providers and endorsement of attitudes, and involvement of other services



Brfdg =breastfeeding, CAS=Children's Aid Society, PH=Public Health, Peds ID=Pediatric infectious Diseases

All factors listed that influence stigma were selected by the majority of respondents (80.9% to 88.8%), except for partner preference which was only selected by 60.5% of respondents. The highest rated stigmatizing factor agreed upon was fear of involuntary disclosure of HIV status for not breastfeeding, selected by 88.8% of respondents (Figure 2). The three, which were selected as 'strongly agree' by the majority, were family members, cultural traditions and fear of involuntary disclosure at 54.6%, 55.9% and 55.9% respectively (Figure 4). (Of note, this same question is also asked of women living with HIV in our pilot questionnaire of pregnant and post-partum women.)

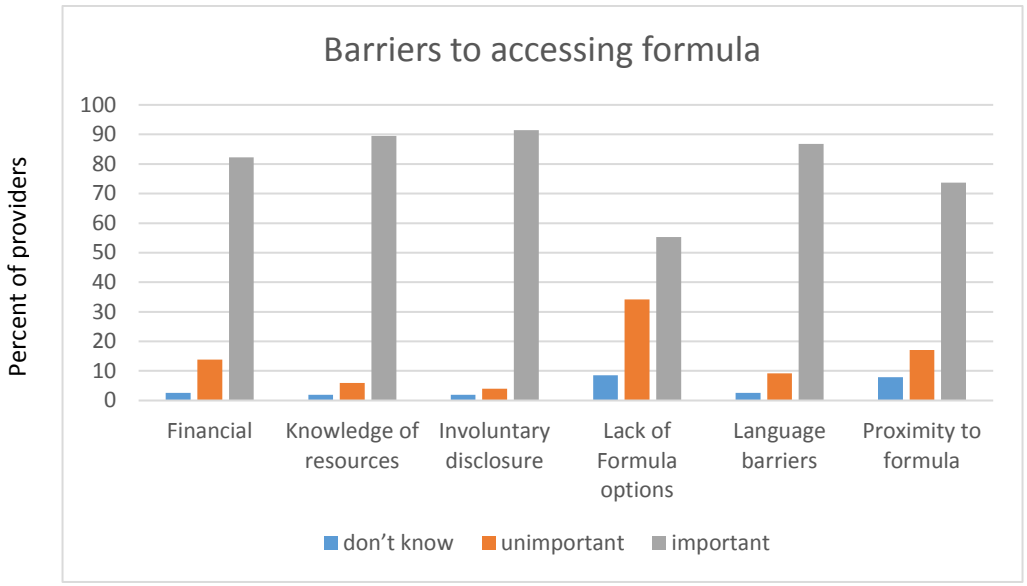
Figure 2: Factors affecting stigma endorsed



Fam: Family, Pref: preferences

Barriers to accessing formula were generally all considered "Important", the least important ones were lack of formula options (considered "Unimportant" by 52, 34.2%), and proximity to formula providers (considered "Unimportant" by 26, 17.1%) (Figure 3). The barriers considered "Very Important": were financial limitations (78, 51.3%), fear of involuntary disclosure (81, 53.3%), and knowledge of resources (72, 47.4%) (Figure 3). (Of note, this question also appears on our pilot questionnaire of women living with HIV.)

Figure 3: Barriers to accessing formula endorsed



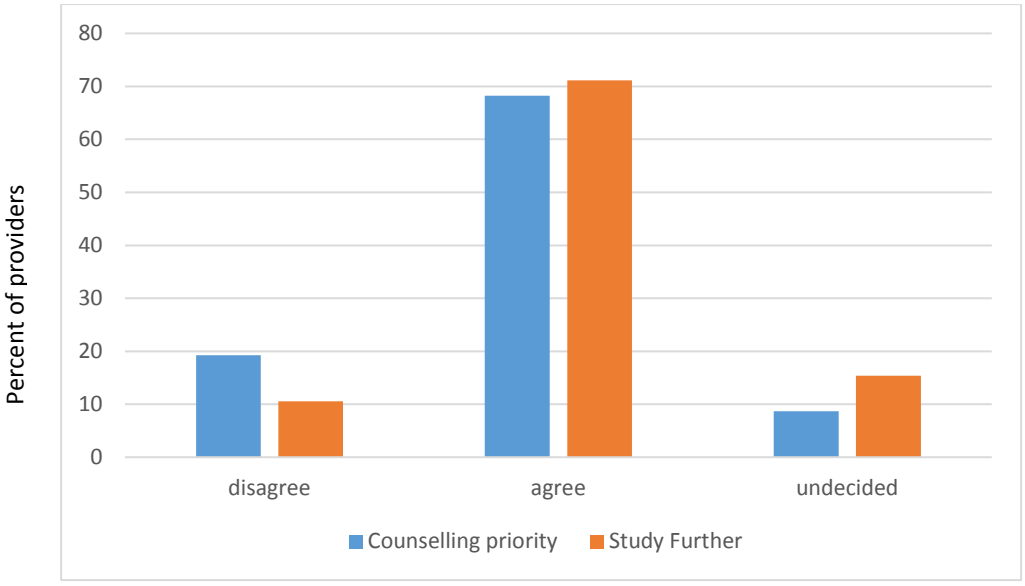
Providers were generally in support of funding formula access, with majority of providers n=119, 78.3%) supporting funding in all situations and 27 providers (17.7%) supporting funding based on socioeconomic status. HIV providers were asked how the majority of their patients access free formula; the most commonly selected option was through pharmacies, according to 41 respondents (39.4%), which is the format for the Ontario program where 36 respondents (37.5% of respondents) endorsed being from. The next most commonly reported answer, by 35 respondents (33.7%) was that they did not know how their patients access free formula. When asked where the provider refers patients the majority of respondents stated the Teresa Group in Ontario 22 (22.9%), and the Oaktree clinic in Vancouver 15 (15.6%). "I am not aware of any formula services available to my patients" was endorsed by 18 (18.75%).

HIV providers were asked if "Women are asking more about breastfeeding over the last 5 years", this was endorsed by 43 (28.3%), "asking the same" by 71 (46.7%), or 'asking less" by 28 (18.4%). Similarly, if "the frequency of women asking why the

recommendations on infant feeding differ in other low resource settings" was rated "More Frequently" by 30 (19.7%), "The Same Frequency" by 83 (54.6%), or "Less Frequently" by 20 (13.2%) respondents.

The HIV providers were asked if infant feeding counselling is a clinical priority in their practice, and the majority of respondents agreed (71, 68.3%), whereas 20 (19.2%) disagreed (Figure 4). HIV providers were asked if further study is needed to determine the biological risk of transmission via breastmilk in the Canadian context and 71.2% agreed while 10.6% disagreed. The topics always counselled on by the clinics of providers were "formula resources" by 42 (91.3%), "mechanism of transmission" by 38 (84.4%), and "explanations as to why they are not breastfeeding" by 33 (71.7%). The elements described as "Seldom Counselled on" were "risk of criminal charges" in 21 (46.7%), and "risk of child protective service involvement" by 20 (44.4%).

Figure 4: Provider endorsement that infant feeding is clinical counselling priority and requires further research

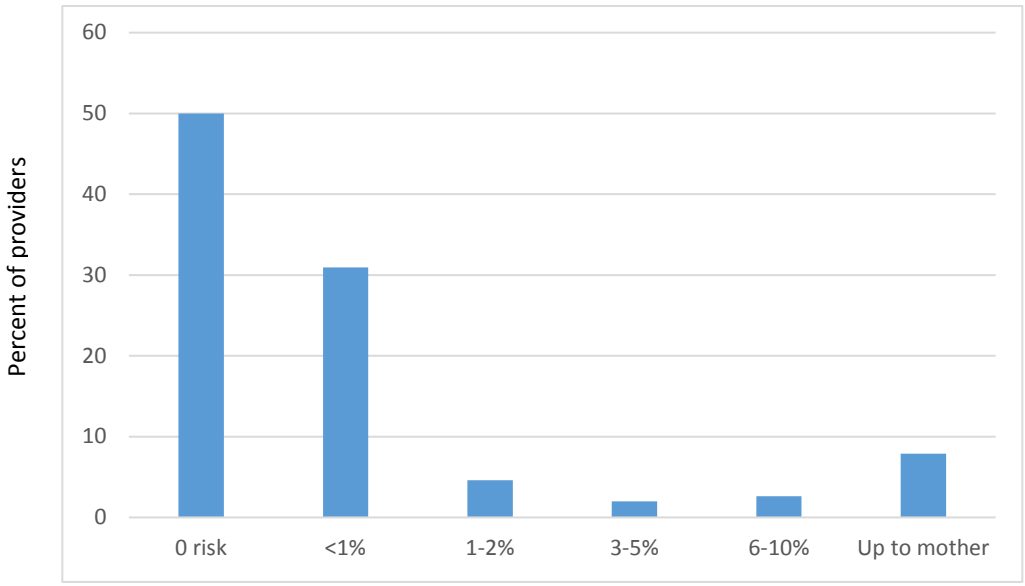


3.2.5.7 Risk Tolerance Attitudes

Attitudes towards HIV being a contraindication to breastfeeding was divided between 73 (43.0%) respondents saying “always”, 52 (34.2%) respondents saying “depends on the scenario”, 13 (8.6%) respondents saying “most of the time”, and 5 (3.3%) saying “never”, with 8 (5.3%) answering “I don’t know” (Figure 1). The majority of respondents (93, 60.5%) felt that breastfeeding should never be considered a criminal activity.

All providers were asked about the acceptable level of risk of breastfeeding transmission in a Canadian context in order to recommend breastfeeding. Half of all respondents (50%) stated “zero risk”, 47 respondents (30.7 %) would accept “<1% risk”, 7 (4.6%) of respondents would accept “1-2% risk”, 3 (2.0%) of respondents would accept “3-5% risk”, and 4 (2.6%) of respondents would accept “6-10%”, 12 respondents (7.9%) stated this is “the mother’s choice regardless of the quantifiable risk” (Figure 5). There was no significant correlation between those who selected zero risk and the knowledge or stigma/barrier scores. However, selecting zero risk was significantly associated with a lower risk tolerance ($B=-0.369$, $p<0.01$). HIV providers were asked if they would be interested in being involved in a study that assessed the biologic risk of transmission of HIV and antiretrovirals in breastmilk in a Canadian context; 22 people, “Maybe” by 23 people, and “Not Interested” by 54 people endorsed this.

Figure 5: The acceptable level of risk to recommend breastfeeding in Canada



There were a few questions, which described scenarios of different women with varying levels of risk of transmission in a Canadian context. The lowest risk scenario was a woman who was on ART, with an undetectable viral load to a woman not on ART, with a detectable viral load. In all scenarios, counselling on the risk of transmission was endorsed by 73.0 to 80.2% of respondents. The scenario in which the woman was unable to afford or access formula resulted in respondents being slightly less likely to counsel on the risk.

Respondents were much more likely to advise to stop breastfeeding in the highest risk scenario with 85.5% of respondents endorsing this. The lowest endorsement (25.7%) for advising to stop breastfeeding was again in the scenario where formula was not accessible. This may appear that providers are willing to tolerate breastfeeding, and contradict the results of 'acceptable level of risk' described in Figure 5. This is likely related to variable interpretation of the scenario and what it means to 'not be able to access formula'. Being 'unable to access any supply of formula' would be rare in almost all locations in Canada, even if dedicated HIV related funded formula programs are not in

place. The lowest risk scenario with undetectable VL on ART also led to only 55.9% of respondents advising to stop breastfeeding. Encouraging breastfeeding was endorsed at a very low rate of 7.2% in the highest risk scenario, and by 20.3% of respondents in the low risk scenario. When formula was not accessible, then 51.9% of respondents endorsed this, again this is likely subject to interpretation of what 'not accessible' truly means.

Involving Child Protective services was endorsed by only 2.6% of providers in the lowest risk scenario and 38.8% in the highest risk scenario. When access to formula was an issue, 7.2% of respondents endorsed this, with occasional free text comments referring to the involvement only to improve access and provide support. Involvement of a Pediatric Infectious Diseases expert was endorsed by 69.1% to 79.6% of respondents in the five scenarios, with the highest endorsement in the highest risk scenario. Involvement of Public Health was endorsed 26.9 to 51.9% of cases, with access higher risk being the highest indication.

3.2.6 Discussion

This is the first study to evaluate health care providers' knowledge, attitudes and practices towards infant feeding in HIV in a Canadian context or a high resource context. Although other qualitative and quantitative work has been completed looking at provider(90)(92)(97)(95)(100) and patient knowledge(91)(93)(94), attitudes and practices to varying degrees they have all been in low resource settings. Preliminary data from a similar survey conducted on American healthcare providers was recently presented at the 7Th International Workshop on HIV and Women in 2017, with a plan for qualitative interviews among health care providers(101).

This study begins to explore the key elements pertaining to health care providers including their knowledge of evidence, their risk tolerance to breastfeeding transmission, and the degree of stigma they perceive their patients face related to infant feeding. A demographically interesting consideration was gender, as the majority of participants were female; this has been seen with previous health care provider surveys(96)(97)(101). Female providers are often more involved in women's health care issues both in Canada and in many low resource settings. The fact that more women responded to our survey may reflect a stronger interest in infant feeding in HIV compared to male colleagues. Nonetheless, gender was not found to be related to knowledge or perceived stigma, but did appear to be related to risk tolerance, with females being more risk tolerant. This was not seen to the same extent in the US healthcare provider survey, where 50% of males were willing to consider breastfeeding for women with undetectable viral load, compared to 44.4% of female providers. However, women were much more likely to respond as 'uncertain' relative to men (37.5% of women versus 10% of men)(101).

Age was not a predictor of any of the scores. Interestingly in the US healthcare provider survey, providers <30 years of age all selected uncertain in their willingness to consider breastfeeding for women with an undetectable viral load. Caring for HIV patients was associated with a lower risk tolerance, but was not associated with perceived stigma or knowledge. The US survey was narrower in their population, with inclusion criteria of healthcare providers who care for women living with HIV or HIV-exposed infants, and had to have counselled a mother regarding breastfeeding in the past 2 years (leading to 13 excluded responses).

Pediatricians had a lower knowledge scores compared to both the infectious diseases and HIV providers. This may be because many of the knowledge questions could be considered to be issues discussed during pregnancy, and pediatric providers are less involved at this time. It is also important to note, these are general pediatricians who may care for HIV-exposed infants, and are less likely the primary care provider of infected youth. This group does not include pediatric HIV or infectious diseases specialists.

The HIV care provider group was associated with a higher perceived stigma/barrier scale compared to the other two groups. This is not very surprising, as HIV specialists receive more training and are more aware of the literature surrounding HIV stigma due to their closer proximity to this population as the primary care providers for this group. Although it is commonly thought that pediatricians are the least risk tolerant in their role as advocates for the infant, this was not borne out in our risk tolerance scale. The US healthcare provider survey had multiple respondent comments from pediatricians stating, “their role is to prevent illness in the child, not to acquiesce to the wishes of the parent”. Other providers stated “we need to get pediatricians on board for their fear is so high and women are not given the option”(101).

Having international experience was not associated with a significant difference in any of the scores among the HIV providers group. This may be due to the fact that international HIV care experience can be very diverse in contexts where women may be predominantly breastfeeding or formula feeding based on various factors. Among the HIV provider group where profession was ascertained, being a physician or pharmacist was associated with a higher knowledge score, when nurses were used as the

comparator group. Profession was not significantly associated with the risk tolerance or stigma/barrier scale.

HIV providers were asked about the ethnicities of their patients, and the majority of patients were African born, however there was a diverse range of ethnicities selected, with Caucasian and aboriginal patients being well represented. This is reassuring in demonstrating that the commonly seen HIV populations were being represented by their providers in this survey. Interestingly, providers highly endorsed that culture influences the desire to breastfeed and the stigma women face (Figure 4). This has been described in previous works where local cultures can significantly influence a woman's ability to follow recommendations. For example in one qualitative study of mothers and health care workers in Burkina Faso, it is customary to give an infant herbal teas as part of preventive care, whereas in the same study women from Cambodia were able to formula feed without suspicion since it is valued as a sign of financial security or a necessity among factory workers(94). Gender and religious values have been shown to shape how health care workers counsel women on transmission and infant feeding(102). Another study from Tanzania also described how mixed feeding is the only culturally acceptable option for women, thereby making counselling a seemingly impossible challenge to nurse-counsellors(100). Although in Canada the WHO's previous AFASS criteria ('Acceptable, Feasible, Affordable, Safe and Sustainable') for formula use aren't applied, the reality that culture influences 'acceptability' of counselling on many aspects of infant feeding in HIV is apparent. This highlights the importance of providers approaching this issue with cultural competency, preferably using knowledge translation (KT) tools developed with input from the different cultural groups.

It is important to recognize an important limitation of surveys of health care providers: they can only be reflective of the perceptions of healthcare providers about the patient populations they serve, and may not be truly reflective of patient beliefs or preferences. This is importantly demonstrated by a question in the US healthcare provider survey where providers were asked if women living with HIV ask if they can breastfeed; 41% of providers stated these women are all or mostly immigrants, whereas 33% said some, very few or none are immigrants. This seemingly contradictory response by US healthcare providers likely reflects how in high resource settings such as Canada and the USA, patient populations are less homogenous. This was demonstrated by the ethnicity question in our survey. Whereas, previous health care providers surveys conducted in low resource settings are of providers that care for more ethnically homogenous patient populations compared to Canadian populations living with HIV.

Provider attitudes towards breastfeeding varied significantly based on the context, but overall most providers did not think it should be criminalized. A similar sentiment is described in the US healthcare provider survey where 28% are concerned about legal implications of transmission, but providers stated, “the legal concern is something that I don’t think should enter one’s decision”. Consensus on contacting pediatric infectious disease was endorsed by most providers. When asked overall if HIV was a contraindication to breastfeeding most providers endorsed ‘always’, but this was not born out in the scenario questions. In scenarios where formula was not accessible, providers did not recommend or counsel against breastfeeding.

It is widely known that fear of involuntary disclosure of HIV status is a major driver for women living with HIV and wanting to breastfeed(103)(104). Other highly selected

factors, which cause stigma, were family members and cultural traditions. These findings were similar to those in the US healthcare provider survey, where providers also selected stigma in family/community, health benefits of breastfeeding, and bonding with the baby as the main concerns patients report about not being able to breastfeed(101). Interestingly, the least relevant factor was partner preferences on our survey, and similarly was not reported in the US data. It will be important to determine the patient perspective on this, for future KT resource development and who to involve in discussions.

Barriers to formula access must be understood with the reality that the majority of respondents came from provinces with free formula programs in place. The greatest barriers were financial limitations, fear of involuntary disclosure and knowledge of formula resources. Twenty percent of US healthcare providers reported formula cost as a concern for patients(101). These are important considerations for recommendations on counselling of pregnant women on infant feeding in the HIV context, and indicate the importance of formula programs. Providers generally believed formula should be provided, especially to those of low socioeconomic status. Surprisingly, a third of HIV providers did not know how their patients access free formula. This may reflect a knowledge gap among providers, and an area in need of KT.

It did not appear overall to providers that women were asking more about breast-feeding, or differences in guidelines. This 'stabilization' in questions on the issue may be a reflection of de-prioritization of this as an issue to providers, patients or both, or may be a reflection that as providers we haven't addressed the issue therefore questions remain at the same rate. The majority of providers did state counselling on infant feeding was a

priority in their practice, with the discussion centering on formula resources, mechanism of transmission, and explanation as to why they are not breastfeeding. However, some of the harder topics such as criminalization and child protection involvement for the most part is not discussed. Potential explanations as to why these topics are not discussed are because providers think breast-feeding will not happen thereby do not see a need to discuss it. Perhaps this is reflective of a knowledge gap among providers, and therefore they tend not to discuss aspects they are less confident in. Providing safe spaces for open discussion on infant feeding, especially the more controversial areas such as criminalization or child protection involvement is critical, and providers and patients' needs to feel comfortable and competent when discussing them.

When asked about the acceptable risk tolerable to recommend breastfeeding, approximately 50% accepted 0% risk, and 30% accepted a <1% risk. In Canada, approximately 200 babies are born to women living with HIV every year, and therefore accepting a 1% risk means two babies infected per year from breastfeeding. Canada has achieved a substantial reduction in confirmed perinatally infected infants from 8 in 2009 (4%) to 2 in 2014 (0.4%) through the implementation of multiple aspects of prevention of vertical transmission(105). If breastfeeding adds a 1% risk of transmission, this would be accepting a 2-fold increase in the number of perinatally infected infants per year in Canada. To a large extent, it may not be a specific risk percentage that providers need to see, but rather a system in place to address all the elements which factor into infant feeding. As demonstrated by many of the scenario questions, formula accessibility, maternal viral load, maternal historical compliance with antiretrovirals all significantly changed provider approaches to scenarios. The US survey alluded to this reality by

asking what mechanisms would need to be in place for a healthcare provider to assist a women living with HIV with an undetectable viral load to breastfeed; 76% of providers stated a society or government guideline, clinical data on the benefit of breastfeeding, and legal protection. From our survey, most people felt this area needs further study, but many were not interested in participating in a study on risk of transmission in a Canadian context. Our survey begins to elucidate some of the highly nuanced aspects of infant feeding for providers and patients in Canada.

3.2.7 Limitations

There are several limitations to this small survey, which had a low participation rate and may not be representative of all providers across the country. The challenge with conducting a detailed survey is that responders are likely to be those with a vested interested in the topic. The generalizability of the study is also limited by the regional predominance of providers from Ontario, Quebec, and British Columbia. These are the 3 provinces with the most pregnancies among women living with HIV.

This tool has not been validated for a specific population, and so the reproducibility of these results is limited. Overall we had a poor response rate among infectious diseases group, but reached 16% and 17% of the community pediatrics and HIV providers groups, respectively, which is not out of keeping for a narrow topic health care provider survey. Our recruitment method was not highly costly, (gift card draw), but perhaps was not as effective as hoped for.

For the most part those answering the survey did care for pregnant women living with HIV or HIV exposed infants, despite us not forcing this as an inclusion criteria.

Overall, we were able to obtain over 100 responses from varied groups; however, we lacked input from midwives which is an important group of care providers.

3.2.8 Conclusions

This survey provides a descriptive analysis of a complex area not previously explored in the literature on provider perspectives on infant feeding in HIV in Canada. This survey provides insight into topics for which knowledge is limited in the literature, but did have many similarities with a survey conducted among US healthcare providers. This survey elucidated some knowledge gaps among providers, such as knowledge of formula resources, interpretation of guidelines, and aspects which are excluded from counselling. Despite these knowledge gaps, providers do see infant feeding as an important topic, and support further research in this area.

The survey provides support for a standardized approach to counselling as a means to improve the consistency of messaging that women receive. The survey provides data for the development of KT resources and clinical guidelines for providers. The need for providers to be culturally competent in their approach to this issue for the populations being served was highlighted, and also involvement of family members in these discussion due to the role they play in decisions on infant feeding. This survey also highlights the importance in understanding how the community's perspective on some of these issues differs, so that providers can understand the patient perspective to facilitate conversation on a complex topic.

Providers feel that formula should be provided to these patients, and socioeconomic status should not be a barrier. Providers do not believe that breastfeeding should be considered a criminal activity in the HIV context. These are important elements,

which should inform policy on infant feeding practices and legislation drafted by government.

Overall, it appears that providers are still reticent to recommend breastfeeding due to the potential risk of transmission, which unfortunately is not quantifiable in our context due to the ethical considerations of study on this topic. Providers do feel further research is needed to understand this better. Specific research gaps are understanding how often breastfeeding is occurring in the Canadian context, and for what duration. Supporting formula feeding is a greater priority among providers given the lack of clear quantification of the risk of breastfeeding. Further study on risk minimization of breastfeeding done in an ethical manner is needed, but would be logistically challenging in a Canadian context. Future guidelines and KT resources are needed for both providers and patients to standardize the counselling, and improve the understanding of this complex issue.

3.2.9 Appendices

Table 7: Table of Specifications

Table of Specifications	Knowledge	Attitudes	Practice
Importance of breastfeeding	X	X	
Infant feeding guidelines in HIV	X	X	
Criminalization of breastfeeding	X	X	X
Calling Child Protection Services for breastfeeding	X	X	X
Experience with counseling on infant feeding			X
HIV Stigma with route of feeding	X	X	
Barriers to accessing formula	X	X	X
Interest in study in infant feeding		X	

CHAPTER 4: Canadian Infant Feeding in HIV Network (CIFHN): Provider Meeting for enhancing research and clinical capacity in Canada

4.1 Abstract

Infant feeding in HIV is increasingly being recognized as an area needing further study to answer remaining clinical and research questions. Among care providers and families affected by HIV, there remains gaps in knowledge, counselling, and variability in practice, which needs further exploration. Canadian HIV care providers with an interest in this area met for a two-day meeting in Jan 2016 to describe local challenges, needs, and resources, discuss the latest evidence from researchers including basic scientists, social scientists, legal experts, and clinical experts. The discussions culminated in a World Café format where the priority areas were identified, a network was developed (The Canadian Infant Feeding in HIV Network), and targeted next steps focusing on areas of specific Knowledge Translational needs for the HIV community, and consensus clinical guidelines for Care providers

4.2 Introduction

4.2.1 Background of Infant Feeding in the Context of Maternal HIV-Infection

Vertical transmission of HIV can occur *in utero*, during labour and delivery, or via breastfeeding. With appropriate preventative interventions, including combination antiretroviral therapy (ART) for the mother during the pregnancy, intravenous zidovudine during labour, 6 weeks of oral zidovudine to the infant and exclusive formula feeding, the rate of vertical transmission of HIV can be reduced to less than 2%(106). In Canada, the overall vertical transmission rate between 1997 and 2012 was 2.9%. Among mothers

started on combination ART prior to delivery the risk was 1% and 0.4% for infants whose mothers were started ART more than 4 weeks before delivery(106).

In Canada, statistics suggest that 82.6% of women who are known to be HIV-positive in pregnancy receive combination ART, and another 4.1% receive some form of ART(107). While the use of ART to prevent vertical transmission is widely accepted in Canada and around the world, issues surrounding avoidance of breastfeeding as a prevention effort remain contentious and often complicated by diverse guidelines and recommendations around the world. The 2010 World Health Organization recommendations indicate that national authorities should decide on the most appropriate strategy for their populace. Two options are suggested: (a) exclusive breastfeeding with concurrent antiretroviral therapy of mother or infant or; (b) exclusive formula feeding. Formula should be meet the acceptable, feasible, affordable, sustainable and safe (AFASS) criteria(56).

Studies, mainly from lower resource countries, have assessed the importance of viral load and/or proviral DNA in cells in breastmilk with respect to vertical transmission of HIV. These studies have suggested that viral load in breastmilk and/or the presence of cells containing proviral DNA in breastmilk are significant risk factors for transmission of HIV (4,5). There are also limited data, mainly from Africa, on passage of antiretroviral medications into breastmilk (6-9). In addition there are several clinical trials on ART to prevent breastmilk transmission, which show significant risk reduction(10,11). These trials, in low resource settings, demonstrate maternal ART and infant antiretroviral therapy can significantly reduce, but not eliminate vertical breastfeeding transmission of HIV. The applicability of these interventions to resource rich countries is uncertain.

4.2.2 Canadian Context

At this time there is no detailed document delineating infant feeding recommendations for HIV-infected mothers in Canada. Health Canada and the Canadian Pediatric society recommend an acceptable alternative to breastfeeding for mothers who are living with HIV and this is the recommendation implemented by practitioners. One ongoing challenge with this recommendation is that not all provinces have subsidized formula programs in place, which potentiates issues of access. Recently the Canadian Pediatric and Perinatal AIDs Research Group and the Society of Obstetricians and Gynecologists published a statement on Prevention of vertical HIV transmission and management of the HIV-exposed infant in Canada(69). Exclusive formula feeding is recommended in this document and recommendations against automatic child protective services referral if a mother discloses ongoing breastfeeding. The absence of clear guidelines, particularly in reference to child protection services, further complicates care for HIV positive mothers and their families. It is argued that in the absence of such guidelines in Canada, a grey area related to infant feeding practices and required supports persists.

4.2.3 Community Perspective

There is an emergence of interest in this topic within the community. Our team has anecdotally observed a movement among women with HIV to better understand their options related to infant feeding, the risk of vertical transmission, and how to discuss infant feeding with their care providers during events organized by the Interdisciplinary HIV Pregnancy Research Group (IHPREG). A community forum hosted in 2013 by IHPREG to discuss the complex issues related to infant feeding with the community

including the true risk of transmission in a Canadian context, the legal and child protection implications of breastfeeding with HIV, and the sociocultural implications of being unable to breastfeed. This event allowed for a frank discussion with community and clinicians on the reality that breastfeeding is occasionally occurring in Canada, and women may not be fully aware of the implications of their infant feeding choices despite the counselling they receive by providers in clinical and community based settings.

4.2.4 Reviewing the literature for possible answers

The true risk of breastmilk HIV transmission in Canada in a woman who has been well controlled for a prolonged period is not known. Breastmilk studies completed in low middle incomes countries provide information, however such data may not be generalizable to a Canadian context. Major population differences when compared to women in Canada include longstanding, reliable access to high quality medication, frequent monitoring of viral load, and in some cases a low HIV reservoir if treated very early in life (as is the case in many children who were vertically infected in Canada that are now of childbearing age). What is clear from international studies, is that plasma viral load doesn't correlate with breastmilk viral load, when compared to other body fluids (e.g. semen)(38). Also antiretroviral medications pass into breastmilk at variable levels based on the drug class. A systematic review published in 2015 of 24 studies demonstrated that NRTIs accumulate in breastmilk at a breastmilk to maternal plasma ratio of 0.89 to 1.21, NNRTIs from 0.71 to 0.94, and PIs from 0.17 to 0.21(59). From the infant's plasma measurements, this was equivalent to ingesting the infant having ingested 8.4, 12.5, and 1.1% of pediatric dosing of lamivudine, nevirapine, and efavirenz. Increasing multi-drug

resistance has been seen to be emerging in infants who are breastfed by mothers on combination antiretroviral prophylaxis due to this ongoing low dose exposure(4,5).

This paucity of data from a comparable high resource setting is a concern. However, to study breastmilk in Canada would require patients to consent to expressing breastmilk (on an ongoing basis) for the purposes of analysis only. This may not be acceptable to women, nor considered ethical given the feelings of guilt a woman may face by not being able to feed her breastmilk to her child. Alternatively, in the context of a study with informed consent of risks, expressed breastmilk could be utilized for both biological analysis, and breastfeeding purposes with close monitoring of both infant and mom. This study may make longer duration of breastmilk analysis possible, but also may be considered unethical given that in the Canadian context, formula can be made available to all, and therefore the infant is being exposed to undue risk. Furthermore, if women were breastfeeding their infants as part of a study this could get misconstrued by others that breastfeeding is safe, especially because it is so widely done in other contexts where formula is not available.

Many providers have varying opinions on the true desire of women to breastfeed, the challenge being unable to breastfeed poses for women, the degree of counselling provided, the accessibility of formula, and the true risk in a well-controlled woman on antiretroviral therapy. Similarly, there appears to be differences in opinion, priorities, and research questions, which women living with HIV face when, compared to their providers. This was seen at the IHPREG Community Forum in 2013, but also voiced in previous focus groups held with women.

Given the paucity of knowledge in this field and this emerging dialogue among both the HIV patient community and providers, the need to engage in a dialogue between providers and patients has been identified. This conversation is imperative in order to establish priority research and to better inform available care and services in a Canadian context.

The ongoing debate and lack of consensus among care providers as to what infant feeding options should be available in Canada, and the sensitive nature of the topic for women living with HIV made it challenging to try to have a meeting with both provider and patient groups. Recognizing that the perspective of women living with HIV needs exploration, and is an essential part of this conversation, we opted to host a focus group for women living with HIV, where their knowledge, attitudes and experiences surrounding infant feeding could be discussed in a safe space. The findings from this focus group were then presented to the HIV research and clinical providers at a two-day research and clinical planning meeting. Key spokespersons from the community with previous research experience (Peer research associates) were present at the meeting as well to offer a community presence as well. Followed by a frank discussion with the research and clinical community as to what resources are in place, challenges faced, and future direction on coming to consensus both from a clinical and research perspective to begin to answer the remaining questions, and standardize and optimize the care provided.

4.3 Goals of the planning meeting

1) To understand if a multicenter cohort study enrolling women willing to express breastmilk for the purposes of research is feasible. Such research would be the most effective way to measure the biologic factors that increase the risk of transmission,

viral loads, cellular reservoirs, medication levels from breastmilk. Through the focus groups, we aimed to bring together community stakeholders to understand the psychosocial elements women face during pregnancy and postpartum to determine the feasibility of a study which would require breastmilk expression by women after delivery, but not allow breastfeeding.

2) To share knowledge across multiple Canadian centers to explore their experiences with infant feeding to determine the most effective method to recruit patients in a sensitive manner. How to sample, store, and test the breastmilk and blood specimens to understand the risk of transmission of HIV was a focus of the planning meeting.
3) To determine clinical consensus based on current data on what aspects of counselling are essential regarding infant feeding, and optimizing the accessibility of formula for all women living with HIV in Canada. This will in turn lead to the development of an evidence based clinical practice guideline
4) To determine the infant feeding in HIV knowledge translation needs based on community and provider perception.

4.3.1 Purpose and Objectives

Purpose: The objective of this component of my research was to host a 2-day meeting, in addition to community focus groups, to discuss how to best engage women to participate in a study involving expression of breastmilk. The meeting brought together HIV researchers and clinicians, with the aim of developing research priorities, and begin a discussion towards consensus clinical management and KT needs surrounding infant feeding in the HIV context in Canada.

4.3.2 Anticipated Outcomes of the Planning Meeting and Focus Groups

1) Gain a shared understanding of the issues surrounding infant feeding across Canada, and identify challenges, successes, and interventions used in current practice. This will help in Planning Research for Infant Feeding in HIV Study establishing common goals and desired outcomes for future collaboration (e.g. formalize group and define terms of reference);
2) Define research questions and plan project(s) for future research grant funding applications; specifically design a multicenter breastmilk cohort study.
3) Generate a meeting report and make recommendations for inclusion in future grant applications.
4) Submit conference abstracts and manuscripts pertaining to the report details and overall meeting outcomes.

4.4 Community Consultation - Focus Groups with Women living with HIV

To ensure this work was founded in a patient oriented approach we opted to conduct focus groups with the community in order to understand the experiences, and research priorities of women living with HIV in a safe space. The findings of this focus group were presented at the planning meeting to the provider/scientist group. Thereafter the planning meeting results were presented to the community in a follow up focus group with the same participants. Ethics approval was obtained for the focus groups and meeting from the Hospital for Sick Children.

The first Infant Feeding Focus group was held in January 2016, the participants were recruited from local HIV community based organizations. The first focus group consisted of 11 participants, and the second focus group was 3 of the previous

participants, and 1 new participant. The demographics of the 12 participants are reported in aggregate form to protect the participants' identity. The women were all aged 30s-40s, of which 9 were African, 2 were Caribbean, and 2 were Canadian born. All women had more than one child, 62% of participants had a pregnancy/delivery in a low resource setting and all had a Canadian pregnancy/delivery experience. Six participants were single, 5 identified a partner in their life, and 1 participant did not disclose her relationship status.

The first focus group was conducted using a semi-structured interview guide allowing for spontaneous participant driven discussion. The second focus group was a discussion on knowledge translation solutions, clinical strategies, and feasibility of infant feeding research. The focus groups were audio recorded, and transcribed for analysis thereafter. Directed content analysis of transcripts was undertaken by two investigators (SK, and VLK) using previous research on infant feeding(112,113) rather than specific qualitative theory. Each investigator read the transcripts and identified main recurring subject areas. Investigators then met to discuss the specificity of the emerging codes, and then read the transcripts again independently with more specific codes to classify the responses. The investigators met again and obtained consensus on the final coding of all responses. The three categories related to infant feeding and HIV identified that were both novel in the literature and could be actualized through research, programming and/or advocacy were: 1) New perspectives on the lived experiences of infant feeding for women living with HIV in Canada, 2) Solutions and changes to supports for women living with HIV and 3) Research considerations in a Canadian context on this topic.

4.4.1 New perspectives on the lived experience of infant feeding for women living with HIV in Canada.

Novel experiences that were shared by the participants included: the realities of women who had previously had a child in an HIV endemic country; the issue of 'choice' or lack thereof; the ongoing grief and loss experienced by women relating to feeding decisions; and the strength and resilience of women despite challenges.

Previous birth in an endemic country: Participants described how the infant feeding experience in an HIV endemic country could vary significantly when compared to Canadian experiences and that these experiences have lasting impressions. Experience in an HIV endemic country was described as creating confusion for some mothers in Canada. One participant who self-identified as being from Africa shared with the group how these confusions manifest themselves in the experiences of mothers who are post-migration:

> The problem I find with Canada [is that] most people…in the groups are immigrants….and we came from countries like Africa where HIV was educated differently…Like back home people say 6 months constantly breastfeeding with nothing else, your child won't be infected. And now you come to Canada, no breastfeeding.

Some women found that having been able to breastfeed, given its social and cultural acceptance, allowed for normalization of their motherhood experience. For those who had a previous baby where they had been counselled to breastfeed, being told they should not breastfeed in the Canadian context lacked clarity and seemed out of date. Women explored how the trade-off between zero risk of transmission and breastfeeding was highly situated in their experiences as post-migrant women and could not simply be defined by guidelines in the Canadian context. While women expressed the importance of protecting their infants from HIV-transmission, they also discussed having been

counselled outside of Canada that current data supports a low risk of transmission from breastfeeding a. As one woman said:

> I know they are saying that in the third world countries, there is that option of breastfeeding because of the lack of resources to bottle feed but…I tell you it's zero. Right now in my country it is zero for those who follow the guidelines for exclusively breastfeeding for 6 months, their children turn out negative.

Choice: The value of being offered a choice regarding infant feeding was highly regarded by participants. For those who had experienced choice, it was remembered as an empowering experience as women and mothers. As one participant who had experience with breastfeeding following her HIV diagnosis described: "Me personally I chose to breastfeed but not because of resources…I chose to breastfeed because I was given a choice…My son I chose to breastfeed for 6 months exclusively. I am told in Canada I will be in jail because it is not allowed but back home it's going on to breastfeed exclusively for 6 months or you choose not to."

The issue of choice, or lack thereof, came across as both an experience, but also a potential solution to address the perceived loss of autonomy. As an experience, the concept of choice related to how an infant would be fed. The opinions around what choice participants would make were not unanimous. Some would not breastfeed if given the option. As one participant stated, "I felt psychologically satisfied when I breastfed my baby but I believe infant formula is the way to go", while others had made the choice to breastfeed, as described above. It was not the notion of what was right or wrong that resonated with the participants, but instead an open discussion about the right to choose.

The ‘lack of choice’ was felt as unnecessarily inflexible, and the way clinicians counseled on infant feeding was often perceived as patriarchal. As the conversation emerged about choice, and women who had experienced more of a sense of choice shared what that had been like. One Canadian-born participant reflected,

> “I hate to say it about my own country but I sometimes feel that Canada is a little stuck up. And they’re just kind of like, it’s the way it is so just do it. And we’re not giving you an explanation. Just do it. And it’s not very nice”.

Ongoing grief and loss: The women in this focus group were particularly vocal about the ongoing grief, and lifelong burden that many mothers carry with them following the lost experience of breastfeeding their babies. The complexities of the grief that accompanies this loss were captured in women sharing personal, and culturally informed, beliefs about the benefits of breastfeeding. As one mother put it, “…because culturally breastfeeding…kids are more intelligent…we have those norms and if you don’t breastfeed and he does not do well in school”

The beliefs were also about the emotional benefits of breastfeeding. For one participant who had breastfed a child before her HIV diagnosis, she reflected on the differences between the two motherhood experiences:

> You know, I have two kids. One is 18 and breastfed and [I am more connected to that child]. Maybe it is my mindset that for me, in my culture, breastfeeding builds some bonds. Maybe in my mind I still have it that I never breastfed this baby…Anything she tries to do which goes another way, my mind says oh it’s because she never drank. Psychologically it’s something that is still with me.

The long-standing impact that mothers discussed relating to infant feeding were much more complex than intelligence and bonds. There were beliefs and practices that were shared by the participants that they felt would impact their children’s health, futures, and even relationships. Most of these beliefs had never been discussed with providers

even though they caused ongoing loss for mothers as their children grow. Several participants reported that the personal and cultural implications of formula feeding remain a concern well beyond the newborn period. This is not something discussed between women and their providers. Participants often associated this lack of discussion with a disregard by providers for traditional beliefs about the value of breastfeeding and breastmilk.

One participant spoke about cultural traditions being disregarded by Canadian health care providers, or not discussed. Another participant echoed her, 'So we don't kill and bury our beliefs. We go with them but we just don't talk about it." Finally, women's experiences of grief were characterized by the persistent connection that children have to the act of breastfeeding as they grow.

> My daughter when she sees me without my bra she want my breast and there are times when I go to bed and I'm just wearing a tank top, she is sleeping beside me, you see her put her hand on my breast. She want to play with it, she want it in her mouth.

The fascination children had with their mother's breasts resulted in a variety of reactions, including anger,

> "This breastmilk you don't want to put these kids in this situation. So I don't like it when [NAME] tried to play with my breast. I am so angry. Take your hands off. If you know what these breasts have done to your siblings you will not play with it. So it's like a different thing."

Strength and Resilience; On many occasions throughout the focus groups women voiced their perseverance despite challenges and a more positive lived experience narrative arose based on their obligation to bottle feed. One woman had a preference not to breastfeed regardless of her HIV status, an important narrative to consider when describing the experiences of infant feeding for mothers living with HIV. As she explained:

> I didn't want to breastfeed HIV or not. Even if I was negative I would not have breastfed. I just was not cool with it and I didn't want to do it and it actually became a benefit that I had HIV and couldn't do it so no one pushed it on me.

Even several of the concerns related to personal and cultural beliefs were countered in a supportive way. Women described their own narratives of intelligent, thriving young children. Participants supported one another and resisted the tendency to comply with the norm that breast is best:

> And I'm like well they said that breastfeeding makes you smart. Look at me and you. Our parents breastfed us and are we like scientists? Like there is no genius between me and you and we have been breastfed, you know? And so, if I got breastfed and I'm not a doctor or a scientist and you got breastfed and you are not that, if my daughter get breastfed, what are the chances she is going to be a genius?

The reactions of others and the stigma that mothers living with HIV have experienced was echoed amongst this group of mothers, as has been found in the past. Despite the many comments on the stigma that women had faced, there was also much commentary on the resilience of women, and reconciling the challenges of HIV stigma, particularly in the context of infant feeding.

> And it's very painful. It brings your self-esteem down. And I've fought a long time to be able to have self-esteem. So I don't want anybody to come in and destroy that. I don't know who you are. I don't know if I tell you if you're going to be comfortable with me or not. I don't care. I don't want to tell you. There's no need for you to know.

4.4.2 Novel solutions and changes to supports for women living with HIV.

The lived experiences that were shared emerged as practical solutions including education, support for all women facing a prescriptive breast is best environment, exploration of opportunities for choice, options of home based and alternative care, and using a holistic and comprehensive approach.

Education as a solution. Several participants discussed where opportunities for further education were needed. They expressed concerns about how little they actually knew about formula feeding. Several participants described a lack of education about how formula is an adequate nutritional substitute to breastmilk. This impeded their ability to accept this as an infant feeding alternative. Lack of education about the specifics of how to safely formula feed their infants was also discussed. For those participants who continued to have a desire to breastfeed, the lack of comprehensive education about the risk of HIV transmission via breastfeeding was an ongoing area in need of further education.

The needs for education were diverse, ranging from actual hands on bottle-feeding practice to learning about different formulas, intolerances, weight gain, volume control, and why it was a safe option but everyone identified a deficit in what they had been counselled on before initiating bottle-feeding.

One participant's comment really summarized what the entire group was saying:

> Give us some information. Help us here because we're just, because really all Canada is doing and it's all great and dandy that you're not allowed to like breastfeed your babies but like give us some information behind it. You're just told and you've just come from that culture and you're told you can't do it. And when you have any questions, they're like ok well we're wasting our time here. You want to go to jail? But they want answers. You have the right to answers. You deserve them.

Solutions were evident to participants such as spaces that education could easily be offered. As one mother described her experience as an in-patient after delivery, she explored how there had been no real education offered to her about how 'best' to formula feed her newborn:

> When you have a child they don't have how to bottle feed your child classes. You notice they [hospital] make announcements. Those [of us] that are there that cannot breastfeed our children were like…why are they announcing breastfeeding classes this time, breastfeeding classes at this time. Why not how to bottle-feed your child classes this time too? …Some people have never even held a bottle to a baby's mouth before.

Participants were clear that this education needed to be offered in a systematic way in advance of delivery. Women who were educated in advance on HIV and pregnancy issues were empowered, and earlier introduction to infant feeding resources allowed for an easier transition to the process of actually bottle-feeding, not just the idea of it:

> So then my doctor … educated me on getting pregnant, how to get pregnant, if and how the level of my viral load is, how safe I am, how not safe I am. She really educated me…Yes, I was very well informed. …. She said there is a group that will give you formula and will provide everything that you need to feed a child that you don't have to put a lot of stress on yourself

When discussing what resources were available regarding bottle-feeding, participants reported feeling that, they were minimal. Again, when discussing education and how it could be improved, multiple suggestions were described including language consideration, pictorial information, accessibility of online resources, and the need for resources that limit potential involuntary HIV disclosure. For one participant who was given a resource, the content on infant feeding was limited:

> …like a huge book that literally took me through the first 3 months. …It was literally you could refer to anything …the book was more focused on like breastfeeding but if you have to bottle feed here is a couple of little instructions and hope for the best, right. But then they had this whole chapter on breastfeeding. And I'm like I got 3 little points here.

A participant described why more education is so important:

> You guys you just tell us information. You don't show us any pictures. I find HIV in Canada is way different to the one in Africa...Those are the information we used to get back home. Here in Canada is zero tolerance for breastfeeding. Now we try to challenge this that if these are developed countries and developing countries that kids have been breastfed and nothing is happening, what is different? You need to tell us and convince us why. Why should we not do? Because we have seen people positive who are breastfeeding their kids and they are all grown up.

And participants had ideas on how to share this information:

> I'm just thinking in terms of like if there's a print resource – a how to guide that had a section on the bottle-feeding. Could you create a video though that was on YouTube or something so that if somebody who couldn't read or English wasn't the first language, an actual video.

Another participant highlighted the need to consider these types of novel educational resources as conventional opportunities, as support groups did not always meet the needs of all women:

> [ASO] classes and then you mention that some people are not comfortable going there. So how can it be made in such way that if I'm not comfortable going to [ASO] that I still get the information that they offer? Can it be in the hospital, can it be with the public health nurse?

Choice as a solution. Even in the absence of a definitive choice to breast or bottle-feed, participants discussed how choice and autonomy could be facilitated. With many women, accepting some aspects of their infant feeding was not a choice, they explored what choice meant to them and how it could address their needs. One of the potential choices that can be offered to women is breastmilk suppressants, some woman had experience using these in places they had given birth in Europe. As one participant said, "And another thing is about the pill you mentioned. I had some persons say no I wouldn't take it but is it something that can be offered to moms and they decide for themselves?"

Another choice raised was donor milk or alternatives to formula feeding. While the primary story was primarily a negative experience, others considered this as an option.

> You know you tell me not to give my milk but I should give milk from another woman? Yeah because the baby is premature and whatever. No matter the baby is premature. Sometimes the sensitivity.

Home based and alternative care as solutions: When many stories focused on obstetrical and HIV providers, several participants discussed other resources that had assisted them with their experience of bottle-feeding. Home visits from public health nurses and even child protective services in home visitor supports were mentioned as a source of education and support. These types of supports were seen as solutions that addressed concerned participants had such as involuntary disclosure by attending groups, discussions while in hospital due to privacy, time pressures during rushed clinic visits and the opportunity for rapport to develop over an ongoing relationship in a safe, private, and supportive environment to really open up about personal and often cultural issues around infant feeding.

> This public health nurse used to visit me because in [hospital] I told them that I got a lot to say but not in hospital. The nurse who used to see me at home, I was more open to her about everything. I was in my comfort zone. Because I told her I can't talk here because now I just want to concentrate on my baby to get out of whatever and I told my doctor there should be something that I as a positive mother tell you what I need to hear because some music we hear in HIV. It's all music and then message is not there.

Another participant shared her beneficial relations with child protection services:

> Like are they getting enough nutrition but nobody mentioned anything about that to me either. There's all these little, and I'll be honest as much as I hated CAS being brought in, they are the ones that helped me! They were the ones who were like its ok, don't worry about it, keep going.

A holistic and comprehensive approach to support as a solution. Each participants' needs were unique and they all shared aspects of their care and support that were lacking. All participants discussed the multiple ways more support was needed. Because needs were individualized, participants explored ways that everyone woman's needs would be met, the first being comprehensive educational needs.

Because many participants described needing more information, but also often feeling overwhelmed by a lot of information at once. Women also described the need for information to be given in a systematic way when multiple providers are involved. This led to the discussion of a Pregnancy Passport to ensure consistent and complete patient education is being given, and providers are informed of the patients' current health status and education needs. This was seen as a solution that would eliminate a lot of unnecessary repetition at the same time:

> It's really so repetitive to have public health, CAS (Children's Aid Society), the social worker, the midwife, the doctor, the nurse and a whole bunch of nurses at the hospital tell you the same thing over and over and you're just like I get it. I've been told this a thousand times like literally it was 6 months of being told the same thing over and over. I was going to kill myself. It was crazy. It's like enough. Yeah just more people reading over notes and just like oh ok she's already been told this 400 times.

Participants proposed other resources they felt would create an environment of more holistic and comprehensive care such as regular social work support, efforts at more continuity of care, and more follow up after delivery when needs often increase. As one participant shared:

> Because I was seeing a doctor, a midwife and a nurse but there was no social worker. They said you could have a problem, let us know and you could have a social worker. But it's hard to just say I have a problem. By the time I have a problem you have been with it for several months. But if I know this person and I need the social worker like the midwife and doctor I will trust this person and get

> to know this person, develop relationships. So if I have a problem it will be easier for me to share it. Is it possible to have a social worker on the team from the beginning? She is there and I know. If I have an issue it will be easier for me to raise it.

4.4.3 Research considerations in a Canadian context on this topic.

Given the focus on HIV and infant feeding in resource rich settings at a clinical and community level, a guided discussion was needed to explore community investment and priorities in developing a Program of Research. Research discussions were informed by the experiences and solutions that were discussed during the focus group in addition to research ideas that had been proposed by various stakeholders over the past five years. Research considerations emerged that are community priorities, basic science research, and feasibility issues.

Community research priorities. The strong focus on the long-term cultural implications of infant feeding practices was apparent throughout both focus groups. The participants learned from each other about how breastfeeding is viewed and valued throughout the world. Participants' shared personal and cultural beliefs about how bottle feeding could potentially impact their children indefinitely. This was seen as one area for research. It was felt that gaining this insight would allow for more cultural humility by providers when working with families who were facing bottle feeding: "But even we should even like do something in Canada as a whole about maybe start looking at other people's culture. We say we're so diverse and we're so blah blah. Well how come we don't know this and how come I don't know this?".

Basic science research: Participants were prompted to explore what we know about HIV and infant feeding, and risk of transmission, from basic science. The specific

question posed to them was if Canada needed its own basic science research agenda. Some women felt that the basic sciences literature on breastmilk from low resource contexts was adequate to answer the transmission risk question, “I think if it’s all based on the same thing then I don’t think it matters where it came from. Just so long as it has scientific proof to back it up”. Other women felt that the need for local research to verify the true transmission risk in our context was necessary. As one participant stated:

> I think it should be done here in Canada too so that we have like tangible evidence from the country itself from the people that are in it so we aren’t relying on information from out. Why can’t it be done here?

Feasibility: The feasibility aspects of a study on expressed breastmilk were also raised; the challenges to recruiting women for such a study, the psychological and ethical challenges of having women express milk for the purposes of research. While most participants expressed an interest and value of such a study, many considerations emerged that would need to be addressed before embarking on such a project. One participant cautioned whose opinions to get regarding feasibility, “I don’t plan to have another child, and it’s certainly different from a person who is thinking of getting pregnant”. A common concern among community-advocates was raised about the ethics of asking for milk samples in a setting where breastfeeding is discouraged, “Who really wants to, if you don’t have to, who wants to sit there milking their boobs for 6 months just so these people can have a sample?”

The focus groups allowed for high yield discussion on the community’s experience, and needs as it relates to infant feeding. These findings are important to understand how to move forward with the research and clinical discussions on this topic.

4.4.4 Key findings from our focus group communicated at the planning meeting

1. The experience of infant feeding is unique to all women. The role of each of the following varies from individual to individual, such as culture and social location, and the desire for choice and autonomy.

   What was also important was the gaps between a woman's experience, and their providers understanding of that experience. Although the provider-client relationship was not a major focus of the participants, as an actionable finding, the realization that a lot is left unsaid between woman with HIV and their care providers regarding infant feeding is an important consideration.

2. The concept of choice was a concern for many women – not necessarily the choice to formula or breast-feed but the many other aspects, which could be empowering for a woman. Respecting the situated freedom of new mothers living with HIV, i.e. supporting choices may be one of the single most important findings of this study. It is something that we know as clinicians, but may have lost sight of in this specific scenario. Choice was explored not only in the lived experiences but also in solutions and thus presents itself as an important consideration for the future

3. The literature thus far has acknowledged the acute grief, feelings of loss, and sadness women feel when they are unable to breastfeed their infants due to an inherent sense that it is an intrinsic part of the mothering experience. What has not been as well reported are the ongoing struggles that mothers living with HIV face regarding infant feeding practices. Understanding these experiences longitudinally for mother and infant is an important consideration as we develop ongoing support for families affected by HIV.

4. Solutions were almost entirely linked to the lived experience with a focus on choice, individuality, holism, and of priority to the participants' education. Participants in this study appeared to readily provide solutions that would address their needs, within their situated freedoms, that are actionable and are due consideration. When asked about solutions, ideas were plentiful signaling the need for ongoing community-engagement in developing strategies to better support women living with HIV in settings where bottle-feeding is recommended.
5. With respect to research questions, the greatest priority was for research pertaining to cultural beliefs to better inform practice that respects those beliefs. When directed, participants did open up to a discussion about basic science research but presented many challenges in terms of feasibility of such a project in the Canadian-context, where women are recommended exclusively to bottle feed.

4.4.5 Limitations of the focus group approach

The qualitative methodology used, the sample of 12 women, and the potential selection bias limit the generalizability of the findings of this study. However, situated within the broader body of literature on this topic, the study offers a substantial contribution about moving forward to address issues surrounding HIV and infant feeding in resource rich settings. The study is limited by the absence of certain communities of women living with HIV in Canada, particularly indigenous women, and this is due further consideration as research and programming plans are developed. Recruitment through community-based agencies may have biased the sample to include women who are more actively engaged in their HIV community; however, participants did identify disclosure and willingness to attend community agencies as a possible issue when discussing education.

Participants were all from Toronto, which may bias the results in terms of transferability to other parts of Canada. Finally, one limitation of this manuscript is that several incidental findings were not reported as they fell outside the scope of the project. This is an inherent challenge with qualitative research and the researchers intend to consider publication of additional findings that are of clinical significance.

4.5 The Planning Meeting

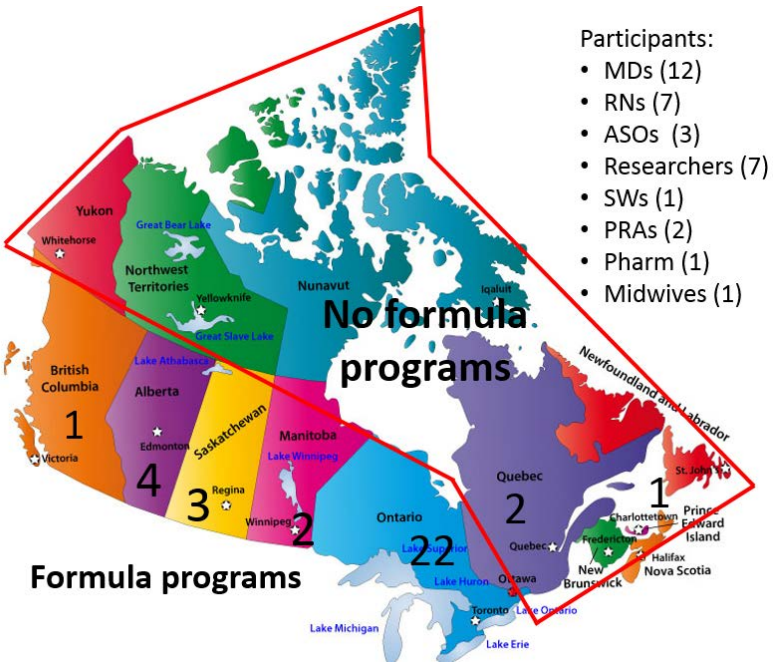
The two-day planning meeting involved an invitation to clinicians, service providers, and researchers with an interest in this area. Part of this invitation also required voting to select which priority topics should be focused on during the World Cafe. (See Appendix A for a full list of attendees/ contributors).

The meeting was structured with both an open-ended discussion format to encourage dialogue and brainstorming, and individual presentations from different Canadian sites and organizations. SK and VLK guided the discussions with key questions. The remainder of this chapter will focus on the proceedings that took place Jan 21-22nd, 2017 at The Sick Kids Research Institute and includes recommendations and next steps for the development of the now named Canadian Infant Feeding in HIV Network (CIFHN). The complete agenda for the meeting can be found in Appendix B.

4.5.1 Participants and Presentations

Participants were from all clinical sites across the country (Figure 1). In total, there were 34 participants. See appendix for attendees list.

Figure 6: Distribution of participants, and their respective professions



MD – Medical Doctors, RNs – Registered Nurses, ASOs – AIDS Service Organizations, SWs – Social workers, PRAs – Peer Research Associates, Pharm – Pharmacists

In an effort to elucidate the current infant feeding issues and practice across Canada, maternal/child HIV clinical sites were asked to present at the meeting. Each site was asked to describe their infant feeding processes, strategies, resources, and challenges.

Presenting Sites included (Summary data presented in Table 1):

1. Oaktree Clinic (Vancouver, BC)
2. Stollery Children's Hospital [Edmonton, AB]
3. Winnipeg Regional Health Authority [Winnipeg, MB]
4. Regina Qu'Appelle Health, [Reginal, SK)
5. The Children's Hospital of Eastern Ontario [Ottawa, ON]
6. The Hospital for Sick Children [Toronto, ON]
7. McMaster Special Immunology Services [Hamilton, ON]
8. Centre Hospitalier Universitaire Saint-Justine [Montreal, QC]
9. Memorial University [St John's, NFLD]

The combined data suggests that approximately 180 pregnancies occur per year in women living with HIV. The regions with the highest numbers are Toronto, Edmonton and Vancouver.

The site presentations on Day 1 elicited discussion amongst attendees on the variability in practice around infant feeding. Although the consensus was that providers were all recommending formula feeding, and if possible were providing information on how to access formula, the depth of the counselling varied. Generally, physicians would discuss the exclusive formula feeding recommendation, and allied health care would provide further teaching on practical aspects of formula feeding, though this varied in depth.

Major variability was seen in the following aspects

1) The majority (6 of 9) of the clinics offer a shared care model where HIV care of adults and children are done within the same clinic, whereas other centers offer separate adult and pediatric care. This may contribute to the overlap in messaging that may occur, or the diffusion of responsibility on the depth of counselling on infant feeding, and breast care
2) Some centers provide mothers the opportunity to make formula to ensure comfort level with this. No sites identified dedicated teaching on how to sterilize bottles, or challenges that may occur with formula feeding such as choice of formula, bottle or nipple.
3) The accessibility of formula varied (the 3 territories, and 5 provinces – Newfoundland, New Brunswick, Prince Edward Island, Nova Scotia, and Quebec do not have formal

formula programs). Providers often struggle to find a sustained formula supply through informal means.

4) Breastmilk suppression using Dopamine agonist Cabergoline that is commonly used in Europe has only been used at two sites, Vancouver and Montreal.
5) Variability was described with respect to the populations served, and the potential that this may impact the feeding preferences of the different populations.
6) Variability in the resources available in each clinic (e.g. dedicated allied health care – dietician, OT, PT, Pharmacy, Social Work)

The site presentations were followed by a variety of presentations from different stakeholders.

1) The AIDS Service Organization, which provides support for moms and babies and is the designated formula provider for the province of Ontario, described their programming. They outlined their programs for pregnant women and new moms (pre-natal support group, welcome home baby package delivered by a family support coordinator at home or in hospital, new mom's group, toddler group, parent club, counselling). The prenatal support group is a 2-day session with presentations from multiple care providers to prepare mom for labour and delivery, confidentiality and infant feeding. The formula program is province wide, and uses pharmacies for local dispensing. They also shared their infant feeding resources: Is Formula good for My Baby (developed by the Teresa Group and Community AIDS Treatment Information Exchange (CATIE),) as well as a breast care leaflet. There were a few webinars hosted by Interdisciplinary HIV Pregnancy Research Group, and CATIE including: Planning pregnancies, Infant Feeding; A complicated dilemma, and Life with Baby.

2) The Primary Investigator of The HIV Mothering Study also presented key findings from observational, mixed-methods, community-based study which enrolled 77 women from March 2011 to December 2012. In-depth interviews with 37 women in their 3rd trimester, as well as data from questionnaires on loneliness, perceived social support, depression, HIV stigma. There were some very compelling quotes from the participants on the challenges of not being able to breastfeed, fear of involuntary disclosure, grief/loss and feelings of failing as a mother. The degree of planning required for women to be able to explain why they are not breastfeeding and the feelings of dishonesty when using excuses justifying why they are not breastfeeding to family. The other key finding was how women moved forward and reclaimed agency, wanting the best for their child, the faith in formula as a good alternative to breastmilk. Also feelings of resistance, having healthy formula fed children, and bonding with the baby through other means. The Mothering Study provided important recommendations on how women living with HIV can be supported by their providers in coming to terms with other infant feeding choices, and recognize the ways culture, gender, race, and stigma affect infant feeding.
3) An HIV lawyer and policy analyst who has been involved in the criminalization concern around HIV and infant feeding. She outlined the potential for legal intervention or child protection in the context of HIV transmission through feeding. The discussion centered around how Criminal Law, Child Protection Law, and Human Rights Law might be relevant in infant feeding and HIV. The Hamilton Mother case is the precedent; this mother pled guilty to failure to provide the necessities of life. The circumstances of breastfeeding after birth are where Criminal Law applies (as a fetus

has no right) if the transmission occurred from breastfeeding – which is unclear in that case. However, the precedent of applying the Criminal Code remains unclear because in this case, the defendant pled guilty and so no ruling was required. Child protection law is provincially determined; examples of when a referral to child protection is suggested include; physical harm, inadequately cared for, medical treatment to cure, prevent, alleviate physical harm or suffering and is not provided it. Breastfeeding or not providing antiretrovirals to prevent transmission could fall within this context. The obligation on CAS is to investigate, and then protect that child as needed. In the Hamilton Mother case, the child was infected with HIV and the judge ruled that the child be removed from the home; but it was not specifically because of the breastfeeding; but because of the lack of disclosure, weak parenting skills, concerned of ability to provide care for herself and the child. Legal intervention due to breastfeeding alone is unlikely to occur; it is more of an issue if there are other concerns about the health of the child. There is variability among care providers about feeling the need to refer to child protection if a woman may breastfeed. Human rights include reproductive freedom, and to have appropriate care to make these decisions free of discrimination, coercion and violence. Woman have the right to information, services, confidentiality, privacy, non-discrimination.

4) We also heard from one of the authors of a systematic review to determine the risk of perinatal transmission through breastmilk among women with an undetectable plasma viral load on ART. Ten studies were included in the review, of which five were combined in a meta-analysis. The risk of transmission was 2.9% (95% CI 2.2-3.8) at one month, 3.6% (95% CI 2.7-4.0) at three months, 4.0% (95% CI 3.1-5.2%) at six

months, and 5.1% (95% CI 4.0-6.5%) at 12 months. Transmissions occurring at 1 month were thought to be related to transmission *in utero* and less likely breastfeeding. Therefore, by subtracting the 2.9% risk this would bring the risk at 3 months down to 0.7%, at 6 months 1.1%, and at 12 months 2.2%.

5) We also heard from a Survey conducted on the Knowledge, Attitudes and Practices of Health care providers related to infant feeding. The survey was delivered to 3 groups of providers; National HIV care providers (HIVP), National Infectious Diseases/Medical Microbiologists (ID/MM), and Toronto based General Pediatricians (GP). The survey was delivered via email using network email lists, with interval reminders. In total, 152 responses were received (HIVP = 104, ID/MM=21, and GP=27). Knowledge questions pertained to risk of transmission by breastfeeding, feeding strategies, formula availability, and knowledge of Canadian and WHO recommendations. Attitude questions pertained to criminalization, child protection and public health involvement, government funding of formula, barriers to accessing formula, factors that cause stigma, and whether HIV is considered a contraindication to breastfeeding. Practice questions pertained to experience with calling child protection, and management scenarios. The knowledge scores were higher among HIVP, but gaps remained among all three groups. Attitudes were similar across most groups on when involving child protection only in higher risk scenarios. The level of transmission risk required to recommend breastfeeding in Canada was essentially 0-1% risk, and overrides patient preferences.
6) A basic scientist at Toronto General Hospital presented some key facts about breastmilk, in terms of the immunological benefits in breastmilk and different forms of

HIV present in it including cell-associated virus (mammary epithelial cells, latent CD-4 T cells, activated CD-4 T cells, macrophages), and cell free virus. Whether HIV or antiretroviral therapy affects the immune benefits of breastmilk is not clearly known, but some data suggests lower anti-oxidant levels, lower B vitamins, and different bacterial compositions. Latent CD-4 T cells are not affected by antiretroviral treatment. Macrophages express DC-SIGN, which may help transport HIV to the baby's gut, and increase cell-to-cell infection of infant T-cells. The other key aspect is that undetectable plasma viral load, does not mean an undetectable breastmilk viral load due to local mammary gland inflammation. The other reality that some antiretrovirals are able to reach the breastmilk at varying concentrations, which may act to induce antiviral resistance in infants who receive low level of exposure to antiretrovirals, in addition to the potential for antiretroviral toxicity. We also heard from a staff member at the National Microbiology Lab about possible cell based and plasma based assays that are available for research purposes if future breastmilk study was to be pursued.

4.5.2 Breakout Discussion: World Café

Prior to the meeting participants were asked to vote on priority topics related to infant feeding for the breakout discussion. The topics were selected by content experts, with suggestion from the participant group. A second opportunity to vote was given after the first day of presentations. In total 25 of 38 participants voted on the topics. The topics selected for discussion were:

A) **Advocacy for national formula access**: Currently formula programs are provincially organized, and vary in their organization and development. If the National recommendation for women living with HIV is exclusive formula feeding, we should ensure access to formula for everyone.

B) **Basic science research on breastmilk in the HIV context in Canada**: We do not know the quantifiable risk of HIV transmission through breastfeeding in Canada.

C) **Consensus clinical management of infant and mom, if a woman chooses to breastfeed**: A situation may arise (albeit rarely) in which a woman living with HIV may breastfeed. How could this be handled in terms of clinical management of both the mother and baby in the current clinical context?

D) **Cultural considerations** - approach in different populations in Canada: Women living with HIV in Canada are a diverse population and may experience infant feeding (or not breastfeeding) in a myriad of ways.

E) **What is required to decide if breastfeeding is an option in Canada:** What data, research, study, consensus, community engagement is needed in order for there to be a recommendation on breastfeeding?

The format for the breakout discussion was a World Café, with a facilitator at each core station. This format was chosen for the breakout discussion as it allows participants to rotate individually through each station for twenty minutes to build upon the discussion. This strategy allowed for cross-pollination and progression of ideas, evokes the collective intelligence of the group, and fosters equitable participation. The goal of the process was

to have a productive discussion on infant feeding and HIV, with a focus on the priority topics identified, to build toward consensus, and identify actionable deliverables to furthering the understanding/management of infant feeding and HIV in a Canadian context.

Notes were transcribed in the sessions by a note taker (see attached instructions in appendix), and a facilitator led the group through the discussion with guiding questions. (See Appendix)

A) Advocacy for national formula access:

The questions in this group focused on models to ensure national formula access that is sustainable, research to understand the health benefit to individual and cost to system through formula programs, and case examples from other contexts (provinces or countries) on how to implement. Given that, one transmission of HIV is extremely costly (hundreds of thousands of dollars in antiretroviral costs alone over a lifetime). The discussion centered on the different programming available per province. A needs assessment to determine the differences in needs of different provinces (e.g. if clean water is not available in some regions and therefore ready to use formula is needed), the most sustainable method to have formula reach clients in a confidential and reliable way. A challenge raised was the development of infrastructure for an issue that perhaps affects a small minority, as is the case in the Maritime Provinces, and the Territories. The idea of local pharmacy providers managed by a central (provincial or national) agency as is the case in Ontario. Alternatively, coupons or vouchers for formula are easy to implement, but harder to regulate and control. Using HIV clinical settings as formula dispensaries also would likely become less regulated, and potentially more cumbersome for patients

who travel distances to access HIV care, or who are followed less closely or less engaged in care.

Priorities and Deliverables identified related to advocacy for national formula access:

- A needs assessment to determine the regional needs (i.e.: areas without formula or water readily accessible, the actual numbers of deliveries occurring per year)
- Processes that could work on a regional, provincial or national level to implement programming (considering existing programs which function through clinics, pharmacies etc.)
- A cost benefit analysis on reduction or transmissions, optimization of nutrition and infant outcomes was thought to be a useful tool, which could sway policy makers on the need to ensure access to formula for all women living with HIV with infants in Canada.
- Qualitative research on the benefits families receive by having formula provided compared to regions where not as readily accessible
- Discussion with policy makers (Federal Ministers of Health, and Aboriginal Affairs) on the need and most appropriate next step

B) Basic Science research on breastmilk in the HIV context in Canada:

The discussion initially was very adamant for further basic science research to quantify the risk of transmission from breastmilk in a Canadian context, but very quickly faded once the ethical and practical aspects arose it became clear it was not feasible. The ethics around asking women to express breastmilk for research purposes only, and to recommend formula feeding for her infant. Similarly, the emotional trauma of having

breastmilk available but being unable to provide it to one's own child. Supports would need to be provided to help women cope with the cognitive dissonance with not being able to breastfeed the infant while pumping for a study.

If a woman was allowed to breastfeed her child in the study, the concerns remain about the known reduction in compliance to antiretrovirals, which occurs post-partum due to the competing demands. The feasibility questions related to what duration could this be studied over (how long would a woman be able or be expected to pump for?). In addition, how much information this would add above what we have from breastmilk study in the low-middle income countries. The numbers required to determine the actual risk are unlikely possible to be obtained in Canada alone. However, Canada could lead this type of research given the resources available, and it could be highly useful information for all developed regions.

Is milk testing useful in an individual patient situation to provide further risk assessment data? However, by the time the milk test results are returned transmission to the infant may have already occurred. Social breastfeeding is another phenomenon discussed where in specific social situations a women living with HIV will breastfeed her child. The risk of this scenario is also not well understood.

Doing this type of study in a context similar to ours where breastfeeding is actually occurring, such as urban South Africa may be of more utility and higher yield.

Milk testing to understand drug levels in milk will be very challenging to quantify given the pharmacokinetic and pharmacodynamic changes, and timing of medication administration to pumping.

The reality is this type of work needs to be community based, with a community co-investigator. If there is a clear want and need from the community for this type of research, then this is potentially feasible. Timing of when to involve the community was also discussed such as, after a protocol is developed and the scientific community is clear on what they want to look for (immune factors, virus, drug levels, inflammatory factors, ways to make breastmilk safe) versus early in protocol development. The compensation needs to be in proportion to the task being asked of the community, there is a high risk for this to be perceived as coercive, especially among new immigrants. There may be cultural or religious issues that may need to be considered.

Priorities and Deliverables identified related to basic science research:

- Qualitative research and Community engagement on the questions and what research is feasible
- A scoping review to generate a list of key aspects of milk components, viral aspects, immune and inflammatory components, nutritional aspects, medication information, and viral inactivation methods from the existing literature, considering HTLV and HIV viral literature
- Collaborate with other HIV/Basic Science researchers based on the review of the literature from other high resource contexts to see if a protocol could be developed to obtain the numbers needed to make significant progress on understanding the risk in the high resource context

C) Consensus clinical management of infant and mom, if a woman chooses to breastfeed:

Situations that may arise where a woman may breastfeed in Canada that were discussed included: isolated remote communities without formula access, a woman who delivers in Canada but is planning to move back to country of origin with the infant where formula will not be available, philosophical reasons why a woman is adamant about wanting to breastfeed, a woman who is in a risk domestic situation where she is unable to formula feed due to family pressures and the late-diagnosis mom already breastfeeding and infant already infected. The challenge of a mother making a long-term decision for her child was a struggle for many.

In such situations providers discussed that the frequency of monitoring and prophylaxis offered to the infant is based solely on expert opinion, as there are no clear-cut guidelines for high resource settings with access to ART and testing. Providers varied between preferences of single drug versus triple drug prophylaxis to the infant. Hesitations around the ongoing exposure to antiretrovirals to infants in the long term being unknown.

Concerns about counselling needing to be in depth, with all the relevant family members who are influencing medical and infant feeding decisions. The importance for this counselling to be done in a safe space for discussion is critical due to the fear of potential criminalization and child protection involvement related to breastfeeding in the HIV context. A significant degree of counselling would need to be provided to these women on the risks of transmission, breast care, management of gastrointestinal or oral mucosal illness in the child, antiretroviral compliance, and frequency of testing. Another

challenge is the need for specialist involvement (pediatric or adult infectious diseases) especially in remote settings. In addition, the challenges of trying to ensure all the necessary resources are in place to support this close degree of management (testing, drugs). The ability to do directly observed therapy would be a more invasive but reliable option to ensure antiretroviral compliance in mom and baby while breastfeeding. The question of the utility of testing breastmilk as a counselling or diagnostic tool in this context was also discussed.

A discussion was also had about the potential for misinformation to spread in the community if a woman was breastfeeding, and a discussion on how to try to mitigate that risk. The medico legal implications for providers if a woman is not adequately counselled and a transmission occurs. This should be vetted through the Canadian Medical Protection Agency.

Deliverables and action items for Consensus Clinical Management:

- Development of a working draft of a counselling guideline to ensure consistency of care using information provided by each site – for further iterative revisions by CIFHN and community
- Development of a working draft of a clinical management guideline after review of existing guidelines and protocols available – for further iterative revisions by the CIFHN
- Consultation with the Canadian Medical Protection Agency to understand the medico legal and liability considerations for providers based on the guidelines being drafted

D) Cultural considerations:

The discussion around the importance of breastfeeding in certain cultures was discussed, and the need for providers to have a better understanding of this. For example, in Caribbean cultures the desire to breastfeed is not as much of a concern, whereas there is significant variability across African and Aboriginal cultures. Different cultural considerations include not only ethnicity, religion, region, sex-trade work culture, substance use, homeless and incarcerated populations each share their own cultural dynamics, which may or may not influence infant feeding decisions. It was felt that some populations have been over-researched, whereas others have not been fully explored. To some extent an individual's family, partner involvement, and degree of association with their cultural community in Canada may also have a major influence on the strength of the desire to breastfeed. In addition, the likelihood of travel back to their country of origin was another consideration that affects the desire to breastfeed and the fear of involuntary disclosure if they are not breastfeeding. In some cultures, exposing the breast in public is a concern, and may reduce the desire to breastfeed. Relatedly, religion is a driver to want to breastfeed as an obligation of the faith. However, it was also recognized that each individual woman was different in her personal beliefs and family circumstances. Another challenge is language barriers for communicating important aspects about feeding such as risk of transmission, challenges a woman is facing. Sometimes this translation is done through a family member, which can be a male who may not be able to communicate breastfeeding issues or concerns. Family members may also not be translating accurately due to their own preferences and biases.

The “breast is best” culture and messaging in Canada acts as a major challenge for women to worsen the feelings of grief and loss from being unable to breastfeed. Other systemic issues, which are more relevant in certain marginalized populations (incarcerated, homeless, sex trade work) or remote communities is access to formula. In these situations, healthcare providers need to be flexible and work within the constraints of the populations. Peer supports may be an important asset in this context to be able to understand the cultural differences and nuances that providers may not catch.

Deliverables and action items for cultural considerations

- Providers need to understand the cultural significance of breastfeeding in their patient populations, to ensure the conversations are sensitive and targeted.
- Providers need to feel comfortable using a translator and have appropriate resources to do so
- Specific approaches may need to be taken in specific high risk populations with unique considerations (e.g. homelessness, substance abuse)

E) What is required to decide if breastfeeding is an option in Canada?

Providers were not comfortable recommending breastfeeding, but the demand at a community level was recognized. Many providers believed when the community is adequately informed, they often prefer not to breastfeed. Discussion focused on the need for effective counselling by providers prior to delivery, the messaging of breast is best poses an ongoing challenge. Providers felt that visits are often already long with a lot of content discussed, this can make it challenging to cover too many topics in fear that the content will not all be retained. Having a checklist would be helpful to ensure all aspects

of counselling are covered between the multiple care providers. If breastfeeding was to be recommended, a clear understanding of the risk was necessary (ideally being able to quantify this risk in the Canadian context), education among all stakeholders (mom, social work, child protection) as to the science of transmission. Providers felt the focus should be on ensuring formula access to all infants.

The key deliverables and action items for what is required to recommend breast-feeding in Canada

- Clear counselling guideline or checklist
- Knowledge Translation for both providers, patients and other stakeholders (Child Protection services) would be helpful

4.6 Outcomes for the planning meeting

The two-day meeting was a success in that it allowed a national discussion on infant feeding to occur with many of the relevant stakeholders. It allowed for sharing of knowledge, resources and commonly identified challenges amongst care providers. It brought to light plainly the differences in needs of the various populations being served by HIV providers across Canada, making it clear that a multi-pronged approach was needed to address this issue holistically in Canada.

A network entitled The Canadian Infant Feeding in HIV Network was developed with multiple working groups within it.

The action items were divided as follows:

A) <u>Community Engagement:</u>

1) Further funding is needed to have meaningful community involvement in the development, writing and review of guidelines and KT resources

2) A national community advisory board (CAB), or regional CABs with multicultural and multi-community engagement will be essential in informing this work

B) <u>Advocacy for national formula access</u>

1) Formalized document at policy level – national mandate
    i. Speak to MOH and minister of immigration privately prior to public level endorsement for private conversation on the need for equitable access on a National level, especially areas that wouldn't meet AFASS Criteria
    ii. Citizenship Immigration Canada – need a commitment that Interim Federal Health coverage would cover formula for new refugees in this context
2) A national statement on the need for universal access in Canada should be drafted, authored by the Canadian Pediatric HIV and AIDS Research Group (CPARG)
    i. With endorsement from other stakeholders
        1. National agencies which do advocacy – Canadian AIDS Treatment Information Exchange (CATIE), Public Health Agency of Canada (PHAC), Interagency Coalition on AIDS and Development (ICAD), Canadian HIV/AIDS Black, African and Caribbean Network (CHABAC) (community involvement)
        2. Society of Obstetricians and Gynecologist of Canada (SOGC)-ID committee
        3. Canadian Association of Nurses in HIV/AIDS Care (CANAC)
        4. Canadian HIV/AIDS Pharmacists Network (CHAP)
        5. Association Medical Microbiologists and Infectious Diseases (AMMI)

C) <u>Cultural considerations - approach in different populations in Canada</u>

1) Consider a recommendation to have an Infant feeding champion on all teams – with cultural sensitivity training, and create safe spaces for discussions

2) Qualitative work to understand what breastfeeding and breastmilk means to me in different cultures

3) KT Resources that are simple enough to accommodate any population
    i. CATIE to develop pictorially based culturally sensitive documents w/ community consultation (Teresa Group working on this) (ie: Breast Care leaflet, formula preparation, bottle cleaning, how to formula feed your baby)

4) KT resources working group with community engagement

D) <u>Consensus clinical management of infant and mom, if a woman chooses to breastfeed</u>

1) Begin conversations with other relevant high resource bodies (BHIVA, DHHS) that have experience, began writing guidelines in this context
2) Consensus on **counselling guideline** is able to be made now, and is needed
    1) Counselling Checklist – what every family should know about infant feeding
    2) B) If breastfeeding scenario – how to manage to be authored by CPARG and published in a Canadian ID/HIV journal
    3) This statement could include the consensus: formula access priority, not a criminal action (need to have a statement from CMPA, Canadian HIV Legal network, CPARG, SOGC ID)
3) Counselling tools are needed (see KT above)
    1) Brief 1 page – basic science KT for patients and families
4) Education of Health Care providers
    1) Consider ensuring this is a learning objective with the Royal college for Infectious Diseases training

4.7 Challenges moving forward

1. Community engagement: This meeting centered mainly around provider input, although there were focus groups conducted prior to and after the meeting. The reality is for this work to be meaningful and to have the buy-in of the community there needs to be clear partnership in moving the clinical, KT and research agenda forward. Part of the challenge is ensuring representation from the multiple communities affected by HIV nationally.
2. Securing funding: Ongoing work in this area will require funding, especially to having meaningful community involvement and input. The feasibility of accessing financial and human resources to advance this KT and research work is an issue. With the diversity of ideas presented during the meeting, novel funding opportunities may need to be considered to support various activities related to CIFHN.

4.8 Conclusions

This Community focus groups and the provider planning meeting were successful in identifying priorities and opportunities related to advancing the needs related to infant feeding in HIV in Canada. Although the discussion started with input from the community based research, which has triggered the need for this discussion, it became more evident that this work needs to be fully community informed in its next steps. It is necessary for all providers to work together with community to come to consensus on the counselling and management related to infant feeding to optimize outcomes for families affected by HIV. It is important to recognize the unique considerations based on region, culture, and resources available. We are hopeful that CIFHN can act as a network to build upon and advance this work.

4.9 Planning Meeting Acknowledgements

We thank the Canadian Institutes of Health (CIHR) for funding this two-day meeting that has facilitated new and exciting national collaborations. We acknowledge the highly competitive nature of these funding competitions and thank the CIHR for appreciating the need to advance Canada's research landscape related to the health and well-being of women living with HIV, and their children and families affected by HIV, specifically as it pertains to infant feeding.

We also wish to thank The SickKids Research Institute in Toronto, Ontario for allowing us to host our national meeting within their institution and the CIHR Canadian HIV Trials Network for their support in planning for the meeting.

In addition, we would like to thank the service providers whose work on the front lines of the HIV epidemic cannot be forgotten, particularly the role they plan in the lives of families

affected by HIV. Thank you to the researchers, clinicians, and experts who played a key role in guiding the discussion. Finally, we wish to acknowledge all women living with HIV in Canada, but particularly the members of our community advisory board and our peer research assistants (M.K. & G.K.). Thank you for selflessly sharing your knowledge.

The following people are acknowledged for participation through the planning grant process:

- Logan Kennedy
- Ari Bitnun
- Stanley Read
- Mark Yudin
- Mona Loutfy

4.10 Appendices

Table 8: Planning Meeting Attendees List

Name	Province	Role	Details
Alison Symington	Ontario	HIV Lawyer	Canadian HIV/AIDS Legal Network, Toronto
Allyson Ion	Ontario	Social Work Researcher	School of Social Work, McMaster University
Ari Bitnun	Ontario	Pediatric ID	The Hospital for Sick Children, Toronto
Cheryl Arneson	Ontario	Pediatric Research Coordinator	The Hospital for Sick Children, Toronto
Dorothy Odhiambo	Ontario	Family Support Coordinator - ASO	Teresa Group, Toronto
Faisal Kordy	Ontario	Pediatric ID	The Hospital for Sick Children, Toronto
Fiona Smaill	Ontario	Adult ID	McMaster University
Georgina MacDougall	Ontario	Pediatric Clinic RN	The Hospital for Sick Children, Toronto
Gladys Kwaramba	Ontario	Peer Research Assistant	The Hospital for Sick Children, Toronto
Jason Brophy	Ontario	Pediatric ID	Children's Hospital of Eastern Ontario, Ottawa
Jay MacGillivray	Ontario	Midwife	St. Michael's Hospital
Josephine Etowa	Ontario	Nurse Researcher	University of Ottawa
Kellie Murphy	Ontario	Obstetrician	Mount Sinai Hospital
Lehana Thabane	Ontario	Statistician	McMaster University
Lena Serghides	Ontario	Scientist	Toronto General Research Institute

Logan Kennedy	Ontario	Nurse Researcher	Women's College Research Institute
Mark Yudin	Ontario	Obstetrician/Gynecologist	St. Michael's Hospital, Toronto
Medys Kihembo	Ontario	Peer Research Assistant	St. Michael's Hospital, Toronto
Muna Aden	Ontario	Research Coordinator	Women's College Research Institute
Nicci Stein	Ontario	Executive Director - ASO	Teresa Group, Toronto
Robyn Salter	Ontario	Social Work	The Hospital for Sick Children, Toronto
Saara Greene	Ontario	Social Work Researcher/Educator	School of Social Work, McMaster University
Sandra Seigel	Ontario	Pediatrics	McMaster University
Sharon Walmsley	Ontario	Adult ID, Researcher	University Health Network
Stanley Read	Ontario	Pediatric ID	The Hospital for Sick Children, Toronto
Fatima Kakkar	Québec	Pediatric ID	
Isabelle Boucoiran	Québec	Obstetrician	CHU Sainte-Justine, Montréal
Ariane Alimenti	British Columbia	Pediatric ID	Oak Tree Clinic, BC Women's Hospital and Health Centre of BC
Chasity Vermette	Saskatchewan	Regional HIV Coordinator	Access Place, Prince Albert
Debbie Rodger	Saskatchewan	Nurse Consultant/Clinic Nurse	Regina Qu'Appelle Health Region, Regina

Nicole Kimball	Saskatchewan	Clinic Nurse	Positive Living Program, Royal University Hospital, Saskatoon, SK
Dr. Debbie Kelly	Newfoundland	Associate Professor, researcher and clinic pharmacist	Memorial University and Eastern Health, St John's
Maria Stadnyk	Alberta	Clinic Nurse & Prenatal HIV Nurse Designate	Northern Alberta Program: Royal Alexandra Hospital satellite site
Sara Berger	Alberta	Clinic Nurse	Northern Alberta HIV Program
Jared Bullard	Manitoba	Pediatric Infectious Diseases & Medical Microbiology	University of Manitoba
Paul Sandstrom	Manitoba	Research, Lab Support for Patient Diagnosis and Monitoring	Public Health Agency of Canada, Winnipeg

Table 9: Planning Meeting Agenda

Time	Thursday Jan 21	Friday Jan 22
8:30 -9am	Breakfast	Breakfast
9-9:30am	Introductions & Check in	
9:30 – 10:15	-Community engagement -Focus Group results	
10:15 – 10:30	Break	
10:30 – 12:15	Clinical Site Presentations * -BC, Alberta, Manitoba -Sask, ON (Hamilton, TO, Ottawa) -QB, East Coast	Breakout sessions** Rotations through the top 4 priorities with facilitated discussion Rotation 1 and 2
12:15 – 1:15	Lunch	
1:15 – 1:45	-Teresa Group	
1:45 – 2:30	-Mothering study -Legal aspects	
2:30 – 3:45	Break	
3:00 – 3:40	-Systematic review results -HCW Survey results	
4:15 – 5:00	Basic Science • Review resources/assays for breastmilk analysis at NML	
Closing	Consensus Priority Survey send out and Dinner at Nandos (832 Bay Street at 7:30)	

Table 10: Summary of Resources for Infant Feeding at Presenting Sites

Site and Cities	Demographic	Population size	Clinical Team Members	Feeding Information	Formula and Breast Care	Other/ Needs
British Columbia 26births/year Family care model Oak Tree Clinic in Vancouver (remote pregnancy care provided by Nurse clinician by phone)	**By Ethnicity /race** -30% aboriginal -22% ACB -11% South Asian **By HIV Acquisition:** -30% IDU -70% heterosexual	**# HIV positive kids** -32 infected -28 transitioned -20 died or moved **# HEUs, followed until:** >500 since 1994, followed until 18 months, efforts to follow until age 5 and beyond	- MDs: OB, MED, PED - RN clinician: pregnant women only - NP - RD - SW - Pharmacist - P/T Counselor (addiction, trauma, safety groups, art therapy) - P/T Psychiatrist (repro. mental health available) - P/T Lab technologist - Research team	- OB - RD: teaches bottle prep, sterilization - Peds at 32-36 weeks - Regulated donor milk program in BC (HEUs are low priority, cost for processing, donor milk only in hospital)	Provincial program provides 1 year of formula (since 2007) **Cabergoline** (lactation suppressant, 1 dose), since mid-2015, variable uptake	-Data shows poor adherence to ART occurring 4-8 months postpartum -further study on Cabergoline
Alberta 40 births/ year	**By Ethnicity /race** -40% aboriginal	**# HIV positive kids**	- Adult ID clinical team (RD, RN, - Psychologist,	- standardize - order sheets for vertical transmission	- Program pays for formula for 1st year	- ~$1500 cost per infant = $31,500 /year (@21 births/year in

	-42% endemic country -15% Caucasian **By HIV Acquisition** (South Alberta only) -IDU 26% -heterosexual 40.4% -other 1.5%	-not reported **# HEUs, followed until:** -Followed until 2 years (20/year)	- Pharm - SW on call work) at q week/month - OB q 1-3month - If pregnant see peds ID, followed after baby born - weekly phone calls, home visits to monitor ART compliance and formula	protocol since 2000 - HIV point of care testing at 12 hospitals	(previously donated) - Specialty formula can also be funded - breastmilk banks (limited)	Northern Alberta only) - Cabergoline implementation
Manitoba 16 births/year Mostly Winnipeg with rural/ northern access as well	**By Ethnicity/ race** - -50% aboriginal -50% endemic country **By HIV Acquisition** -majority sexual -minority of IDU	**# HIV positive kids** 9 kids **# HEUs, followed until:** -100 HEUs -3-5 years	- MDs: OB, MED, PED - RN	- standardize order sheets for vertical transmission protocol since 2010	- initial consult with RD – formula application and prescribe formula - funded by Manitoba Health Healthy Living and Seniors - Administered by Provincial HIV Program/ Nine Circles Community	- Cabergoline implementation

Ontario **-Hamilton** 60% -Niagara 20%, -Waterloo 10% -South West Ontario Family based clinic 11 births/year	**By Ethnicity/ race** - -79.3% African, -13.8% North America -3.4% Caribbean -3.4% Asian **By HIV Acquisition** -66.7% via heterosexual transmission -4.8% IDU -19% more than one risk factor -9.5% unknown	**# HIV positive kids** 8 kids **# HEUs, followed until:** indefinitely though a lot lost to follow up after sero-reversion documented	- MDs: OB, MED, PED - RN - Pharmacist - Social worker	- Adult HIV, OB - occasionally see Peds in prenatal consult	- Provincial Formula Program(Teresa Group)	-Criminal Case in 2004 -Cabergoline implementation
Ontario **Ottawa** 15-20 births/year	**By Ethnicity/ race** - -42% white -46% ACB -12% Asian -4% Latina **By HIV Acquisition** -70% sex -19% IDU -15% Perinata	**# HIV positive kids** -not reported **# HEUs, followed until:** -seen at 1,4,6,12,18 months then yearly thereafter	- Adult ID, HIV GP, HR OB, Peds ID - adult care is in building attached to CHEO (TOH) - counseled by MD, RN, SW - RD, pharmacist, other team members - AIDS Committee of Ottawa: Afro-Caribbean	- Peds at 30 weeks GA	- Provincial Formula Program (Teresa Group	- Cabergoline implementation - ACB support group – 1/month - supervised activities for kids - Peer support, home visits - Food bank, diapers, social program navigation - Dedicated prenatal/postnatal groups - Qualitative research with HCWs

			support worker			- Actual transmission risks with breastmilk
Ontario **Toronto** 25 births/ year	**By Ethnicity/ race** -mainly ACB, non-Canadian -Single moms **By HIV Acquisition** Not reported	**# HIV positive kids** 75 **# HEUs, followed until:** -250-300 HEUs -followed at 1,2,3,6,18 months, then yearly until 5.5y	- MDs: OB, MED, PED - SW - RN - Midwife	- Peds sees in late pregnancy	- Provincial Formula Program (Teresa Group)	- Cabergoline implementation starting at 1 site - Pilot study on pregnant and post partum women Knowledge, Attitudes and Experiences Questionnaire
Quebec	**By Ethnicity/ race** - 50% ACB - 20% Asian **By HIV Acquisition** - 64% endemic, - 21% heterosexual - 12% IDU	**# HIV positive kids** -not reported **# HEUs, followed until:** Not reported	- MDs: OB, MED, PED - Research RN 1 - PT 1, OT 1, SW 1, RD 1 - Pharm - Research lab tech - Research team (PhD 1, students/ post-docs)	- Dedicated RN (Peds and OB) - 2 OB - 2 Pharmacist - 1 SW	No provincial program Lactation inhibition (Cabergoline 1mg)	Cost per year for formula: - Powder: 1195$ - Liquid: 1374$ - Needs per year ≃298 800ml - biobank: stored samples of colostrum (n=71) from 1990 to 2000

Maritimes - Nova Scotia - Prince Edward Island - Moncton, New Brunswick - St John, New Brunswick - Newfoundland 3-5 births/ year	**By Ethnicity /race** - Some sites (NL) indicated pregnancies increasingly occurring among refugee moms **By HIV Acquisition** -majority heterosexual (endemic country)	**# HIV positive kids** -not reported **# HEUs, followed until:** -not reported	- MDs: OB, MED, PED	- Not reported	- free infant feeding program anywhere - income support for 1year if MD letter (Moncton) - If tube feeds, qualify for nutritional support if followed by IWK MD and RD (Nova Scotia), SW, - Pharmacist advocates on case-by-case	- formula program - Cabergoline implementation - Cultural issues Language barriers

IDU = Intravenous drug use, ACB: African Caribbean Black, HEU: HIV Exposed Uninfected infant, RN: Registered Nurse, SW: Social worker, P/T: part-time, OT: Occupational therapist, ID: Infectious Disease MD, Peds: Pediatrics, OB: obstetrician, RD: registered dietician, MD: medical doctor, Repro – Reproductive, ART – antiretroviral therapy, transitioned – Transitioned from pediatric to adult care

Priority Topics Vote Form

Infant feeding in HIV in Canada - Priority Topics Vote

The following are a list of priority areas for discussion during the breakout session that we want your input to decide which 5 will be selected. Please select only 5 topics, feel free to enter other topics that you see fit.

You will have another opportunity to review the list prior to the meeting.

Please select the top 5 topics you believe should be discussed during the breakout sessions during this National Infant Feeding in HIV Research Planning Meeting. *

Use your local experience, in addition to consideration of what national needs exist.

- [ ] Advocacy for national formula access
- [ ] Basic science research on breastmilk in the HIV context in Canada
- [ ] Counselling priorities for women about infant feeding risk of transmission
- [ ] Developing an approach to medicolegal aspects of breastfeeding in Canada (ie: Calling CAS, Public Health, Criminalization)
- [ ] Breast care consensus management
- [ ] Consensus clinical management of infant and mom, if a woman chooses to breastfeed
- [ ] Balancing priorities for the mother, the child and the family
- [ ] Psychosocial support - optimizing coping
- [ ] What is required to decide if breastfeeding is an option in Canada
- [ ] Cultural considerations - approach in different populations in Canada
- [ ] Other:

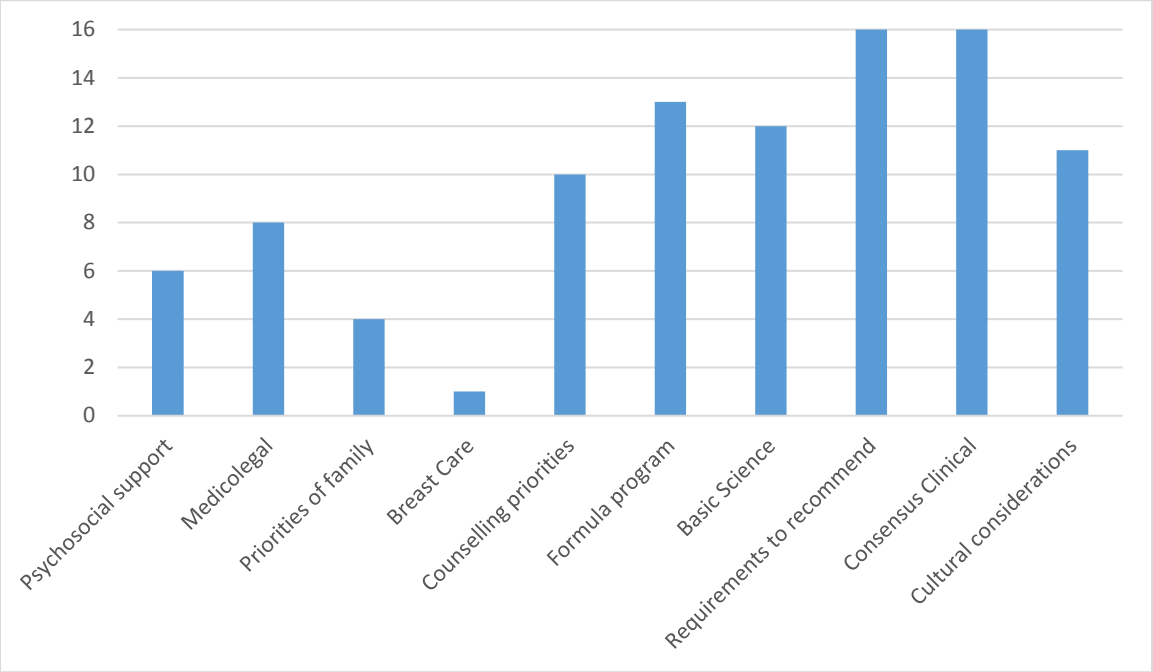
Vote Results from World Café

Total of 25 respondents from 38 attendees

Top 5 Selected Topics

1. Counselling priorities for women about infant feeding risk of transmission (10)
2. Psychosocial support - optimizing coping (6)
3. Developing an approach to medicolegal aspects of breastfeeding in Canada (ie: Calling CAS, Public Health, Criminalization) (8)
4. Balancing priorities for the mother, the child and the family (4)
5. Breast care consensus management (1)

Figure 7: Votes results for priority topics



World Café Facilitator and Note Taker Guidelines

About The World Café:

The World Café is a small group conversational process that allows participants to discuss various topics. These conversations link and build on each other as people cross-pollinate ideas and discover new insights into issues specific to the meeting theme. As a process, the World Café evokes the collective intelligence of the group and ensures that all participants are able to contribute. The figure below depicts the principles behind the World Café method (www.theworldcafe.com):

Session Purpose:

The purpose of the small group discussions is to allow participants to react to, reflect and build upon, and advance the ideas covered by the presenters. It is also an opportunity for the participants to provide some feedback about the workshop and identify some key next steps.

Session Description:

Five facilitators will be seated at tables with **chairs for**

7 to 10 other people. Each table and facilitator will be assigned one of five topics. The Topics and Guiding Questions will be reviewed with the group as a whole from 10:30-10:45, facilitators will be introduced (make sure you are seated at your designated table) then participants will be asked to move to a Table representing their topic of choice. Over the course of the session (10:45-11:10am), the facilitators will discuss their assigned topic with one group. Each participant will go through one round of the small group discussions and cover one topic. A two-minute warning will be provided so groups can summarize their ideas and confirm what they would like to share with the larger group. In total there will be about 20 minutes at each of the 5 stations for discussion.

All participants should rotate through 2 topics before the lunch break, and the remaining 3 topics after the lunch break. Try to ensure you aren't travelling in groups but as individuals so that you get to rotate who you work with at any given station.

Facilitator Responsibilities:

In the 25-minute session: Table facilitator will do a brief (1 minute) introduction to the issue, and then pose the first discussion question. After approximately 5-7 minutes, the facilitator should move on to the second discussion question. Make sure that all participants have equal opportunity to provide input should they want to, and avoid having individuals dominate the discussion.

Note taker Responsibilities:

The note taker will stay with the facilitator through the entire session. S/he will take detailed notes on their laptops to capture the content of the discussions. Note takers should do their best to capture discussions as comprehensively as possible. Note takers

should save their notes frequently throughout the session, and email final notes to Sarah Khan sarahz.khan@sickkids.ca

Table 11: World Café Topics and Facilitators

Topic	**World Café Facilitators**	**World Café Note-Takers**
1 Advocacy for national formula access	Angela Underhill	Julie
2 Basic science research on breastmilk in the HIV context in Canada	Logan Kennedy	Chantel
3 Cultural considerations - approach in different populations in Canada	Kaitlyn Mellor	Nadia
4 What is required to decide if breastfeeding is an option in Canada –	Muna Aden	Parker
5 Consensus clinical management of infant and mom, if a woman chooses to breastfeed	Sarah Khan	Leo

Guiding Questions for each station in World Café

Advocacy for national formula access

-Currently formula programs are provincially organized, and vary in their organization and development. If the National recommendation for women living with HIV is exclusive formula feeding we should ensure access to formula for everyone.

- How is formula access currently facilitated in health and/or social service settings? How was this system established? Should the system through which women living with HIV access formula be changed/improved?
- Is a Needs Assessment required? If yes, how should we go about this Needs Assessment and who should be responsible for its completion?
- What are the potential models to ensure national formula access? (e.g. Governmental: Federal, Provincial, Municipal; ASO Based; Private: Drug or formula company based) What model is most feasible, sustainable, and appropriate? What model(s) do you recommend?
- How can we ensure that national formula access is sustainable?
- Is there any data to suggest that access to formula for women living with HIV leads to better outcomes (health, social, economic, etc.)? Should any research be done in this area? If yes, what kind of study is possible (e.g. retrospective experiences, Database research)? Should this research be pursued? By whom?
- Are there examples from other countries that we can learn from regarding facilitating access, needs assessment, and access research?

Basic science research on breastmilk in the HIV context in Canada

- We do not know the quantifiable risk of HIV transmission through breastfeeding in Canada.
- Should we measure the risk of transmission through breastfeeding using basic (and/or clinical?) research approaches?
- What are the pros and cons of conducting basic science research on HIV in breastmilk? E.g. to be able to counsel in an informed way and to make a clear recommendation when delivering care to women living with HIV
- What basic science research has been done internationally exploring HIV in breastmilk?
- What are appropriate ways to engage the community of women living with HIV on this issue?
- What are the Ethical considerations?
    - Psychosocial, sociocultural issues around asking women to express milk
- What are the parameters necessary to conduct basic science research on HIV in breastmilk?
    - E.g. does the duration of time that women express milk matter? Does the amount of milk that women express matter? How long would women have to express milk in order to draw sound conclusions? What about ART – how does Mother's ART factor into this?

- What basic science research questions should be explored regarding HIV in breastmilk (i.e. what are the most feasible and important research questions that should be prioritized)?
    - Examples:
    - What are we looking at (Cell associate, Cell free virus, immune factors)?
    - Ways to kill/de-activate HIV in breastmilk (solutions)?
    - Mother on ART and measuring mother's reservoir, correlations with other reservoirs including blood, mucosal, etc.
- Who will fund this research? Who should conduct this research (including collaborators with international researchers)?

Cultural considerations - approach in different populations in

Women living with HIV in Canada are a diverse population and may experience infant feeding (or not breastfeeding) in a myriad of ways.

- From your observations/communications, what are some of the ways that women living with HIV experience infant feeding/not breastfeeding
- What are the immediate concerns/thoughts that come to mind when you think about not breastfeeding among women living with HIV?
- From your observations, how is the experience of infant feeding connected to women's overall lived experience (if at all)?
- Considering the needs of women regarding infant feeding, what are some ways we could modify our practices and the support offered to these women?
- Thinking about the health care system on a large scale, are there areas that could be modified to address the primary concerns for women living with HIV and their experiences with infant feeding? For example, how can/should health and social care providers and the system of care that women access consider and respond to women's lived realities and social/cultural circumstances?
- How can we reach women living with HIV across Canada and engage them with this issue, taking into consideration different social locations and individual experiences?
- Is a Needs Assessment required? If yes, how should we go about this Needs Assessment and who should be responsible for its completion?
- Is more research needed in this area? E.g. scale up of the HIV Mothering Study across Canada? If yes, who will fund this research? Who should conduct this research (including collaborators)?

What is required to decide if breastfeeding is an option in Canada?

-What data, research, study, consensus, patient engagement is needed in order for there to be a recommendation on breastfeeding?

- As a provider, do you think breastfeeding should be an option for women in Canada?
    - In your perception, do you think breastfeeding is wanted at a community level?
- If not to both or either of the above, what are the priorities for next steps with regard to infant feeding and HIV?
- If yes:
    - What basic science “answers” are required, e.g. quantifying the risk?
    - What does this mean for clinical management? What changes/ practice shifts would be needed? What
    - Are the considerations for “compliance” and “engagement” of the mother and her family? How can this best be optimized? Can we learn anything from employing a “harm reduction” approach?
    - What community engagement is needed?
    - What political engagement and advocacy work is needed?
    - What are legal considerations and responses? E.g. clarify the legal requirements, public health implications, child protection, CMPA, etc.
    - Who are the actors and what are the critical next steps in these areas?

Consensus clinical management of infant and mom, if a woman chooses to breastfeed

A situation may arise (albeit rare) where a woman living with HIV may breastfeed. How could this be handled in terms of clinical management of both the mother and baby in the current clinical context?

- What are situations that this rare situation may arise, and how would that change management? (PROBE: moving to a Low middle income setting, community coercion, abusive relationship)
- What level (frequency, duration, etc.) of clinical monitoring of both the mother and baby is recommended? Based on what evidence?
- What factors would be considered in the clinical management of this scenario? E.g. level of “reservoir”
- What kind of counseling/information should the mother receive, e.g. regarding risks and benefits of breastfeeding? What are the counseling/information guidelines based on – practice experience? Research evidence? Other knowledge/experience?
- What is the legal requirement of the physician (CMPA involvement)?
- Can we learn anything from harm reduction approaches to apply to this area?
- What are the recommendations for liaising with child welfare services and/or public health?

CHAPTER 5: Conclusions and future directions

Vertical transmission remains a concern for both adult and pediatric HIV care providers in Canada and globally. Although great strides to minimize the risk of transmission in utero and peripartum have been made, postnatal transmission through infant feeding remains a controversial topic for families affected by HIV. In Chapter One we explored the literature on what is known about breastfeeding transmission. This chapter summarized the relevant literature from the first cases of breastfeeding transmission, isolation of cell free and cell associated virus in breastmilk, the known maternal, infant and feeding related factors which increase the risk of transmission, to the use of antiretroviral interventions as a means to further minimize the risk.

Chapter One further summarized how the above evidence has shaped guidelines developed by the WHO, intended for low and middle income countries. These WHO recommendations are contrasted with those written for high resource countries such as Canada. The medical recommendation for the Canadian general population for optimal health of mother and infant is to breastfeed. This among other factors has led to a 'breast is best' prevailing societal view. Women living with HIV are within the narrow population of mothers where breastfeeding is not recommended. However, data from the United States and cases described in the literature from Canada reveal that breastfeeding is occurring in high resource countries despite these recommendations. Some of the challenges that complicate this issue further, are the legal and child protection implications, which are less well delineated in the literature. Chapter One serves to summarize the relevant background to provide context for the need for an exploration of provider perspectives on infant feeding in HIV in Canada.

There is a body of literature exploring knowledge, attitudes and practice of health care providers in low and middle-income countries on infant feeding in HIV. However, there is a paucity of data from high resource settings, where infant feeding issues differ significantly. The survey developed for this thesis was a knowledge, attitudes and practices survey of Canadian HIV care providers. The survey developed in consultation with content and measurement experts had a variety of question styles in order to elucidate some of the nuance related to infant feeding. Questions included multiple choice, Likert scales, and scenario based questions. The populations included HIV, Infectious Diseases, and Pediatric providers, which were sampled using national and regional networks. The survey allowed for the development of knowledge, risk tolerance and perceived stigma/barrier scales. The main predictors set a priori included age, gender, years in practice, clinical experience with HIV patients, and provider group explained some of the variance in the scores but not all. There was consensus overall, that providers would not recommend breastfeeding because of the non-zero risk of HIV transmission to the infant. Providers agreed that formula should be provided for women living with HIV in most situations, though some providers felt this should be provided only based on socio-economic need of the woman. Providers were somewhat varied in their decision to involve child protective services, but overwhelmingly they did not believe breastfeeding alone merited criminal charges. The survey identified common knowledge gaps among providers, including aspects of guidelines, and areas where knowledge translation is required for providers, including aspects of counselling which should be considered standard of practice.

Several limitations were identified for the survey including the small sample size, and inability to generalize results to all providers. Specifically, we were unable to reach pediatric providers nationally and instead this data is reflective of a much narrower Toronto-based pediatric provider group. This is an important limitation due to the reality that infant feeding and HIV issues vary from cultural community, regional area, and resources available despite some issues, which are shared across Canada. Ideally, using a validated survey among health care providers in high resource settings would have been a more reliable method for data collection, however upon review of the literature no existing survey was found. This is likely due to the novel area being studied. There were issues with specific questions which made them more challenging to interpret, and therefore were not included in the combined analysis to avoid adding any error in interpretation. Similarly, some knowledge questions were reduced to a dichotomized right or wrong answer, rather than allowing half points for partially correct responses. Although this leads to a more clear-cut interpretation for objective areas such as knowledge, it may not quantify the true extent, or gaps in knowledge. After our data was collected, a survey was completed in US Healthcare workers, and their use of comment / free text options allowed for participants to provide direct quotes, which added further context or nuance to responses. We had intended for a quantitative analysis, however this did limit the interpretation of some of the answers participants provided. Our questionnaire was also lengthy, in an attempt to cover a lot of content; this may have contributed to the low response rate, especially among Infectious Disease providers who may be less invested in the topic. Likely, our respondents were those who treat women or children with HIV or have an interest in this subject area, thereby limiting generalizability to other providers.

Future studies intending to measure similar concepts could use some of the higher yield questions from our survey. Alternative approaches for future studies could include in-person surveys at provider meetings. This would improve response rates, and allow for a more generalized sampling of the provider population, however would be more resource intensive. Our approach to incentivize survey completion was a draw for gift cards, which was costly and not as effective as intended. Researchers attempting to study this area in the future can use these limitations and lessons.

Survey findings were further corroborated by the provider meeting presented in Chapter Four. To explore provider input further and develop consensus on research and clinical needs on this topic in Canada we hosted a two-day meeting. Prior to this meeting community consultation occurred in the format of focus groups to discuss the experiences and priorities for women living with HIV in Canada around infant feeding. Rich discussion occurred in these focus groups, and using directed content analysis of transcripts key themes emerged including: novel perspectives on the lived experiences of infant feeding for women living with HIV, solutions and changes to supports for women living with HIV, and research considerations in a Canadian context on the topic. Women strongly voiced the importance of culture and social location in the infant feeding decisions, and that providers were not adequately informed on the role this plays. Women were interested in research on this to improve knowledge and awareness of the role culture plays in infant feeding and HIV care experiences. The long-term impact infant feeding decisions has for women, and their relationship with their children was an important finding that again providers may not be aware of. The most enriching aspect of the focus groups was hearing many solutions women had to improve their infant feeding experience, thereby

reinforcing the importance for community consultation when deciding upon knowledge translation tools, and resource development for both community and providers.

The planning meeting held mainly for providers had important overlap with the focus groups with the community. Both groups felt that knowledge translation was the greatest need related to infant feeding. Women generally feel inadequately informed on the risk of transmission, and unsure as to why guidelines differ in low versus high resource countries. Providers felt that knowledge translation resources would improve their ability to counsel women on important aspects such as the risk of transmission, aspects of breast care and breastmilk suppression, and resources to support formula feeding. Providers also felt that a consensus clinical guideline would help unify aspects of care; and improve the counselling they provide to their patients. The provider meeting allowed for an open discussion of current resources available, and challenges faced across the country pertaining to infant feeding in HIV. Providers recognized that women living with HIV may have a strong desire to breastfeed for various reasons including: optimal bonding, nutritional concerns, fear of involuntary HIV disclosure to undisclosed friends or family, cultural preference, pressure from partners or family members, lack of a clear understanding of risks of breastfeeding, or feelings of inadequacy in the role of mothering. Despite providers overall feeling that the recommendation should not change, and that formula feeding is the safest option for infant feeding in Canada, they did recognize situations in which formula feeding may not be the reality. Providers were able to begin to discuss how they would manage such scenarios; however, this required broader discussion and the need for a process to develop an evidence based guideline for such circumstances.

Unfortunately, what remains unknown, despite our survey, focus group discussions with community, and provider meeting is how often women living with HIV in Canada are breastfeeding. Even more difficult to quantify is the actual risk of breastfeeding transmission of a woman living with well-controlled HIV for a prolonged period, monitored closely while breastfeeding in Canada. The best estimate taken from systematic reviews of trials from women with undetectable plasma viral loads treated and monitored in low-middle income countries suggests the risk is likely between 1-5% over a 6 to 18 month period of exclusive breastfeeding. Uncertainty typically lends to diverse approaches in clinical practice. HIV Care Providers differed in their approach to this challenging scenario in clinical settings as demonstrated by the survey responses, and the provider meeting discussions.

Infant feeding in HIV remains a contentious issue for providers and families affected by HIV, with strong opinions despite some areas lacking clear evidence. The Canadian Infant Feeding in HIV Network discussed in Chapter Four; offers a promising start towards the development of evidence based knowledge translation, clinical guidelines, and ethically sound research, which can continue to address the ongoing unanswered questions and challenges remaining on this important aspect of HIV care for families in Canada. This thesis only begins to examine the gaps and needs of providers, and starts to open a broader conversation on this subject. An important gap in this work was meaningful community voices and exchange on this subject.

Future directions for this work include a more in depth analysis of the variable needs of specific communities in Canada regarding infant feeding. Because HIV affects diverse communities in Canada, the infant feeding needs and priorities likely differ greatly.

An in depth discussion with communities through qualitative exploration across Canada is needed to understand the patient important outcomes to begin to answer these questions through community based research approaches. Implementation science would be an important research approach to consider when designing clinical solutions around infant feeding for families affected by HIV in Canada.

This thesis has been a learning process for me as a clinician and researcher. I have been humbled from the first day meeting community members who through their lived experience began to educate me on the realities of how HIV impacts every aspect of life. My interest was in infant feeding as an area of clinical care, which overlaps with pediatric, women's, and family-centered HIV care. What I did not recognize was how highly nuanced this issue is for both providers and community. After two years of this small undertaking to elucidate provider knowledge, attitudes and practice, I very quickly learned I would need to understand the intersection between provider and patient on this issue, where they meet and where they remain disconnected from each other. I sincerely hope this body of work will begin to uncover some of the deeper issues, but clearly many questions remain. What risk would be acceptable to allow breastfeeding in Canada? According to who? What level of risk would be defensible in a criminal case if a transmission occurred? What implications would such a transmission whether in consultation with HIV care providers or not, have in relation to child protection services, a lifelong mother-child bond, and the healthcare system? What are the quantifiable benefits and harms in the short and long term to mom or infant from breastfeeding when HIV infection and antiretrovirals are a factor?

This thesis did allow for the development of some clear next steps needed. The two most highly demanded next steps by both community and providers were Knowledge Translation tools. These need to be developed by communities, for communities. As a step towards this we have acquired a CIHR Dissemination Grant in order to bring together community leads to 3 key KT resources: 1) Breast care and lactation suppression information, 2) Basic science information on breastmilk transmission, 3) How to bottle feed your infant safely. This needs to be driven with and by community co-investigators, and the format of which this KT is developed needs to be tailored to the needs of different populations based on cultural, regional, and language needs.

The second high priority next step as highlighted from the provider meeting is a consensus clinical management guideline for providers to ensure that care and information discussed by providers is correct, thorough, and clear for women to feel fully informed. A counselling checklist may be a useful tool to ensure all aspects of infant feeding are adequately discussed, including aspects which providers may be less comfortable with, such as child protection and legal aspects. This ideally will be done in consultation with the Canadian Medical Protection Agency, HIV Provider and Community groups, and developed using a Delphi consensus among content experts within CIFHN. It may be useful after release and dissemination of these guidelines to repeat a similar but more tailored survey among care providers to assess if provider knowledge, attitudes or practices have changed.

Although questions remain, I look forward to taking part in the next steps moving this body of research further. I advocate for a community based, interdisciplinary approach to understanding the issues surrounding infant feeding in Canada. I believe the

Canadian HIV experience with infant feeding can contribute to a global discussion for other high resource countries that are starting to explore th1e issue, and how it affects their families living with HIV.

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