LAYING THE GROUNDWORK FOR PRENATAL DIETARY ASSESSMENT RESEARCH AMONG FIRST NATIONS WOMEN AT RISK FOR ALCOHOL USE: IMPLICATIONS FOR FETAL ALCOHOL SPECTRUM DISORDER

by

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Abstract

Fetal Alcohol Spectrum Disorder (FASD) is a health concern that is over-represented among First Nations peoples. Optimal prenatal nutrition plays a role in the severity of FASD. Prenatal nutrition as it relates to fetal brain development and fetal alcohol exposure is an under-researched area, especially among pregnant First Nations women. Finding current dietary intake patterns of pregnant women who drink alcohol could lead to developing a nutrition provision strategy. However, there is no appropriate dietary assessment research tool that is specific to this population. This study aims to develop an effective, culturally appropriate and interactive dietary assessment research tool using participatory methods to engage with women and communities in the process. We used community health priorities forums, information sessions, volunteering, collaboration with programs, and a trauma-informed approach as methods to engage with pregnant women. To develop the research tool, top sources of fetal brain development nutrients were determined for the food frequency component, several prenatal health workers reviewed the tool, and a pre-test with 20 pregnant women of the target population was completed. Pre-test results show the tool is being well-received. All of this ground work will help pave a path for further prenatal nutrition research with First Nations women. This research will inform programs and policies which strive to improve food and nutrition security and reduce the severity of FASD.

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Dedication

I would like to dedicate this work to the mothers I had the privilege of meeting during this project. Even when life seems to be waging against you, you still love. That is strength.

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LIST OF ABBREVIATIONS

Abbreviation	Term
5-HTOL/5-HIAA	Ratio of 5-hydroxytryptophol/5-hydroxyindolylacetic acid
ADH	Alcohol dehydrogenase
ALT	Alanine aminotransferase
AMC	Assembly of Manitoba Chiefs
AMC HIRGC	Assembly of Manitoba Chiefs Health Information Research Governance Committee
ARND	Alcohol-Related Neurodevelopmental Disorder
AST	Aspartate aminotransferase
AUDIT	Alcohol Use Disorders Identification Test
BAC	Blood alcohol concentration
BMI	Body Mass Index
CAGE	Cut down Annoyed Guilty Eye-opener (see Table 2)
CCHS	Canadian Community Health Survey
CDC	Centers for Disease Control and Prevention
CDT	Carbohydrate deficient transferrin

CFS	Child and Family Services
CNS	Central Nervous System
CPNP	Canadian Prenatal Nutrition Program
CVD	Cardiovascular Disease
DHA	Docosahexaenoic acid, C22:6n-3
DNA	Deoxyribonucleic acid
EtG	Ethyl glucuronide
EtOH	Ethanol
FAE	Fetal Alcohol Effects
FAEE	Fatty acid ethyl esters
FAS	Fetal Alcohol Syndrome
FASD	Fetal Alcohol Spectrum Disorder
FFQ	Food frequency questionnaire
FNFNES	First Nations Food Nutrition and Environment Study
GGT	Gamma-glutamyltransferase
HIRGC	Health Information Research Governance Committee
LGBT	Lesbian Gay Bisexual Transgender
MCV	Mean corpuscular erythrocyte volume
MEOS	Microsomal ethanol oxidizing system
NIAAA	National Institute on Alcohol Abuse and Alcoholism
NMDA	N-methyl-D-aspartate (NMDA)
PC	Phosphatidylcholine
PEth	Phosphaditylethanol
pFAS	Partial FAS
PHAC	Public Health Agency of Canada
PLD	Phospholipase D
PUFA	Polyunsaturated fatty acids
RDH	Retinol dehydrogenase
RHS	Manitoba First Nations Regional Longitudinal Health Survey
ROS	Reactive oxygen species
SAMHSA	Substance Abuse and Mental Health Services Administration
SES	Socioeconomic status
SF-MCH	Strengthening Families Maternal Child Health
T-ACE	Tolerance, Annoyed, Cut down, Eye-opener (see Table 2)
TCA	Tricarboxylic acid cycle
VLT	Video lottery terminal

CHAPTER 1: LITERATURE REVIEW

Introduction

Canadian First Nations populations are often faced with the brunt of the health problems in Canada, which is a growing health equity concern. In particular, First Nations populations have a higher birth rate and younger demographic compared to non-Aboriginal populations (Statistics Canada, 2014a). Also this population has high alcohol consumption rates (Williams and Gloster, 1999) and potential high incidence rate of fetal alcohol spectrum disorder (FASD) (Williams et al., 1999). This is a concern considering the existing maternal and child health problems, food security issues, and other health concerns in this population.

Unhealthy eating patterns, in addition to food insecurity, contribute to the prevalence of chronic diseases such as diabetes and cardiovascular disease (CVD), which are commonly seen in Canadian First Nation populations. The quantity and quality of food intake plays a significant role in health, quality of life, and contributes to the decrease of many chronic diseases. This indicates that diet is a major modifiable risk factor for overall improvement of health. Furthermore, optimal nutrition status may reduce the risk for a number of disorders including FASD. Prenatal alcohol consumption affects maternal and fetal nutrition status in various ways plus poor nutrition status increases the risk for FASD. Proper overall nutrition status and possibly supplementation of certain nutrients could reduce the effects of alcohol on the fetus. However, in order to plan a nutrition strategy that aims to reduce the severity of FASD, we must know the current dietary intake patterns of pregnant women at risk for alcohol consumption. To determine dietary intake patterns we need an appropriate dietary assessment tool that focuses on nutrients related to fetal brain development and fetal alcohol exposure.

This review will focus on FASD and how a nutrition intervention could potentially reduce the severity of FASD, and will point to the need for a population-specific, FASD-focused dietary assessment tool among First Nations peoples. First, FASD will be defined, prevalence will be discussed, risk factors will be explored and existing interventions and treatments will be introduced. Second, alcohol will be discussed further to explore how alcohol is metabolized, what the prenatal alcohol consumption rates are, and how biomarkers can help confirm alcohol exposure. Third, the importance of nutrition during pregnancy for the potential mitigation of the effects of alcohol exposure will be discussed in detail. Fourth and finally, the state of prenatal nutrition research among First Nations women and the need for a population-specific dietary assessment tool will be highlighted.

Fetal Alcohol Spectrum Disorder

Diagnostic Terms

Fetal alcohol spectrum disorder (FASD) is the umbrella term for a range of effects resulting from prenatal alcohol consumption. FASD is not a clinical diagnosis by itself. Instead, a person may be diagnosed with one of three disorders which are included in the Canadian diagnostic criteria (Chudley et al., 2005). From most dysmorphic to least dysmorphic, these are Fetal Alcohol Syndrome (FAS), Partial FAS (pFAS), and Alcohol-Related Neurodevelopmental Disorder (ARND). Diagnosis for FAS requires evidence of pre-or-postnatal growth retardation, three facial anomalies, impairment of three or more central nervous system (CNS) domains (decreased cranial size at birth, structural brain abnormalities, neurologic hard or soft signs), and confirmed maternal alcohol exposure (Chudley et al., 2005; Stratton et al., 1996)

Partial FAS requires evidence of two facial anomalies, impairment of three or more CNS domains, and confirmed maternal alcohol exposure. The diagnosis of ARND requires evidence of impairment of three or more CNS domains and confirmed maternal alcohol exposure (Chudley et al., 2005). The term Fetal Alcohol Effects (FAE) is not well defined (Sampson et al., 1997) and the term Alcohol-related birth defects (ARBD) refers to a list of congenital anomalies which are not necessarily a direct impact of alcohol exposure (Chudley et al., 2005; Stratton et al., 1996). Both terms are not included in the Canadian diagnostic criteria; however, ARBD is included in the Institute of Medicine criteria (Stratton et al., 1996).

Prevalence of FASD

It is difficult to accurately assess the prevalence of FASD. Underreporting due to lack of awareness, lack of resources, and lack of trained and skilled professionals in diagnosis are reasons why prevalence is unknown in many countries (Chudley, 2008; Kilgour and Chudley, 2012). Evidence from studies in Europe, South Africa, United States, and Canada show incidence and prevalence of FASD.

Prevalence around the world

According to Abel (1995), the overall estimated incidence of FAS in European countries and other non-North American countries was 0.08 per 1,000 births, whereas, in the USA the incidence was estimated at 1.95 per 1,000 births (Abel, 1995). The rates in the United States were more recently reported at around 0.5-2 per 1,000 births (Centers for Disease Control and Prevention, 2002). However, a recent study conducted with school-aged children in mid-Western USA revealed an estimated prevalence of FAS ranging from 6 to 9 per 1000 children, PFAS from 11 to 17 per 1000 children, and the total rate of FASD was at 24 to 48 per 1000 children

(May et al., 2014). In the Lazio region of Italy, the prevalence of FAS was 3.7-7.4 per 1,000 births and prevalence of FASD was 20.3-40.5 per 1,000 births (Abel, 1995). Prevalence of FAS in South Africa is around 40-74 per 1,000 births (Centers for Disease Control and Prevention, 2003; Viljoen et al., 2005). Clearly the rates are quite varied around the world.

Prevalence in Canada and in Canadian First Nations communities

It is estimated that 9 in every 1000 babies born in Canada have FASD (Public Health Agency of Canada (PHAC), 2005). However, this rate is an estimate based on data from the USA (Sampson et al., 1997). A recent study in the province of Alberta indicates an incidence of FASD of 14.2 to 43.8 per 1000 births, depending on year and the length of follow-up (Thanh et al., 2014). This is based on annual data from 2003 to 2012 that indicates 739 to 1884 people were born with FASD in Alberta (Thanh et al., 2014). These rates are much higher than the commonly cited rate of 9 per 1000. Ultimately, there is no overall prevalence rate of FASD in Canada as a whole.

While prenatal drinking rates may be high, there is no overall or regional prevalence of FASD in Canadian First Nations communities. Some studies have shown estimated prevalence but the range is wide. For example, the incidence of FASD in a First Nations community in North-Eastern Manitoba in the late nineties was about 7.2 per 1000 live births (Williams et al., 1999) and another study found an estimated prevalence of FAS to be 61 per 1000 live births in another First Nations community in Manitoba (Square, 1997). The later estimate is based on a study that found that 46% of the school-aged children studied had been exposed to alcohol *in utero*. Of the 178 children studied, 11 were identified as having FAS and 7 children were identified as having pFAS (Kowlessar, 1997). Prevalence estimates in Manitoba are generally

higher than in Saskatchewan, where estimates are about 0.6 per 1000 births (Habbick et al., 1996) in British Columbia, where estimates are about 24 per 1000 births (Asante, 1985). However, overall, these rates are outdated and may not represent the actual or current prevalence.

Tait (2003) points out that much of Canadian research on FASD is focused on Aboriginal peoples and supports a common belief that prenatal substance abuse is more frequent among Aboriginal women than non-Aboriginal women. However, the overall prevalence of FASD in both Aboriginal and non-Aboriginal populations is not known and therefore we cannot confirm that FASD rates are in fact higher among Aboriginal populations (Tait, 2003).

Risk factors of FASD

Since alcohol can easily cross the placenta, any alcohol that a pregnant woman consumed is delivered directly to her fetus *in utero* (Cook, 2003). There are a multitude of factors that contribute to whether or not a baby is born with the effects of prenatal alcohol exposure and to what extent they are affected (Abel and Hannigan, 1995; May and Gossage, 2011) (See Figure 1 and Table 1).

Figure 1: Maternal permissive and provocative factors and fetal factors leading to FASD
Source: Modified from (Abel and Hannigan, 1995) and (May and Gossage, 2011)

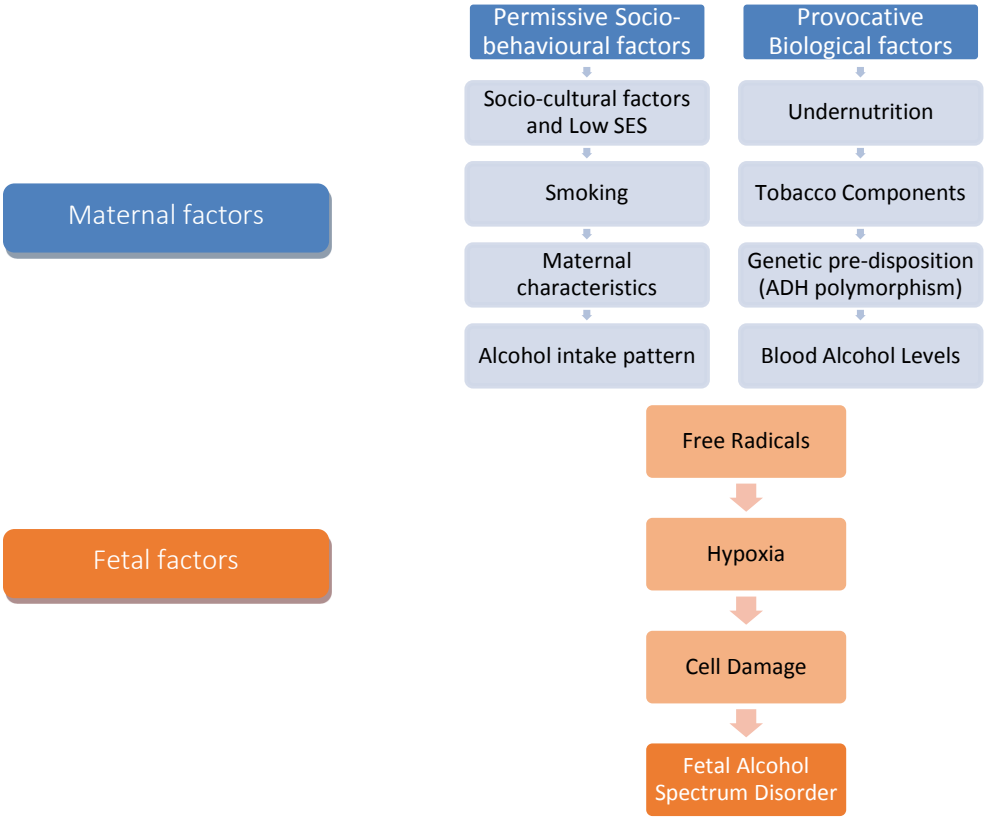

Table 1: Maternal risk factors for FASD
Source: Modified from (May and Gossage, 2011)

Host	Agent Exposure	Environment
Mother's age ≥ 25	High BAC from large quantities of EtOH	Low SES
Gravidity ≥ 3	Binge drinking (3+ per occasion)	Not married, but living with partner
Parity ≥ 3	Length of drinking career	Culture accepting of heavy drinking
Higher rates of stillbirth and miscarriage	Frequent smoker (lower birth weight)	Family of origin of heavy drinkers
Infrequent practice of religion/spirituality	Beer is beverage of choice of a majority of FASD mothers in most populations	Partner is a heavy & frequent drinker
Low maternal education	Drinking outside of meals	Alcohol-centered recreation popular
Smokes cigarettes	Polysubstance abuse in urban studies	Social isolation from mainstream economy & society
Depression/psychological distress	Change in gastric ADH activity	Little or no knowledge or awareness of FASD
Short stature	Change in nutritional status during pregnancy	
Low weight		
Low BMI		
Nutritional deficiency		
Particular alcohol dehydrogenase polymorphisms		

Alcohol intake pattern

The quantity, frequency, and timing of exposure to alcohol are all important factors that influence FASD (May, 1995; May and Gossage, 2011). Maternal binge drinking, as some studies define as three or more drinks per occasion (May et al., 2007; May et al., 2008) is considered to be most dangerous for fetal development because of the high blood alcohol concentration (BAC) it produces (Abel, 1998; Maier and West, 2001; Pierce and West, 1986; West and Goodlett, 1990). A regular pattern of binge drinking produces high and frequent blood alcohol levels indicates that FASD will likely be severe (Khaole et al., 2004). Population studies have shown that high rates of FAS and pFAS are produced when weekend binge drinking is common among women (May et al., 2000; May et al., 2007; Urban et al., 2008; Viljoen et al., 2005).

Timing of alcohol consumption is also key. The facial characteristics that define FAS and pFAS are developed at 6-9 weeks gestation (May and Gossage, 2011). The cognitive and behavioural traits in FASD may occur at various times throughout gestation but certain parts of the brain may be particularly vulnerable to exposure of alcohol at certain times (Guerri et al., 2009; Mattson et al., 2001; Riley and McGee, 2005). Quantity, frequency, and time of exposure to alcohol are all factors; however, the exact criteria will depend on the other cofactors that exist such as maternal nutrition status (May and Gossage, 2011). Clearly, the effects of prenatal alcohol exposure are more complicated than the exposure alone.

Maternal characteristics: age, gravity, parity

The severity of FASD is influenced by certain characteristics of the mother. Even if two women report the same quantity, frequency, and time of exposure to alcohol, their offspring could be affected in different ways (May and Gossage, 2011). Several studies from various

regions in the world have compared maternal characteristics of women who have children with FASD and those who do not (Jacobson et al., 1996 1998; May et al., 1983, 2005, 2006, 2007, 2008). These studies have revealed three main maternal risk factors: age, gravidity, and parity. If a woman is older and has had more pregnancies and births, her offspring are more likely to have FASD (May and Gossage, 2011).

Abel and Hannigan (1995) reviewed some of the reasons why these risk factors have an impact. The older a woman is, the more possible years of alcohol consumption she has (Abel and Hannigan, 1995). Over time, her tolerance to alcohol may increase, which means that offspring born later on in her life would be exposed to higher levels of alcohol, and more prone to FASD (Abel, 1998; Iosub et al., 1981; Lipson et al., 1983). Furthermore, any maternal alcohol-related medical problems that a woman has will be more severe as she has more years of alcohol consumption (Khera, 1987). The more births a woman has, the more drastic a decrease in blood flow to the fetus due to increased uterine and placental collagen and elastin which can contribute to fetal hypoxia (lack of oxygen being delivered to the fetus) (Robertson and Manning, 1974; Woessner, 1963). Hypoxia makes the impact of alcohol exposure more severe (Abel and Hannigan, 1995). It is also possible that age, gravity, and parity relate to the amount of physical and mental stress a woman goes through which could impact her alcohol consumption rates and the effect that alcohol has on the fetus.

Nutrition and BMI

Poor nutrition status of a pregnant woman can increase the fetus's vulnerability to the effects of alcohol exposure because of a decrease in the "nutrient pool" which supports fetal growth and maintains maternal health (Abel and Hannigan, 1995; Dreosti, 1993). Alcohol

consumption alone is a cause of primary and secondary malnutrition (Lieber, 2000). Also, results from animal studies show that even when alcohol consumption rates are equal, alcohol metabolism is slowed by undernourishment which increases the BAC and increases the fetal alcohol exposure (Mendelson, 1970; Villarroya et al., 1985).

Population studies in South Africa show that FASD is more common in regions where major nutritional deficiencies are present among pregnant women (May and Gossage, 2011). May (2004) found that pregnant mothers of children with FASD had lower intake of riboflavin, calcium, and docosahexanoic acid (DHA), an omega-3 fatty acid (May et al., 2004). Other nutrients such as zinc, B vitamins, copper, and choline may play a role (Keen et al., 2010; Tamura and Picciano, 2006; Thomas et al., 2004). The specific nutrients that may have an impact on alcohol and role of nutrition in mitigating FASD will be discussed further in the nutrition section.

Body mass index (BMI) has been shown to impact FASD rates in various epidemiologic studies around the world (May and Gossage, 2011). Mothers of children with FASD are often of lower height, weight, and BMI than women without children with FASD (May et al. 2008). It is possible that this is related to overall malnutrition. More important is that BMI has an impact on BAC. Higher BMI reduces the blood alcohol concentration and therefore reduces alcohol exposure to the fetus.

Smoking

Smoking is a risk factor of FASD for two reasons. First, smoking, alcohol use, and poverty are correlated in increasing the risk for FASD (Abel, 1995). Secondly, specific ingredients in tobacco smoke can decrease blood flow and oxygen content (Abel, 1984) and

reduce the availability of nutrients (Fisher et al., 1984) which could increase growth retardation and teratogenic affects by forming free radicals leading to the signs and symptoms of FASD (Abel and Hannigan, 1995).

Genetics

Alcohol metabolism can vary between different women (Badger et al., 2005; Frezza et al., 1990; Shankar et al., 2006,2007). This variance could be due to genetic and environmental factors (May and Gossage, 2011). One of the major enzymes involved in alcohol metabolism, alcohol dehydrogenase (ADH), has protective genetic variants (ADH1B*2 and ADH1B*3). People with these variants of the enzyme tend to have a more intense response to alcohol and a reduced risk for alcohol abuse and alcoholism (May and Gossage, 2011). Women with this protective variant have fewer negative metabolism-related consequences than those who do not and are less likely to have children with FAS (Khaole et al., 2004).

Low socioeconomic status

Epidemiologic studies on FASD have shown that most of the families affected by FASD are living in poverty (Abel and Hannigan, 1995). For instance, African Americans and Native Americans in the United States of low socioeconomic status (SES) were 10 times more likely to have children with FAS than Caucasian children of middle and upper SES (Abel, 1995). Poverty can have a clear impact on many of the other factors involved, such as education, employment, nutrition, stress, and the environment in which a pregnant woman might feel the need or pressure to drink alcohol. Individuals living in poverty are at risk for micronutrient deficiencies, namely, vitamin A, folate, and choline, and macronutrient deficiencies and explains that low SES is the one common risk factor of FASD (Ballard et al., 2012).

Population-based studies in South Africa have revealed that the highest rates of FASD occurred in areas where "living conditions are the worst, nutrition of the women is poorest, and weekend binge drinking is a regular practice" (May and Gossage, 2011). Also, many women who have children with FASD have "lower levels of education and more frequently are unemployed or underemployed" (May and Gossage, 2011). Poverty can affect so many aspects of a person's life and could predict the likelihood of a woman to drink while pregnant. It is likely that similar conditions occur in Canadian women with FASD, but it is not well documented.

Socio-cultural factors

The risk factor, culture, as described by Abel and Hannigan (1995), is focused on the idea that different cultures around the world might be more or less likely to diagnose a child with FASD. There are cultural factors that "can influence a physician's decision to diagnose a child with FAS or not" (Abel and Hannigan, 1995). Although this is likely an influence, it is not a factor that relates specifically to whether or not a woman would drink while she is pregnant. However, a culture that is accepting or encouraging of heavy drinking, especially regular binge drinking, could impact a woman's decision to drink. May and Gossage (2011) list "culture accepting of heavy drinkers" as an environmental risk factor for FASD. Another social-related factor is paternal drinking. If the father or the woman's partner is a heavy drinker, the woman is more likely to drink (Eni et al., 2014; May and Gossage, 2011). All of these risk factors point to the complexity of FASD.

Interventions for FASD

Ideally FASD could be prevented by stopping or reducing maternal alcohol consumption. Some initiatives like warning labels on alcoholic beverages or public health messages like "With

Child, Without Alcohol" of the Manitoba Liquor and Lotteries may increase awareness of the effects of alcohol and promote some reduction in alcohol consumption. However, these methods are not the only solution and may not effectively reach the target population of women who are most likely to drink alcohol during pregnancy.

Unfortunately, many women still drink alcohol while they are pregnant (Centers for Disease Control and Prevention, 2009; Public Health Agency of Canada, 2008) and some may not know the consequences of alcohol on their unborn baby. The knowledge of FASD among First Nations peoples is largely unknown. However, one study showed that only 36% of the Native people who participated in the study were aware of FAS (Williams and Gloster, 1999). If this result is indicative of the awareness among other First Nations people in Manitoba and Canada, there is a need to increase awareness. However, as previously discussed, awareness is only one part of the solution. Therefore interventions that minimize the effects of alcohol exposure are necessary (Idrus and Thomas, 2011). This review will focus on the prevention of FASD using interventions that target the mother.

Experimental Interventions

Some experimental interventions aim to block alcohol from disrupting fetal development in certain mechanisms. Idrus and Thomas (2011) well summarized six potential interventions. First, the use of N-methyl-D-aspartate (NMDA) receptor antagonists could protect against brain cell damage during the withdrawal period of maternal binge drinking (Idrus et al., 2011; Stepanyan et al., 2008; Thomas et al., 2001). Second, serotonin agonists could also prevent alcohol induced cell death (Druse et al., 2004; Zhou et al., 2008). Third, reducing the effects of alcohol on L1 neuronal cell adhesion molecules, could reduce alcohol's teratogenic effects

(Arevalo et al., 2008; Chen et al., 2001). Fourth, administration of neurotrophic growth factors, such as brain derived growth factors, could reduce teratogenic effects by mitigating alcohol-induced motor deficits or increasing neuron survival (Barclay et al., 2005; McGough et al., 2009; Mitchell et al., 1999b). Fifth, the use of antioxidants such as vitamins E, C, and β carotene have been shown to block alcohol's effects by reducing oxidative stress (Cohen-Kerem and Koren, 2003; Siler-Marsiglio et al., 2005). Finally, other nutritional factors could have an influence. Malnutrition has been seen to increase risk for FASD (May et al., 2000). Studies which supplement specific nutrients like zinc, folic acid, DHA, choline, vitamin A have demonstrated potential mitigating effects.

It is important to note that supplementing only one nutrient may not be the most effective solution and could actually have negative effects in terms of nutrient absorption. For example, iron supplementation can reduce zinc absorption (Idrus and Thomas, 2011) and vice versa (Sandstead, 1995) and therefore, could cause more harm than good. Rather, a balanced diet of many nutrients would likely be the most effective nutrition intervention (Idrus and Thomas, 2011).

Ballard et al. (2012) further emphasize that more research should be completed to see if a nutrition intervention could be a cost-effective method of reducing FAS. They state that although preventing alcohol consumption during pregnancy would be the best approach to prevent FAS, it is a difficult goal to achieve. They suggest that more work should be done to determine the effect of increasing vitamin supplementation in the population, especially among those of low socioeconomic status (Ballard et al., 2012). It is important to know the deficiency rates of these nutrients among pregnant women prior to intervening.

FASD programs in Canada

In Canada, there are many programs and organizations dedicated to FASD prevention and treatment (Canada FASD Research Network, 2015). The PHAC has developed a "Framework for Action" which includes five broad goals: increase awareness, develop and increase capacity, create effective national screening, diagnostic, and data reporting tools, expand knowledge base, and increase commitment and support for FASD (Public Health Agency of Canada, 2005). This framework can help guide future action on FASD. The Manitoba government and Healthy Child Manitoba have their own strategy called "Together We are Stronger" which has more specific goals such as ensuring that all Manitobans know that drinking during pregnancy can cause FASD, that information, support and services are provided to women of childbearing age, that assessments and diagnoses are available to anyone who might have FASD, that supports and services are evidenced based, and that service providers know the impact of FASD (Manitoba Government, 2007). Furthermore, the Manitoba FASD Centre in Winnipeg is involved in the multidisciplinary team diagnosis, treatment, and prevention of FASD. The four key pillars of the organization are assessment education, training, and research (Manitoba FASD Centre, 2015).

Some programs such as the Fetal Alcohol Spectrum Disorder Program target First Nations Canadians specifically. This program has five main objectives: "Building awareness of FASD in First Nations and Inuit communities, targeted interventions for women at risk of having a child with FASD, collaboration with communities to address broader determinants of health, education and training for front-line workers and health professionals, and early diagnosis and intervention for pre-school aged children with FASD and their families" (Stout and Harp, 2009).

The Strengthening Families Maternal Child Health and FASD programs that run in Manitoban reserves are also doing a great deal to prevent, diagnose, and treat FASD. However, there is limited data on the effectiveness of these initiatives which may be due to a lack of funding for program monitoring and evaluation. Unfortunately, FASD still exists and pregnant women still drink alcohol. Further interventions need to be initiated, specifically those that address the root causes of FASD and do not focus solely on informing pregnant women to stop drinking alcohol.

Alcohol and Fetal Alcohol Spectrum Disorder

To further understand how prenatal alcohol consumption affects the fetus we need to understand alcohol metabolism. This will lead to our understanding on how alcohol affects certain nutrients in the body and that nutrition could be a possible intervention for FASD. The rates of prenatal alcohol consumption will be discussed to further establish a need for intervention. Finally, biomarkers for alcohol exposure which help to confirm prenatal alcohol exposure will be highlighted.

Metabolism of alcohol

Alcohol, in the form of ethanol, is absorbed through the gastrointestinal tract, transported into the bloodstream, and then oxidized in tissues. In the liver, it is converted to acetyl aldehyde and then to acetate. The acetate is converted to acetyl CoA and oxidized by the TCA cycle producing energy. This occurs in the liver and tissues peripheral to the liver. One gram of ethanol produces 7 kcal of energy and it is metabolized by three key enzyme systems: alcohol dehydrogenase (ADH), the microsomal ethanol oxidizing system (MEOS), also known as the cytochrome P-450 system, and catalase, in the presence of hydrogen peroxide. However, most

(~98%) of alcohol is metabolized by the ADH or MEOS/cytochrome P-450 system (Gropper et al., 2008).

Alcohol is involved in many metabolic pathways such as glycolysis, the Krebs cycle, fatty acid metabolism and many other pathways. According to Ballard and colleagues (2012), "alcohol indirectly damages neurons by causing massive shifts in the flow of metabolism". Ballard also states that there is a correlation between FAS and certain polymorphisms in alcohol dehydrogenase (ADH). Some Native Americans may lack the FAS-protective ADH polymorphism, making them more susceptible to FAS (Ehlers et al., 2004; Green and Stoler, 2007). This could be true for Canadian First Nations peoples as well, but research is needed for this to be confirmed. According to Ballard and colleagues, "these massive shifts in metabolism and findings on ADH polymorphisms suggest there may be key players in the metabolic pathways that are inhibited or induced by alcohol" (Ballard et al., 2012). They explain that these "key players" could be specific nutrients such as vitamin A, which is metabolised by ADH, or other nutrients such as folic acid and choline that are involved in methylation pathways (Ballard et al., 2012).

Alcohol affects nutritional status by displacing the intake of nutrient dense foods and by affecting digestion and absorption of nutrients (Zajac and Abel, 1992) (See Figure 2). Furthermore, there is evidence from animal studies that some specific nutrients may mitigate the effects of alcohol on the fetus such as vitamin A (Kot-Leibovich and Fainsod, 2009; Yelin et al., 2007), folate (Craciunescu et al., 2004; Hewitt et al., 2011; Xu et al., 2006, 2008), docosahexaenoic acid (DHA) (Burdge, 1998) and zinc (Carey et al., 2003). These, and other nutrients, will be discussed in further detail in the nutrition section.

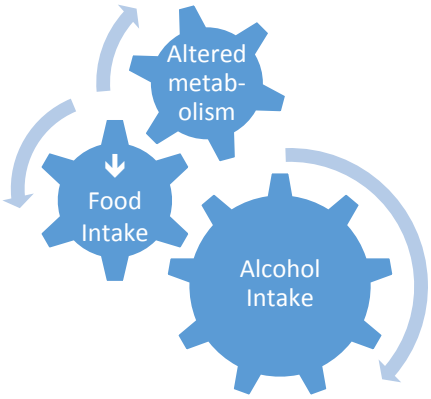

Figure 2: **Alcohol intake alters metabolism and decreases food intake**

Prenatal Alcohol Consumption Rates

Most of the data on alcohol consumption during pregnancy are based on reported rates which may be inaccurate because women may underreport their consumption patterns. Some studies have shown that when women are asked about alcohol consumption after the birth of the child they are more truthful and accurate (Alvik et al., 2006; Czarnecki et al., 1990; Floyd et al., 1999; Hannigan et al., 2010; May et al., 2008). This may be because to admit prenatal drinking patterns can be associated with a lot of shame, stigmatization, and trauma due to child apprehension and other child welfare interventions. Therefore alcohol consumption data from pregnant women who are drinking can be inaccurate.

Rates around the world

Maternal alcohol consumption rates vary around the world. In the United States, about 10.2 to 16.2 % of pregnant women report drinking during the previous month, and two percent report binge drinking during the previous month (Centers for Disease Control and Prevention, 2009). Australia and many European countries report higher prevalence (Malet et al., 2006;

O'Callaghan et al., 2003; Polygenis et al., 1998). In France, one study found that only 53% of women reported complete abstinence during pregnancy (Malet et al., 2006), indicating that almost half of the women included in the study continued to drink while pregnant. A study in Israel revealed that 14.1% of women reported alcohol consumption during pregnancy (Senecky et al., 2011).

Rates in Canada

The Canadian Community Health Survey (CCHS) includes data on heavy drinking, which is defined as having 5 or more drinks on one occasion, at least once a month in the past 12 months. In the latest survey, completed in 2011, over 1 million females 20-44 years old, who are of childbearing age, reported heavy drinking in the past month (Statistics Canada, 2014c). Since around half of all pregnancies are unplanned (Ian McDowell, 2015), women may not know they are pregnant and continue to drink after conception, even if they had intended to stop drinking if they got pregnant. This poses a huge risk for fetal exposure to alcohol. According to the Canadian Perinatal Health Report (2008), the rates of mothers who reported drinking alcohol during pregnancy were between 10.5-12.4% from 2000 to 2005 (Public Health Agency of Canada, 2008). The rates vary by province with lowest rates found in Newfoundland and Labrador and highest rates found in Quebec (Public Health Agency of Canada, 2008). These statistics do not include First Nations women living on-reserve (Statistics Canada, 2014b).

Rates among First Nation Canadians

Few studies have looked at alcohol consumption during pregnancy among First Nations Canadians. However, one study conducted interviews with men and women visiting Thompson from 21 Manitoban reserves and asked about alcohol consumption during pregnancy.

Interestingly, 51% of the women interviewed (n=242) reported that they had consumed alcohol during one or more of their pregnancies, whereas only 35% of men (n=224) reported that their partner had consumed alcohol during pregnancy (Williams et al., 1999). However, these rates may be inaccurately high because later in 2006, results of the 2002/2003 First Nations Regional Longitudinal Health Survey indicated that 15% of the women surveyed (female adults n=1815; female youth n=546) from 26 communities in Manitoba had continued to drink while they were pregnant (AMC Health Information Research and Governance Commitee et al., 2006), a rate that is about 3-5% higher than the national average, as noted above. The highest rate of alcohol consumption are found in females ages 15-17. Around 65% of these young women are consuming alcohol (AMC Health Information Research and Governance Commitee et al., 2006). Given that there are many teen pregnancies in some First Nations communities, this is an alarming rate.

Screening Tests and Biomarkers of prenatal alcohol consumption

As discussed above, alcohol consumption during pregnancy is largely underreported. There are some tools that are used as alcohol consumption screening tests which can identify women at risk for prenatal alcohol consumption. Some commonly used screening tools are AUDIT (Alcohol Use Disorders Identification Test), CAGE (Have you ever felt you needed to **C**ut down on your drinking?, Have people **A**nnoyed you by criticizing your drinking?, Have you ever felt **G**uilty about drinking?, Have you ever felt you needed a drink first thing in the morning (**E**ye-opener) to steady your nerves or to get rid of a hangover?), and T-ACE (**T**olerance: How many drinks does it take to make you feel high?, Have people **A**nnoyed you by criticizing your drinking?, Have you ever felt you ought to **C**ut down on your drinking?, **E**ye opener: Have you

ever had a drink first thing in the morning to steady your nerves or to get rid of a hangover?) (See Table 2) (National Institute on Alcohol Abuse and Alcoholism, 2015). These screening tools can be useful to identify at-risk women, but compliance and accuracy are still an issue.

Biomarkers can determine alcohol consumption up to a couple months after alcohol was consumed (Joya et al., 2012). There are indirect and direct maternal biomarkers for alcohol consumption. There is no single biomarker that perfectly represents maternal alcohol consumption. In fact many researchers suggest that a combination of markers should be used (Cook, 2003; Joya et al., 2012).

Table 2: Alcohol assessment tools
Source: Modified from (National Institute on Alcohol Abuse and Alcoholism, 2015)

CAGE		***T-ACE***	
C	Have you ever felt you should **cut down** on your drinking?	**T**	**Tolerance:** How many drinks does it take to make you feel high?
A	Have people **annoyed** you by criticizing your drinking?	**A**	Have people **annoyed** you by criticizing your drinking?
G	Have you ever felt bad or **guilty** about your drinking?	**C**	Have you ever felt you ought to **cut down** on your drinking?
E	**Eye opener:** Have you ever had a drink first thing in the morning to steady your nerves or to get rid of a hangover?	**E**	**Eye-opener:** Have you ever had a drink first thing in the morning to steady your nerves or get rid of a hangover?

Indirect maternal biomarkers

Liver enzymes can be measured in the blood to indicate alcohol consumption. Gamma-glutamyltransferase (GGT), aspartate aminotransferase (AST), alanine aminotransferase (ALT), or carbohydrate deficient transferrin (CDT) can all be measured. Also, the mean corpuscular erythrocyte volume (MCV) and plasma ratio of 5-hydroxytryptophol/5-hydroxyindolylacetic acid (5-HTOL/5-HIAA) changes with excessive ethanol use so can be used as a biomarker. The problem is that these indirect maternal biomarkers can only indicate chronic maternal alcohol use (Joya et al., 2012) and thus may not be useful for detecting binge drinking. This is a problem

because, as previously discussed, even small amounts of alcohol could have negative effects on the fetus and binge drinking is also known to be more dangerous to the fetus.

Direct biomarkers

Ethanol or the metabolites of ethanol can also be used as biomarkers. Fatty acid ethyl esters (FAEEs), ethyl glucuronide (EtG), or phosphaditylethanol (PEth) are metabolites which could be measured. FAEEs can be measured in the blood or hair of the mother or in the meconium of the neonate (Joya et al., 2012). Although these measurements might be accurate, the invasiveness of collecting blood, hair, or meconium make them a challenge to collect in a community setting.

Nutrition and Fetal Alcohol Spectrum Disorder

Proper nutrition in the mother (prenatal nutrition) and in the fetus (fetal nutrition) is very important for proper growth and development of the fetus. When alcohol is involved, nutrition status is compromised by decreasing intake and disturbing nutrient metabolism. Therefore, the following section will focus on the importance of prenatal nutrition and how certain nutrients are affected by alcohol. Furthermore, it will be discussed how supplementation of these nutrients in the presence of alcohol can possibly reverse or reduce the negative effects of alcohol.

The following section has two main points: (i) poor nutrition status of a pregnant woman who consumes alcohol can increase the risk that her fetus will develop FASD and (ii) promoting proper nutrition including supplementation of certain nutrients could be a promising intervention for FASD.

Maternal nutrition

Nutrition during childbearing age and pregnancy is very important. If a woman is malnourished during this stage in her life, there can be profound consequences on fetal development. Physiological changes during pregnancy lead to an increased need for macro and micronutrients to meet the nutritional demands of the woman and the fetus (Black, 2001). An inadequate intake of nutrients, as in the case of maternal malnutrition, is predictive of various labour and birth complications and infant and maternal diseases (Abu-Saad and Fraser, 2010; Brough et al., 2010; Garmendia et al., 2014; Gruszfeld and Socha, 2013; Imdad and Bhutta, 2012; Jiang et al., 2013). Nutritional requirements during pregnancy are discussed in this section.

Maternal size and weight gain

During pregnancy one of the commonly used indicators of proper nutrition is maternal size, or height and weight. According to Mahan and Escott-Stump (2007), increased maternal size generally means increased infant size. This is because maternal size is indicative of placental size which means more nutrients and oxygen can be transported to the fetus. Furthermore, maternal size is also related to the presence or absence of disease (Mahan and Escott-Stump, 2007).

Maternal weight gain during pregnancy is another important indicator of proper nutrition. A woman with a normal pre-pregnancy BMI (18.5-24.9) should gain 25-25 lbs or around 11-16 kg during her pregnancy. Women with lower BMIs (<18.5) should generally gain more and women with higher BMIs should gain less.

Obesity during pregnancy creates a risk for the mother and the fetus. Obesity increases risk for gestational diabetes, pregnancy-induced hypertension, caesarean section birth, late

pregnancy, term intrauterine fetal demise or miscarriage (Stephansson et al., 2001), very preterm (<32wks), infant with cardiac defect, macrosomia (birth weight >4000g), and doubles the risk of neural tube defects (Watkins et al., 2003). In fact, the protective quality of folate for preventing neural tube defects is less effective in obese women than women of normal weight (Watkins et al., 2003).

Nutritional requirements

Energy and macronutrients

Given the importance of maternal weight gain during pregnancy, it is clear that appropriate energy intake is important. Pregnancy and fetal growth increase the metabolic demands on the pregnant woman's body and requires more energy. If energy requirements are not met or energy is severely restricted, ketone production can occur, which can negatively affect the fetus.

Energy in the form of protein is also important. Although, since protein deficiency typically occurs together with energy restriction, it is difficult to know the specific effects of protein deficiency. Protein requirements are higher for a pregnant woman (71g/d) than a non-pregnant woman (46g/day) (National Research Council, 2005).

The requirement of carbohydrates for pregnant women is 135-175g/day which provides enough calories to prevent ketosis and enables proper blood glucose levels. Consumption of fibre in the form of whole grain breads, grains, and vegetables and fruits is also recommended. (National Research Council, 2005)

Although there is no specific recommendation for lipids during pregnancy, energy requirements will help determine the amount of fat in the diet. There are recommendations for n-

3 and n-6 (omega 3 and 6) polyunsaturated fatty acids, 1.4g/day and 13g/day respectively (National Research Council, 2005).

Vitamins

Certain vitamin intake levels are increased during pregnancy (see Table 3). Folic acid is required in greater amounts during pregnancy because of the increased demands of maternal erythropoiesis (production of red blood cells), fetal and placental growth, and prevention of neural tube defects. There are other nutrients which are important for reducing the possibility of neural tube defects. Vitamin B12 is a cofactor for methionine synthase, and plays a key role in folate metabolism. Iron, magnesium, niacin (Groenen et al., 2004), thiamine, niacin, and vitamin B6 might reduce orofacial clefts in addition to folate (Krapels et al., 2004). Also, choline plays a role by being a methyl donor (Zeisel and da Costa, 2009; Zeisel and Niculescu, 2006). Furthermore choline is important during pregnancy because of its role in structural integrity of cell membranes, cell signalling, and nerve impulse transmission. Vitamin B6 recommendations are increased during pregnancy because of increases in synthesis of non-essential amino acids in growth and vitamin B-dependant niacin synthesis. Ascorbic acid or vitamin C recommendation is increased. In large population studies, vitamin C deficiency has not been linked to negative pregnancy outcomes, however, some studies suggest a link between deficiency and preeclampsia and premature rupture of the membranes (Woods, 2001).

Table 3: Changes in Dietary Reference Intake recommendations during pregnancy
Source: (Institute of Medicine, 1997; National Research Council, 2001; National Research Council, 2005)

	Recommendations Increase for Pregnant women	Recommendations Do Not Change for Pregnant women
Macronutrients	Protein Carbohydrates Fibre n-3 PUFAs n-6 PUFAs	Fat
Vitamins	Vitamin C Vitamin B6 Folate	Vitamin A Vitamin D Vitamin E Vitamin K Thiamine Riboflavin Niacin Vitamin B12 Pantothenic acid Biotin Choline
Minerals	Copper Iron Zinc Magnesium Iodine	Arsenic Boron Calcium Chromium Fluoride Manganese Molybdenum Nickel Phosphorus Selenium Silicon Vanadium Potassium Sodium Chloride Sulfate

Minerals

The recommended intake of some minerals are also increased during pregnancy (see Table 3). Maternal blood supply is dramatically increased during pregnancy. This indicates a greater demand for iron. Therefore, iron recommendations are increased during pregnancy from 18mg/day to 27mg/day (National Research Council, 2001). Most women require iron supplementation to meet the iron needs of pregnancy. If a woman is iron deficient, her body will not be able to tolerate hemorrhage during delivery which can increase cardiac stress. Low iron levels can also impact the fetus. One possible impact is the reduction in hemoglobin production and therefore, a decrease in the transport of oxygen to the uterus, placenta, and fetus (Mahan and Escott-Stump, 2007).

Zinc is another nutrient that is important during pregnancy. The recommendations are increased by 3 to 5 mg for pregnant woman than for non-pregnant women (National Research Council, 2001). Zinc deficiency has been related to a variety of congenital malformations, abnormal brain development and behaviour in animal studies. Zinc deficient women in developing countries are more likely to give birth to a low weight infant (Rwebembera et al., 2006; Scheplyagina, 2005).

Although maternal copper deficiency may not affect the fetus, the recommendations are increased for pregnant women (National Research Council, 2001). Magnesium recommendations increase in pregnancy, partially because magnesium could reduce preeclampsia and intrauterine growth restriction (Institute of Medicine, 1997). Finally, recommendations for iodine increase during pregnancy. Iodine deficiency can cause neonatal cretinism where physical stunting and

mental retardation occur (Mahan and Escott-Stump, 2007). Adequate nutrition is clearly important in pregnancy, not only for the health of the mother, but the health of the fetus as well.

Fetal nutrition

Maternal nutrition clearly impacts the nutrition of the fetus. Malnutrition of the fetus often means that the birth weight of the baby is low (<2500g) or very low (<1500g). Low birth weight can increase perinatal mortality and other disorders such as necrotizing enterocolitis, respiratory distress syndrome, intraventricular hemorrhage, and cerebral palsy (Bernstein et al., 2000). Developmental delays and learning disorders such as attention deficit hyperactive disorder are also related to low birth weight.

Nutrients Affected by Alcohol

Nutrients are affected by alcohol by drastically changing their ability to be metabolized, utilized by the mother, and transferred effectively the fetus. The following sections will discuss how certain nutrients are affected by alcohol and how supplementation of these nutrients during pregnancy could potentially reduce the effects of alcohol on the fetus. Most of the studies on nutrient supplementation are completed with animals due to obvious ethical considerations which restrict completion of human studies. A detailed review on the nutrients involved in FASD has been published in our lab (Young et al., 2014).

Vitamin A (Retinol)

One of the most well-established nutrient interactions with alcohol is with vitamin A. Excessive alcohol metabolism is associated with a deficiency of vitamin A (Gropper et al., 2008). Ethanol affects retinol dehydrogenase (RDH) which is the enzyme that converts retinol to retinal. RDH is so similar to ADH that it competes with it and inhibits conversion of retinol to

retinal in the liver. A study on zebrafish *in utero* supports that ethanol inhibits acetyl aldehyde (Marrs et al., 2010). Also, alcohol consumption can cause a tolerance to vitamin A which means that the person would require more vitamin A from the diet to be healthy (Gropper et al., 2008). Vitamin A is a gene regulator and involved in neurogenesis (Ballard et al., 2012). Furthermore, vitamin A deficiency in mice has been shown to impair memory, long term potentiation, and signal transmission between two neurons, in mice (Conlon and Rossant, 1992). Ballard et al. (2012) suggest that one of the mechanisms of the phenotypic expression of FAS could be the retinoic acid-mediated pathway. The authors also note that any study on vitamin A supplementation as a mitigating factor of FAS should not fail to consider the teratogenic effects of vitamin A toxicity (Ballard et al., 2012).

Human Studies

There are no studies that look at the effect of vitamin A supplementation on ethanol induced fetal development effects in humans. This is due to ethical constraints. However, it would be of interest to measure the vitamin A status of acute and chronic alcohol users.

Animal Studies

One study examined *in utero* effects of retinoic acid supplementation in zebrafish exposed to alcohol. The alcohol exposed zebrafish had morphological defects and those that received vitamin A supplementation had fewer defects (Marrs et al., 2010). Another study looked at the interactions between ethanol and retinoic acid in Xenopus embryos. The findings suggest that the effects of ethanol is focused on the competition for the available retinaldehyde dehydrogenase activity at the onset of retinoic acid signaling during early gastrulation (Kot-Leibovich and Fainsod, 2009).

Folic acid

Folic acid is converted to tetrahydrofolate and is involved in moving single methyl groups around the cell which means it is a key coenzyme in many metabolic pathways and in the methylation of DNA. Ethanol inhibits folate metabolism, therefore effecting protein expression (Ballard et al., 2012). Ethanol also inhibits the intestinal absorption, renal reabsorption and cellular entry of folate (Hamid and Kaur, 2005; 2007; Hamid et al., 2007). Ballard and colleagues emphasize that "folate deficiency slows down metabolism, increases the number of errors in DNA replication, and induces the activation of many inappropriate genes through insufficient methylation in epigenetics" (Ballard et al., 2012). It is interesting to note that folate deficiency and FASD both have poverty as a risk factor (Ballard et al., 2012). This is further reasoning to promote improved nutrition among people of SES and consider the complex causes of poverty that impact nutrition status.

Human Studies

There are no studies that look at the effect of folate (folic acid) supplementation on ethanol induced fetal development effects in humans. However, there is evidence to support that folic acid supplementation can reduce neural tube defects which have some similarities to FASD (Burdge and Lillycrop, 2012).

Animal Studies

One study looked at the effects of chronic ethanol exposure and folic acid supplementations in the guinea pig. Folic acid supplementation did not prevent a decrease in folic acid in the brain and hippocampus but did prevent a decrease in hepatic levels in both the mother and the fetus (Hewitt et al., 2011). Another study showed that folic acid supplementation

prevents the development of cardiac dysfunction in fetal mice exposed to ethanol *in utero* (Serrano et al., 2010). Folate has also shown effects when acting against oxidative stress (see antioxidant section below).

Choline

There are three main cellular processes that choline and its metabolites are involved in: neurotransmission through acetylcholine, structural integrity of cellular plasma membranes and cellular signaling, and in folate independent pathways as a methyl donor via its metabolite, betaine (Ballard et al., 2012; Zeisel and da Costa, 2009). Choline is converted to phosphatidylcholine (PC), which is incorporated into the cell membrane and then converted to phospholipase D (PLD) for cellular signaling. If alcohol is consumed, the ethanol competes with water for the PLD catalyzed reaction of PC, impacting protein expression (Exton, 2002; Klein, 2005; Zeisel and da Costa, 2009).

Human Studies

There are no studies that look at the effect of choline supplementation on human fetal development when exposed to alcohol.

Animal Studies

A recent study looked at the effect of choline supplementation on specific neurons which are altered in FASD. Pregnant rat dams were fed with an alcohol containing liquid diet or control diet during gestational days 7 and 21 with or without choline. The results suggest that gestational choline supplementation prevents the adverse effects of alcohol on the neurons (Bekdash et al., 2013). Previous research from Thomas and colleagues has shown that perinatal choline supplementation can reduce the severity of FASD, specifically, hyperactivity and learning

deficits (Ryan et al., 2008; Thomas et al., 2000, 2004, 2007, 2009, 2010). The authors also have shown that choline supplementation during the early postnatal period could reduce the behavioral effects of alcohol, specifically those that rely on the functional integrity of the hippocampus (Ryan et al., 2008; Thomas et al., 2000).

A more recent study looked at the effects of developmental alcohol exposure and perinatal choline supplementation on hippocampal M1 and M2/4 muscarinic receptors in rats, which would indicate alcohol-related behavioural affects (Monk et al., 2012). Choline supplementation reduced hyperactivity, did not have an effect on the muscarinic M1 receptors, but had an effect on M2/4 receptors. The authors conclude that choline supplementation could reduce the alcohol-related behavioural changes due to developmental alcohol exposure that cause long-lasting changes in the hippocampal cholinergic system (Monk et al., 2012).

These studies show promising results that prenatal choline supplementation could reduce some of the effects of alcohol consumption on the fetus. They also provide information on the specific mechanisms that choline could be involved in. However, further research should be completed, specifically on any adverse effects of choline supplementation, before it is used as an intervention for FASD in humans.

Docosahexaenoic Acid (DHA, (22:6n-3))

Polyunsaturated fatty acids (PUFA) play various roles in the body such as in structural and functional components of cell membranes, in brain and nerve cells, in the promotion of normal growth and vision, and in gene regulation (Sizer and Whitney, 2014). One important PUFA, especially for pregnancy and fetal development, is docosahexaenoic acid (DHA (22:6n-3)). DHA can be consumed in the diet from fatty fish or it can be produced by the body by

elongation and desaturation of α-linolenic acid which is found in plant based oils such as flaxseed oil (Burdge and Calder, 2005). DHA is particularly important during fetal development because of its role in cognitive, visual, and CNS development (Horrocks and Yeo, 1999; Wen and Kim, 2004). Consumption of alcohol during pregnancy affects DHA status of the developing fetus. Consumption of omega 3 fatty acid rich foods is likely to be compromised when alcohol is consumed. Furthermore, alcohol reduces the bioavailability of DHA in the mother and decreases the transfer of DHA to the fetus through the placenta (Innis, 2007).

Human Studies

Few human studies have been conducted to determine the effect of alcohol on maternal and fetal DHA levels. However, one study compared cord blood serum from a control of women who consumed less than 2mL absolute ethanol per day with women who consumed more than 30mL absolute ethanol per day during their pregnancy (Denkins et al., 2000). The concentrations of DHA were higher in the cord blood of women who consumed more alcohol while pregnant, which is contrary to most of the literature. The authors suggest that this unexpected result could be because the analyses were performed at the end of pregnancy when maternal drinking had decreased considerably, partially due to the counselling provided to the women to reduce alcohol consumption. The authors also hypothesize an alternative view of the effect of alcohol on PUFA concentrations. They suggest that "the main effect of ethanol is to stimulate fatty acid catabolism. Fatty acid anabolism is then stimulated *in vivo* by a feedback mechanism in an adaptive response that serves to maintain tissue PUFA concentrations" (Denkins et al., 2000). Furthermore, the authors point out that although the serum cord blood concentrations of PUFAs were higher with higher alcohol consumption, the concentrations could be lower in specific

organs. For instance, the fetal brain may not be receiving as much PUFA if alcohol is being consumed (Denkins et al., 2000).

Animal Studies

Burdge et al. (1995) found that when adult female guinea pigs had alcohol both before and throughout pregnancy, the plasma and liver PUFA contents were unchanged even though there were decreases in phospholipid DHA concentrations in the fetal brains (Burdge and Postle, 1995). Perhaps the main point is that alcohol does impact PUFA and DHA metabolism and concentrations, which can impact fetal development. However, more research should be completed to determine the full effect of alcohol on PUFA and DHA concentrations.

A study on the effects of DHA enriched tuna oil and phospholipid levels in the brain of fetal guinea pigs exposed to ethanol during development revealed that DHA concentrations were significantly reduced in the group exposed to ethanol alone (Burdge, 1998). The group that received ethanol plus the DHA enriched tuna oil had increased DHA levels and the levels were similar to the control group. According to these results, DHA supplementation could reverse the negative effects of alcohol on DHA concentrations (Burdge, 1998).

Zinc

Zinc is important for fetal development because it plays an important role in DNA, RNA, protein and cell synthesis, and brain development (Cano et al., 2001; Chen et al., 2001; West et al., 1994). Consumption of alcohol during pregnancy reduces the availability of maternal zinc in the plasma and therefore reduces the amount of zinc that can be transported through the placenta to the fetus, which causes fetal zinc deficiency (Ghishan and Greene, 1983; Summers et al., 2009).

Human Studies

Since alcohol induced zinc deficiency and supplementation studies cannot be conducted in humans, we must rely on animal studies for the basis of zinc supplementation.

Animal Studies

Animal studies on alcohol induced zinc deficiency and supplementation have conflicting results. An early study on rats revealed that zinc supplementation did not increase placental uptake and transport of zinc to the fetus (Ghishan et al., 1982). Another study saw that maternal zinc supplementation did not improve ethanol induced Purkinjie cell loss in the fetal rat brain (Chen et al., 2001). However, when pregnant mice were injected with ethanol and fed a zinc supplemented diet, the fetuses had fewer incidences of birth defects than the group that had alcohol injections but did not have the zinc supplemented diet (Summers et al., 2009). Furthermore, the incidence of physical abnormalities among fetal mice was lower in a zinc supplemented ethanol group than those exposed to ethanol alone (Carey et al., 2003). Given the inconsistencies in these studies, it is difficult to say whether zinc supplementation could be used to reduce the negative effects of alcohol on a human fetus.

Antioxidants

Some of the negative effects of alcohol on fetal development have been linked to oxidative stress (Cohen-Kerem and Koren, 2003). In fact, oxidative stress has been recognized as one of the mechanisms to ethanol toxicity (Abel and Hannigan, 1995). Ethanol induces oxidative stress through various mechanisms such as by formation of free radicals and reactive oxygen species (ROS), and by reducing intracellular antioxidant capacity (Cohen-Kerem and Koren,

2003). Antioxidants can reduce oxidative stress at the cellular level. Some vitamins and minerals such as vitamin E, vitamin C, β-carotene, selenium, folate, and zinc have antioxidant activity.

Human Studies

There are no studies on the effect of antioxidants on the alcohol exposed human fetus. However, antioxidants, namely vitamin C and vitamin E, have been shown to reduce the occurrence of pre-eclampsia in women with no adverse effects to the fetus or mother noted (Chappell et al., 1999). However, according to review authors Cohen-Kerem and Koren (2003), there are mixed results from animal studies and therefore, using antioxidants as a treatment for alcohol-induced damage in humans is difficult to justify (Cohen-Kerem and Koren, 2003).

Animal Studies

There are no studies that look at the effects of vitamin C on reducing alcohol teratogenicity however, vitamin C has antioxidant properties and works together with vitamin E to stabilize α-tocopherol (Cohen-Kerem and Koren, 2003).

An early study on vitamin E supplementation to prevent ethanol teratogenicity failed to show a protective effect in rats (Tanaka et al., 1988). Chung et al. (2009) showed that vitamin E supplementation did not inhibit ethanol-induced changes in retinoic acid catabolism or prevent ethanol-induced hepatocyte hyper proliferation in the rat liver (Chung et al., 2009). However, an *in vitro* study showed that vitamin E supplementation reduced alcohol-induced oxidative effects at low levels of alcohol exposure in fetal rat hippocampal cultures (Mitchell et al., 1999a). Rat pups exposed to alcohol consuming a vitamin E supplemented diet had less Purkinjie cell loss than those who were exposed to alcohol with no vitamin E supplemented diet (Heaton et al., 2000).

In alcohol exposed conditions, selenium is sequestered into the plasma to prevent oxidation but this means there is reduced maternal hepatic storage of selenium, therefore reducing the available selenium for the rat pup (Ojeda et al., 2009b). However, selenium supplementation alleviates the oxidative imbalances (Ojeda et al., 2010).

Finally, folate also has antioxidant properties. One study found that high dosage of folic acid reduced oxidative stress in the maternal rat liver and pancreas (Cano et al., 2001). However, the authors did not study oxidative stress in the brain which would be more relevant to FAS, considering brain damage is a concern.

Overall, studies that look at the effects of antioxidants on ethanol-induced oxidative stress have mixed results. Further research is needed to confirm whether or not antioxidant therapy could be used in humans to mitigate or reduce the effects of alcohol on fetal development.

Other nutrients

Other nutrients have been studied in regards to mitigating the negative effects of alcohol. For instance, there is good evidence that zinc and other nutrients, including copper (Cu), iron (Fe), magnesium (Mg), selenium (Se), methionine, choline, vitamin B12, and folate, can modulate alcohol's developmental toxicity (Keen et al., 2010). Some of these nutrients have not been discussed in detail because they lack thorough research into the potential effect on FASD.

It is possible that supplementation of multiple nutrients would be a potential intervention. Some of the nutrients show more promising results than others, namely, DHA, folate, zinc, vitamin A, and choline. However, there may not be one nutrient that could have a "magic" fix for reducing the effects of alcohol but rather a combination of nutrients and overall improvement of

nutrition status. The results from one study suggest that supplementation of both folic acid and vitamin B12 reduces the negative effects of alcohol on the fetus more than supplementation of a single nutrient (Xu et al., 2006). Furthermore, since most of the previously discussed nutrients have not been studied using human subjects it is impossible to confirm that the nutrients would have the same effect in humans as in animals.

Nutritional status among pregnant First Nations women

Importance of nutritional status information and associated factors

There are many implications of malnutrition during pregnancy. Therefore, it is important to know what the nutrition status is of pregnant women. First Nations people in Canada, especially those living in remote or Northern areas, have a unique set of challenges related to nutrition because of lack of access to a variety of foods, environmental contamination of traditional food sources, and other factors (Chan, 2012).

Lack of nutritional status information among pregnant First Nations women

There is a lack of data on food consumption patterns and nutritional status relating to alcohol consumption among pregnant First Nations women. This gap must be addressed before prenatal nutrition interventions can be effectively planned and implemented. The gap in nutrition data among pregnant First Nations women is largely due to the fact that the national health survey, the CCHS, excludes First Nations people living on-reserve (Statistics Canada, 2014b). This means about 55% of the First Nations population in Manitoba are excluded (Statistics Canada, 2010). The report also excludes homeless populations in Canada, because CCHS is limited to Canadians with a permanent address. These populations are often the most vulnerable to food insecurity and malnutrition (Tarasuk et al., 2012). Furthermore, the nutrition related

questions in the CCHS are limited to fruit and vegetable consumption and vitamins and mineral supplement use and there are limited questions that are specific to pregnancy (only alcohol and smoking use) (Statistics Canada, 2014b). One study that includes First Nations people living on-reserve, the First Nations Food, Nutrition, and Environment Study (FNFNES), excludes pregnant and lactating women (Chan, 2012). A few small studies had been completed in specific First Nations reserves, but have limitations, however. For instance, one study conducted in 1999focuses on a single nutrient, vitamin D and the study is 15 years old (Waiters et al., 1999). Another study relied on participant reports of whether or not they usually ate breakfast, lunch, supper and/or snacks and it does not provides a thorough picture of nutritional status during pregnancy (Wenman et al., 2004). A third study, an Aboriginal birth cohort study, is being conducted among pregnant women and their newborns from the Six Nations Reserve in Ontario. A retrospective chart review was completed, resulting in some nutrition-related information like weight gain and smoking during, but no dietary intake assessments were completed (Oliveira et al., 2013). Another study by the same group plans to collect biological data during antenatal visits including hemoglobin, diabetes biomarkers, and lipid profile (Wahi et al., 2013), however the results have yet to be published. Therefore there is a major gap in nutrition research among pregnant First Nations women, especially those living on-reserve.

In spite of this lack of data, there is reason to believe that food insecurity and malnutrition levels are higher among First Nations women than the overall Canadian population. The 2011 CCHS, estimates that 27% of off-reserve Aboriginal households across Canada experience food insecurity, a rate that is more than double that of all Canadian households (Kuhnlein et al., 2014). Rates on-reserve are even higher. According to the First Nations Food Nutrition and Environment (FNFNES), 38% of participants living on-reserve in Manitoba

reported experiencing household food insecurity and 31% of households reported that they could not afford to eat a 'balanced meal' (Chan, 2012).

Furthermore, a comparison of the recommended intakes for nutrients during pregnancy and the typical intake for women of childbearing age in First Nations communities in Manitoba reveals potential deficiencies in fibre, vitamins A, D, C, B6, and folate, as well as minerals, calcium, iron, zinc, and potassium (see Table 4). However, there is no data on pregnant women specifically. Furthermore, experts on FASD in First Nations communities emphasize that there is a need for studies on eating habits and diet of pregnant First Nations women, specifically studies that compare diet with blood and urine metabolites. This demonstrates the need for a study which identifies if pregnant First Nations women are malnourished, if there are any major gaps in dietary intake of certain foods, and what specific nutrients could be lacking. Also, if a nutrition intervention is necessary, potential intervention targets needs to be identified such as what types of foods need to be promoted or if promoting First Nations traditional foods use is possible.

Need for a new dietary assessment research tool

In order to improve upon this lack of data and address this research gap, an appropriate dietary assessment research tool is required. To our knowledge, there is no nutrition research tool that has been developed specifically for pregnant First Nations women who are at risk for alcohol use. The development of such a research tool should have an understanding of First Nations culture, philosophy of health and well-being, food availability and accessibility, food consumption and sharing patterns and should consider the literacy level of some respondents. These issues indicate that it is necessary to develop an effective, culturally appropriate and

visually interactive nutrition research tool that focuses on FASD-related nutrients and is specific to women at risk for alcohol consumption during pregnancy.

Table 4: Comparison of Dietary Reference Intakes for pregnancy and nutrient intakes among women of childbearing age in First Nations communities in Manitoba
Source: (Chan, 2012; Health Canada, 2011)

Dietary Reference Intakes: Pregnancy Health Canada, 2011					**Nutrient Intakes MB FN Women** FNFNES, 2010 Manitoba
Nutrient		**Age**			
	Units	<18 y	19-30 y	31-50 y	19-50y
Reference Values for Macronutrients					
Carbohydrate	g/day	175	175	175	241
Total protein	g/day	71	71	71	75
Total fat		ND	ND	ND	80
Linoleic acid n-6	g/day	13	13	13	14
α-linolenic acid n-3	g/day	1.4	1.4	1.4	1.4
Total fibre	g/day	28	28	28	12
Total water	L/day	3	3	3	ND
Reference Values for Vitamins					
Vitamin A	µg/day	750	750	750	317
Vitamin D	µg/day	15	15	15	3.6
Vitamin E	µg/day	15	15	15	ND
Vitamn K	µg/day	75	90	90	ND
Vitamin C	mg/day	80	85	85	78
Thaimin	mg/day	1.4	1.4	1.4	1.6
Riboflavin	mg/day	1.4	1.4	1.4	1.9
Niacin	mg/day	18	18	18	35.8
Vitamins B6	mg/day	1.9	1.9	1.9	1.3
Folate	µg/day	600	600	600	304
Vitamin B12	µg/day	2.6	2.6	2.6	4.3
Pantothenic acid	mg/day	6	6	6	ND
Biotin	µg/day	30	30	30	ND
Choline	mg/day	450	450	450	ND
Reference Values for Elements					
Arsenic		ND	ND	ND	ND
Boron		ND	ND	ND	ND
Calcium	mg/day	1300	1000	1000	549
Chromium	µg/day	29	29	29	ND
Copper	µg/day	1000	1000	1000	ND
Fluoride	mg/day	3	3	3	ND
Iodine	µg/day	220	220	220	ND
Iron	mg/day	27	27	27	13.9
Magnesium	mg/day	400	350	360	226
Manganese	µg/day	2	2	2	ND
Molybdenum	mg/day	50	50	50	ND
Nickel		ND	ND	ND	ND
Phosphorus	mg/day	1250	700	700	1055
Selenium	µg/day	60	60	60	ND
Silicon		ND	ND	ND	ND
Vanadium		ND	ND	ND	ND
Zinc	mg/day	12	11	11	10.4
Potassium	mg/day	4700	4700	4700	2346
Sodium	mg/day	1500	1500	1500	3264
Chloride	mg/day	2300	2300	2300	ND

CHAPTER 2: RESEARCH PLAN

Rationale

FASD is a public health concern around the world. In Canada, it is estimated that 9 in every 1000 babies born have FASD (Public Health Agency of Canada, 2012) and a much broader range of 7.2 to 61 FASD per 1000 live births among First Nations peoples (Williams et al., 1999; Square, 1997; Asante, 1985). Since First Nations populations have a higher birth rate and younger demographic compared to non-Aboriginal populations (Statistics Canada, 2014a) , it is of particular concern given the host of maternal and child health-related challenges they face.

The main risk factors for FASD are related to alcohol consumption such as intake patterns like binge drinking and socio-cultural acceptance of alcohol consumption. Other risk factors include maternal characteristics like age, gravity, parity, socioeconomic status, and nutrition status. Nutritional status and alcohol consumption interact in several ways. When alcohol is consumed, digestion and absorption of nutrients is altered, and these nutrient-poor calories displace nutrient rich foods (Zajac & Abel, 1992). For the developing fetus, there may be protection from the negative effects of alcohol when the mother consumes specific nutrients important for fetal brain development. Animal models suggest that consumption of vitamin A (Yelin et al., 2007; Kot-Leibovich et al., 2009), folate (Craciunescu et al., 2004; Xu et al., 2006,2008; Hewitt et al., 2011), choline (Ballard et al., 2012; Bekdash et al., 2013; Zeisel, 2011), docosahexaenoic acid (DHA) (Burdge, 1998), and zinc (Carey et al., 2003) could mitigate some of alcohol's effects on the fetus. These findings indicate that foods containing the specific nutrients have potential mitigating the adverse effects of FASD.

The quantity and quality of food intake play significant roles in health and quality of life and contributes to the decrease of many chronic diseases. This indicates that diet is a major modifiable risk factor for overall improvement of health. Knowing that alcohol affects specific nutrients in the mother and therefore compromising the nutrition of the fetus, a healthy nutrition status may reduce the severity of FASD. However, there is limited food habits and diet information on pregnant First Nations women. This poses a gap in the research that needs to be addressed in order for nutrition provisions to be properly informed and effective. Experts on FASD in First Nations communities emphasize that there is a need for studies on eating habits and diet of pregnant First Nations women.

Having an appropriate dietary assessment research tool is critical to address this research gap. Existing dietary assessment tools often focus on a few select nutrients or are specific to a certain population or disease sate. To our knowledge, there is no nutrition research tool that has been developed specifically for pregnant First Nations women who are at risk for alcohol use. That is, including a focus on assessing dietary intake of foods that are rich sources of nutrients which are important for fetal brain development, especially in the case of fetal alcohol exposure. The development of such a research tool should have an understanding of First Nations' culture, philosophy of health and well-being, food availability and accessibility, food consumption and sharing patterns and should consider the literacy level of some respondents. These issues indicate that it is necessary to develop an effective, culturally appropriate and visually interactive nutrition research tool that focuses on FASD-related nutrients and is specific to women at risk for alcohol consumption during pregnancy. This must be done with the involvement of women and key stakeholders using a participatory approach to engage with potential participants and their communities.

Research Objectives

This study, as the first phase of a series of studies will address the research gap by:

(1) Developing a First Nations-specific, interactive tablet research tool, called *Nutrition for Two*, that combines nutrition, alcohol consumption, pregnancy, and the social determinants of health that influence access to food.

(2) Reviewing and evaluating the tool with various groups and pre-testing the research tool with a sub-sample of the population, using participatory methods to engage with women and their communities.

Study Population

This study started with community engagement with on-reserve communities in rural Manitoba. These communities are located 2-4 hours' drive from an urban centre. The food available in the communities is limited and often overpriced. As described in the following manuscripts, this community engagement lead us to further engagement with prenatal programs in Winnipeg, Manitoba. This is where the *Nutrition for Two* tool was pretested.

The target population for *Nutrition for Two* is pregnant First Nations women at risk for alcohol consumption during pregnancy. *Nutrition for Two* was pre-tested with pregnant women living in the Point Douglas area of Winnipeg, Manitoba, Canada. Although these women are not living on-reserve, which is where the major nutrition research gap exists, they have similar socioeconomic status, culture, and access to food. These women, most of whom are First Nations, attend programs for women who may be consuming alcohol and/or using drugs during pregnancy by providing support such as prenatal visits, healthy meals, and social support. Many

of them live fairly transient lives and have experienced trauma and the effects of marginalization and colonization (Mothering Project program manager, personal communication, 2014).

CHAPTER 3: CHALLENGES AND SUCCESSES PARTICIPATORY PRENATAL DIETARY ASSESSMENT RESEARCH AMONG FIRST NATIONS WOMEN AT RISK FOR ALCOHOL USE

Introduction

Fetal Alcohol Spectrum Disorder (FASD) is a health concern that is over-represented in some First Nations communities (Chudley, 2008; Chudley et al., 2005; Public Health Agency of Canada, 2006; Square, 1997) . Many FASD prevention strategies focus on encouraging women to abstain from alcohol during pregnancy. However, since the risk factors for FASD are highly connected to the social conditions within which women live, abstinence is not always a feasible solution (Salmon, 2011). For some women, alcohol use during pregnancy is more than just a decision to drink or not to drink. It is often connected to dangerous, painful, or traumatic experiences (i.e., experiences of violence, sex trade work, poverty, abuse, etc.) (Salmon, 2007). In addition there are a whole host of factors, other than alcohol consumption patterns, that influence the severity of FASD (May and Gossage, 2011). One key factor that has often been overlooked is prenatal nutrition. Improving prenatal nutrition among women who may drink alcohol during pregnancy is a potential harm-reduction approach to FASD. However, there is a lack of data on food consumption patterns and nutritional status relating to alcohol consumption among pregnant women, especially among First Nations women. This gap must be addressed to provide the basis for future prenatal nutrition interventions. To address this gap, research involving pregnant First Nations women who may be drinking alcohol during pregnancy, must use participatory methods. This paper describes the participatory methods used in starting a prenatal nutrition assessment study among First Nations women living in Manitoba.

There are 4 main characteristics that are common for this population: Aboriginal, pregnant, female, and at risk for alcohol and/or drug use. These factors, among others such as poverty, indicate that this population is a vulnerable population. This why it is particularly important that research with this population be conducted with continuous guidance from community leaders and the target group themselves, in order for the whole process to be sensitive to their vulnerability, respectful, and community-specific.

Unfortunately, there is a history of colonizing research among Aboriginal people. It has been argued that research among Aboriginal women conducted by non-Aboriginal scholars is connected deeply to experiences of colonization and imperialism (Smith, 2012). Aboriginal women, especially those living in poverty or those who use substances, have been "treated as objects of study rather than experts of their lives and the conditions that mediate them" (Salmon, 2007). This paper aims to describe methods of respectful research that attempts to give women back their voice in research. We hope to shed light to the fact that the inherent nature of scientific research can be a barrier to respectful research among this population.

Ethical Approaches

This study was guided by the principles of the Canadian Institutes of Health Research Guidelines, "Health Research Involving Aboriginal peoples" and the Tri-Council Policy Statement, "Ethical Conduct for Research Involving Humans". Ethical approval has been granted by the University of Manitoba Health Research Ethics Board (H2013:263). We collaborated in discussions with the regional nurse advisor of the Assembly of Manitoba Chiefs (AMC) and presented the research proposal at the AMC Health Information Research Governance Committee (HIRGC) (Aboriginal health research ethics board) semi-annual board meeting.

Community engagement for research on-reserve

Since there is a large research gap in prenatal nutrition among Aboriginal women living on-reserve, our study started with the goal to ultimately recruit pregnant women who live on reserve. We started to build upon existing relationships with leaders in the community who coordinate health programs.

Round table with community leaders

With an existing connection to the Strengthening Families Maternal Child Health (SF-MCH) program which runs in 14 First Nations communities in Manitoba, an initial presentation was made to the community coordinators. A copy of the study plan and a draft of the research tool, including a food frequency questionnaire (FFQ), was provided to each coordinator. Each question was reviewed for clarity and appropriateness for the target population. An open discussion was held at this meeting and the coordinators provided feedback on ensuring confidentiality, appropriate wording of questions, and what foods to include or exclude from the FFQ. The research tool was revised based on the feedback.

Another presentation was made to the community coordinators of the FASD program that runs in 7 First Nations communities in Manitoba. A discussion was held at this meeting and feedback on the study plan was provided. Community coordinators representing a total of 18 communities showed their interest in being involved in our study and also indicated that pregnant women in their community might be interested in participating.

Based on feedback received from these discussions, it was determined that the research tool should be in a more interactive format than just as a paper questionnaire, especially considering the extensive and detailed FFQ component and the literacy level of some potential

participants. In collaboration with Function Four Ltd. (Winnipeg, Manitoba), a software development firm, the paper form was converted to a tablet version which is named *Nutrition for Two.* This allowed for the FFQ component to be more interactive and easy-to-use for participants.

Community visits and forums

With pre-arrangement, we visited two reserve communities in the Dakota Ojibway Tribal Council region. The purpose of these visits was to identify if our study is in line with the communities' health priorities and to assess if potential participants were interested in our study. We also held on-going communication with health directors and SF-MCH coordinators, especially in those communities that showed particular interest in participating in the study.

Community 1

In collaboration with SF-MCH research team, we held a small forum on health priorities in the community. There were about 20 community members in attendance, with mainly middle-aged women, a couple elders, teen girls and young adult women. There were also 1-2 nurses from outside the community in attendance. The forum began with an introduction of our purpose of the visit. The discussion was about what the main health problems in the community and why. It was a loosely structured discussion, where the community members were encouraged to tell stories and take the discussion where they wanted to. Some of the key contents of this discussion are as follows.

Root causes of health issues

The discussion participants suggested some of the root causes to health problems in their community as mental health issues such as depression, anxiety, or suicidal tendencies, lack of

self-esteem, and imbalance of four components of health: physical, mental, emotional, and spiritual. They suggested that the priority should be on the individuals' balance before the balance of the group/community. They also talked about the lack of self-identity and emotional maturity (knowing how to identify when you are feeling an emotion, what might be causing that, and what to do about it) as causes of health problems in the community.

Problems that stem from these causes

The discussion participants identified the main problems that stem from the causes are relationship issues such as abuse, promiscuity, mistrust, a broken cycle (balance among people was broken by horrors in residential schools, taken away from families), alcohol and drug abuse, malnutrition (becomes a lower priority to feed children when personal and family health/life is unsettled), wasting time and money on VLTs (video lottery terminal) (used as a coping strategy, elders give up and go to VLTs), and a lack of fatherly presence in many homes.

Problem solving methods currently used

To address relationship issues like abuse, one woman reported that she has started a women's support group in the community. It was also discussed that there are shelters for abused women, but they are quite far away from the community in urban centers. Some participants suggested that telling their men to leave the house does not help. Some identified that they do not have the self-esteem to leave relationship because of not feeling good enough, or that they do not deserve better or do not feel loved or worthy of love. Some general health problem solving methods were also identified. For example, it was suggested to get help from community elders, especially for helping to gain self-identity, and to pass on family values and language to the next generation, putting children first in caring for the whole community. There were also a few

programs that were identified as addressing some of the problems in the community such as a women's self-esteem program, a counselling skills program, residential school therapy sessions, and alcoholics anonymous. However, limitations of the programs were discussed. Many of the programs were located outside of the community, were led by non-Aboriginal people, or did not help to address the root causes of the problems.

Suggested solutions

Some of the suggested solutions or changes included an after-hours counselling support for mental health issues, or parenting skills support, which should include aunts and grandmothers. It was emphasized that community members should be trained to help their own community and that future programing should not separate mental, emotional, spiritual, and physical health.

From this forum, it was clear how well the participants were able to identify the main health issues in the community, root causes of the problems, and potential solutions. Based on the discussion, prenatal nutrition among women at risk for alcohol consumption was not identified as a top health priority for this community. While keeping this in mind, we attempted to invite the community to participate in our study with an official invitation letter. There was no response from the community so no further contact was made because we wanted to respect their decision.

Community 2

In collaboration with SF-MCH research team, we held a small forum on health priorities in the community with various community members. There were about 20-30 community members in attendance at this group discussion, including elders, middle-aged people, and a

couple of young people. There were more women than men in attendance. We began with an introduction of the purpose of the meeting and identified 2 key questions to be covered: i) what are the health priorities in your community? and ii) what does research mean to you? We had planned to also include two questions on the resources available in the community but were unable to cover these topics due to time constraints.

Health Priorities

For the first question, we divided the group into small groups to discuss the health priorities for key sub-groups of the community: women, pregnant women, families, youth, and the community at large. Some of the key health priorities identified for women included improving parenting and life skills and passing on traditional cultural and medical knowledge. For pregnant women, improving nutrition and healthy eating education, a focus on preventive care, and supporting women to access regular prenatal care that includes using traditional medicines were identified. For families, improving infrastructure like homes without mold and more play structures for children, as well as having parenting support groups and improving healthy eating were highlighted. For youth, physical fitness and nutrition, as well as mental health and sexual health and education were identified. For the general community, it was discussed that adding more support groups for women, youth, and men, and improving the access to health services by creating awareness, and adding more health workers in the community would be beneficial.

Perspectives on research

For the second question, we asked for participants' perspectives on what research is to them and if it could be part of a solution to address some of these health priorities. The attendees

perceived that research is for new ideas and an opportunity to improve. It was emphasized that research should be up front and open with the community. They mentioned that some researchers in the past had an agenda for the community and did not allow the community to make the research decisions. It was also expressed that research could help the community to know or re-gain the knowledge of why traditional foods are most healthy – to re-learn the traditions. These are all important points that we as researchers have to keep in mind when building relationships with communities to conduct research that aims to improve health outcomes.

Since prenatal nutrition was suggested as a community health priority, we further initiated community involvement in the study with discussion with FASD program and SF-MCH program community coordinators. This led us to present the study to four pregnant women who participate in the Canadian Prenatal Nutrition Program (CPNP) prenatal nutrition class. The study plan was well received and three women indicated their interest in participating in the study. However, after providing an official invitation, the community declined involvement at health director level since another study was selected in the community. No further contact was initiated in this communities except to have the SF-MCH coordinators review our research tool.

Community engagement for research off-reserve

After our attempts at recruiting women living on-reserve, we began the process of recruiting women living in Winnipeg. Winnipeg is a unique place for health research among First Nations people. According to the 2011 National Household Survey (NHS), First Nations people represented 3.6% of the total population of Winnipeg, compared to 1.6% in Edmonton and 0.7% in Vancouver (Statistics Canada, 2014a). A large portion of First Nations people in Winnipeg live in the Point Douglas area. The population in Point Douglas is nearly 30%

Aboriginal, compared to 10% in the whole of Winnipeg. About 60% of the population over 15 years old hold some certificate, diploma or degree, compared to nearly 80% in all of Winnipeg. The unemployment rate is 8.3% compared to 5.2% overall. The average household income in Point Douglas is $40,703 compared to the overall Winnipeg average of $63,023 (City of Winnipeg, 2006).

The target population for our study was pregnant First Nations women at risk for alcohol consumption during pregnancy. These women, most of whom are First Nations, attend programs for women who may be consuming alcohol and/or using drugs during pregnancy by providing support such as prenatal visits, healthy meals, and social support. Many of them live fairly transient lives and have experienced trauma and the effects of marginalization and colonization (Mothering Project program manager, personal communication, 2014). Women may lack appropriate housing and move from house to house, staying with families or friends. Furthermore, women may even move from a remote reserve to an urban centre and back again. Interestingly, statistics show there is a sort of back and forth nature to migration to and from reserves. Overall, the net migration rates of registered Indians on reserves from 1996 to 2006 were positive, meaning more people were migrating back to reserves than leaving. This is contrary to popular belief that suggests that people are leaving reserves to find a better life in the city (AboriginalAffairsandNorthernDevelopmentCanada, 2013).

There are many challenges to locating and inviting women who deal with substance abuse issues to participate in a study that includes questions on alcohol use during pregnancy. This could be partially due to the transient lifestyle that many of the women live, but is more likely also a result of stigmatization of substance use and FASD. Many women who use

substances experience guilt, shame, and trauma during pregnancy (Salmon, 2007). Many of the women who would be eligible to participate in our study may have had traumatic experiences of disclosing substance abuse and having their children apprehended, or having increased observation or investigation by social service, medical, and criminal justice authorities (Boyd and Roach, 1999). These struggles that women face are their reality. It means that the typical recruitment methods recommended by research ethics boards and used by many studies, such as putting up posters and inviting potential participants to contact the researcher, will not work. Some level of trust must exist before women are willing to participate. One method of creating this trust is to collaborate with community leaders (Salmon, 2007) and/or home visitors whom the women trust. In our study, we began by building relationships with women through volunteering and then we collaborating with the Program Manager of the Mothering Project in order to invite women to participate.

Volunteering with community program

The Mothering Project (Manito Ikwe Kagiikwe) at Mount Carmel Clinic (Winnipeg, MB) supports women who are pregnant or have a child up to 2 years old dealing with substance abuse issues. The program serves primarily First Nations women and provides a one-stop-shop for child care, health care, prenatal care, social supports, one-on-one support, group programing, and advocacy. Some of the major strengths of this program are that is it culturally grounded, trauma informed, harm reduction oriented, and has a focus on kindness. When the program was first launched in 2013, 100% of the clients were using drugs and alcohol, 90% reported significant trauma history, and 79% did not have prenatal care. After a two year period, 36% reported they abstained from using drugs and alcohol and 47% reported they have reduced their substance use

(The Mothering Project brochure, Mount Camel Clinic), indicating the program is making a difference.

Through connections with the Program Manager it was found that there was an interest on both sides for a volunteer with a background in dietetics. During the initial meeting there was a discussion on how to incorporate volunteer skills with potential projects for the summer. These included building and planting a small garden and using the harvest to make food for drop-in, teaching women both food skills and nutrition along the way. The benefit of having a physical activity to do, such as planting or cooking with the women and their children, was to provide an informal method of sharing an experience with clients and allowing trusting connections to be built. Relationship building, however, was not quick or simple. It took over 6 months of weekly volunteering to become part of the "landscape" of the Mothering Project. Although the depth and meaning of our relationships were different than that of clients to their outreach workers, women felt comfortable bantering, asking questions, and sharing some of their own stories with us. As noted in our own interactions, as well as that of support workers to clients, humour was integral to making connections. It was necessary to seek constant ideas and advice on what clients wanted to eat or learn to cook so that they would feel like the drop-in was meeting their needs and also to create more interest in participating.

Volunteering at this clinic required flexibility to meet the needs of program at each point in time and respond to changes in seasons, resources, and staff. Most importantly though, was the longevity and consistency of being there. Being a reliable face in the kitchen or garden meant that the effort to get to know each other would not be in vain. A few months in to volunteering, the Program Manager suggested collaboration between the program and a potential research

project. There was strong support within the management team at the Mothering Project for food and nutrition to be part of client care, and this became essential for moving forward with nutrition-focused research.

Collaboration with community leaders

The Program Manager of the Mothering Project, Jane[1], helped us by allowing us to put up recruitment posters at the drop-in area and to attend the weekly drop-in in order to meet and connect with potential participants. Jane recommended that we meet with the Mothering Project Women's Advisory Committee, a group of about 8-10 former and current participants as well as staff and program leaders, to explain the proposed study objectives and design to them, get their feedback and their support to continue meeting with potential participants and begin recruitment. Having a connection with this committee was critical as they guided us on what we should or should not do. Once the committee was informed with our study, they recommended us to attend the weekly drop-in to connect with potential participants and to begin collecting data on the same day as the drop-in. This way, participants would not have to make an extra trip to the clinic to participate. They also recommended that we provide a door prize that any Mothering Project participant could enter as a way of included all of the women in the program, even those who were not pregnant.

The committee also previewed the *Nutrition for Two* research tool. The interactive tablet format was well accepted as a good way to collect information in a way that is easy to understand and more enjoyable than filling out a questionnaire on paper. However, the

[1] We used a pseudonym to protect the identity of the women who participated in the research.

committee felt that the questionnaire may be too long for some participants. This feedback led us to condense the questionnaire as much as we could without compromising the strength of the data.

In terms of providing honoraria to each participant, the committee suggested that it be given in the form of a gift certificate to a local supermarket. They also supported our idea to provide nutritious snacks for the participants during the completion of the questionnaire. The provision of honoraria and food is a way of giving back to participants in a practical and tangible way (Salmon, 2007). Plus, given the SES of the women we are working with, a seemingly small amount of money can go a long way and make an impact on whether a woman is able to participate since it may allow her to afford transportation. Providing honoraria and food can help women to feel respected and they are more likely to participate (Culhane, 2003).

With thorough review on the *Nutrition for Two* research tool, Jane raised a concern that we should ensure to assess the benefits and risks of asking sensitive questions such as how much alcohol is consumed. Since one of the main parameters of the study is alcohol consumption, we could not remove these questions all together, but Jane recommended that we go about asking those questions in a way that minimizes trauma for women. This is because asking questions about alcohol consumption during pregnancy or about pregnancy history could invoke memories of past trauma that many of these women have experienced. Furthermore, as mentioned previously, many of the women have experience with Child and Family Services (CFS) removing their children from their care due to alcohol or other substance use. These traumatic experiences must be acknowledged and respected.

Trauma-informed approach

Jane provided us with training on trauma-informed practise methods, which were incorporated in our study design and methodology. Trauma-informed practices have been defined as those practices that "enable service providers to appreciate the context in which a woman who has experienced trauma is living her life" (Jean Tweed Centre, 2013). According to the Substance Abuse and Mental Health Services Administration (SAMHSA), the trauma-informed approach means, "A program, organization, or system that is trauma-informed: Realizes the widespread impact of trauma and understands potential paths for recovery; Recognizes the signs and symptoms of trauma in clients, families, staff, and others involved with the system; Responds by fully integrating knowledge about trauma into policies, procedures, and practices; and Seeks to actively resist re-traumatization" (Substance Abuse and Mental Health Services Administration, 2014).

Accordingly, our study included a trauma-informed approach in several says. First, in the development of the research tool, *Nutrition for Two*, we entitled the main sections of as "How do I give myself and my baby energy?" (food consumption patterns and nutrient status) and "How do I take energy away from my body" (alcohol consumption and smoking). This was intended to create a non-judgemental space for the participant. Although the questions asked can be sensitive for our vulnerable target population, we wanted to frame it in such a way that everyone adds energy or takes energy away from their bodies, through what we put in our bodies and what we do to ourselves. We also included some open-ended questions to allow participants to reflect and share their opinion and voice rather than just being limited to the quantitative nature of the questionnaire. Second, in the informed consent process, we ensured participants understood that

we would be asking questions about substance use, food and eating habits, and general health. We highlighted that they could refuse to answer any of the questions if they felt uncomfortable and could withdraw from the study at any time. The emphasis was given that their information would be kept confidential and would not share their information with anyone who has any influence on their well-being or the well-being of your child and family. A simple graphic was also provided to help ensure participants understood the key points of the official consent form (see Appendix B). Third, in the implementation of the research tool, we arranged for a former Mothering Project participant and member of the Women's Advisory Committee to administer the part of questionnaire that deals with substance use, height, weight, and other health-related parameters. This allowed participants to complete these questions with someone they knew well and trusted. We also allowed women to take breaks between the parts of the questionnaire and provided snacks.

After adhering to the recommendations of the Project Manager and the Women's Advisory Committee, an official study invitation was submitted and we were approved to recruit participants to collect the data Mount Camel Mothering Program.

Discussion

Strengths

This study employs participatory methods to engage with communities and women in research. Given the importance of participatory methods when engaging in research with women who may be using substances, one of the major strengths of this study is that it does just that. The methods of building trust with potential participants before recruitment is a way of creating a safe space for research in a non-threatening way.

Challenges and barriers

One of the major limitations of this study was that the actual data collection did not occur on-reserve after all of the community engagement that was conducted. However, this also sheds light on some of the challenges and barriers to completing good, ethical, respectful research with pregnant First Nations women on-reserve. For instance, after completing an information session on the study in one reserve community, a group of pregnant women were interested in participating. However, to conduct the study in the community, we needed approval from the Health Director and/or Band Council. Since approval was not granted, the study could not be completed even though potential participants showed interest. The levels of approval for research on-reserve are necessary and important to ensure that unethical research is not conducted and that all research is welcomed by the community. However, it is unfortunate that even when potential participants are interested and willing to participate, studies can be blocked by the upper levels of leadership. That being said, there are many factors involved in approving a study from the community's perspective such as time and resources to support the implementation of the study (i.e. prenatal health workers to help with the recruitment of participants) and sometimes there are other studies that take priority since communities cannot support more than one study at a time. These are some examples of some of the potential barriers that can be faced.

Another barrier or challenge that was identified during this study is that the nature of scientific research does not always align with the needs and realities of community health. For instance, many scientific research ethics boards may recommend using posters as a main recruitment method. In reality, posters are not a sufficient recruitment tool with a population that has experienced trauma in the past. Sometimes the nature of typical scientific study design does

not fit with the needs of the community. This also relates to funding for research. Oftentimes grant providers want to see data or results within a period of time that is impractical if the study involves a process of community engagement and participatory methods. Building trusting relationships takes time. One must not adhere to the needs of scientific approaches and procedures at the expense of the needs and respect of the community and participants.

Conclusion

This thesis describes the community engagement and participatory methods used in starting nutrition research among pregnant First Nations women at risk for alcohol use. This study lays the ground work for further research in this area. The study approaches used in this research attempt to give women back their voice in research and to respect women with the kindness they deserve. Our efforts were not without obstacles and we acknowledge some of the challenges of bridging the gap between the research questions to be addressed and needs of the community. All of this ground work will help pave a path for the continuation of prenatal nutrition research with First Nations women. It could set an example of community engagement principles and methods for further research in this area. Future studies will help facilitate insight into prenatal nutrition status among First Nations women and could inform programs and policies which strive to improve food and nutrition security and reduce the severity of health issues such as FASD. Ultimately, this study could contribute to improvements in maternal and child health.

CHAPTER 4: *NUTRITION FOR TWO*: A DIETARY ASSESSMENT TOOL FOR PREGNANT FIRST NATIONS WOMEN AT RISK FOR ALCOHOL USE: IMPLICATIONS FOR FASD

Introduction

Fetal Alcohol Spectrum Disorder (FASD) is a health concern that is often over-represented among First Nations peoples (Chudley, 2008; Chudley et al., 2005; Public Health Agency of Canada, 2006; Square, 1997). It has been reported that alcohol consumption rates during pregnancy are as high as 51% among First Nations women (Williams and Gloster, 1999). However, according to the 2002/2003 First Nations Regional Longitudinal Health Survey, 15% of the women surveyed had continued to drink while they were pregnant, a rate that is similar to the national average (AMC Health Information Research and Governance Commitee et al., 2006). Although the obvious prevention for FASD is for no alcohol to be consumed during pregnancy, this is not always possible. For some women, alcohol use during pregnancy is more than just a decision to drink or not to drink. It is often connected to dangerous, painful, or traumatic experiences (i.e., experiences of violence, sex trade work, poverty, abuse, etc.) (Salmon, 2007). Plus there are a whole host of factors, other than alcohol consumption patterns, that influence the severity of FASD (May and Gossage, 2011). One key factor that has often been overlooked is prenatal nutrition. Improving prenatal nutrition among women who may drink alcohol during pregnancy is a potential harm-reduction approach to FASD. Based on results from animal studies, improving nutrition during pregnancy has the potential to reduce the negative effects of prenatal alcohol consumption on the developing fetus (Ballard et al., 2012; Carey et al., 2003; Patten et al., 2013; Thomas et al., 2010). However, there is a lack of data on food consumption patterns and nutritional status relating to alcohol consumption among pregnant

First Nations women. This gap must be addressed before prenatal nutrition interventions can be effectively planned and implemented.

The gap in nutrition data among pregnant First Nations women is largely due to the fact that the national health survey, CCHS, excludes First Nations people living on-reserve (Statistics Canada, 2014b). This means about 55% of the First Nations population in Manitoba are excluded (Statistics Canada, 2010). The report also excludes homeless populations in Canada, because CCHS is limited to Canadians with a permanent address. These populations are often the most vulnerable to food insecurity and malnutrition (Tarasuk et al., 2012). Furthermore, the nutrition related questions in the CCHS are limited to fruit and vegetable consumption and vitamins and mineral supplement use and there are limited questions that are specific to pregnancy (only alcohol and smoking use) (Statistics Canada, 2014b). One study that includes First Nations people living on-reserve, the First Nations Food, Nutrition, and Environment Study (FNFNES), excludes pregnant and lactating women (Chan, 2012).

A few small studies had been completed in specific First Nations reserves, but have limitations, however. For instance, a study conducted in 1999, focuses on a single nutrient, vitamin D, is 15 years old (Waiters et al., 1999). Another study relied on participant reports of whether or not they usually ate breakfast, lunch, supper and/or snacks and it does not provides a thorough picture of nutritional status during pregnancy (Wenman et al., 2004). A third study, an Aboriginal birth cohort study, is being conducted among pregnant women and their newborns from the Six Nations Reserve in Ontario. A retrospective chart review was completed, resulting in some nutrition-related information like weight gain and smoking during, but no dietary intake assessments were completed (Oliveira et al., 2013). The same authors collected biological data

during antenatal visits including hemoglobin, diabetes biomarkers, and lipid profile (Wahi et al., 2013), however the results have yet to be published. The lack of data on nutrition status of pregnant First Nations women hinders the provision of appropriate and effective care and improvement of health outcomes.

The high prevalence of food insecurity among First Nations women, may add additional impact on their nutritional status during pregnancy, especially when they consume alcohol. The 2011 CCHS, estimates that 27% of off-reserve Aboriginal households across Canada experience food insecurity, a rate that is more than double that of all Canadian households (Kuhnlein et al., 2014). Rates on-reserve are even higher. According to the First Nations Food Nutrition and Environment (FNFNES), 38% of participants living on-reserve in Manitoba reported experiencing household food insecurity and 31% of households reported that they could not afford to eat a 'balanced meal' (Chan, 2012).

Since none of the above studies targeting pregnant First Nations women focused on dietary intake of fetal brain development nutrients influenced by alcohol exposure, there was no existing research tool appropriate for this population. To our knowledge, there is no appropriate nutrition research tool that has been targeted specifically for pregnant First Nations women who are at risk for alcohol use. The development of such a research tool should have an understanding of First Nations' culture, philosophy of health and well-being, food availability and accessibility, food consumption and sharing patterns and should consider the literacy level of some respondents. These issues indicate that it is necessary to develop an effective, culturally appropriate and visually interactive nutrition research tool that focuses on FASD-related nutrients and is specific to women at risk for alcohol consumption during pregnancy. The present

study focuses the development of a First Nations-specific interactive tablet research tool, called *Nutrition for Two*, that combines nutrition with a focus on fetal brain development nutrients, alcohol consumption, pregnancy, and the social determinants of health that influence access to food.

This study was guided by the principles of the Canadian Institutes of Health Research Guidelines, "Health Research Involving Aboriginal peoples" and the Tri-Council Policy Statement, "Ethical Conduct for Research Involving Humans". Ethical approval has been granted by the University of Manitoba Health Research Ethics Board (H2013:263).

Research tool development

The development of a research tool of this nature involves several steps. The *Nutrition for Two* tool was developed using steps based on Keller et al. (2000) who developed and tested a research tool called 'Seniors in the Community: Risk Evaluation for Eating and Nutrition (SCREEN)'. The 7 key steps to developing an effective health measurement tool are: 1. determine what is being measured; 2. review the literature for tools; 3. critique tools for their development, validation, and reliability; 4. develop a construct for health measurement; 5. write the items, select items for the scale, and consult experts and a target group; 6. pretest items for readability; 7. pretest in a developmental sample; 8. validate the construct and measurement tool; and 9. ensure test-retest reliability (Keller et al., 2000).

Step 1: determine what is being measured

To determine what is being measured, an extensive literature review was conducted on FASD and the associated factors, particularly prenatal nutrition and specific nutrients important for fetal brain development (see Young et al., 2014). The main item of measurement was

determined as food consumption patterns and nutrient status, as measured by a food frequency questionnaire (FFQ) and 24-hour recall. The other key items were alcohol consumption patterns, and basic demographics, with a focus on factors that influence food security.

Step 2: review the literature for tools

The literature search for *Nutrition for Two* used PUBMED (2005 to 2015) database and grey literature (government sites such as Health Canada, Statistics Canada, or PHAC, and Google) to search the terms "nutritional assessment" "nutritional surveys", "diet surveys", or "food frequency questionnaire" crossed with the terms "prenatal" or "pregnancy" and/or "alcohol" or "fetal alcohol syndrome" and "First Nations" or "Aboriginal". There are nutrition several tools that focus on pregnant women but do not deal specifically with alcohol consumption and/or First Nations women (Baddour et al., 2013; Barbieri et al., 2014; Cade et al., 2002; Combet and Lean, 2014; Li et al., 2014; Loy and Jan Mohamed, 2013; Mejia-Rodriguez et al., 2012; Mouratidou et al., 2006; Shatenstein et al., 2011; van Gelder et al., 2013; Vian et al., 2013). The questionnaires used for larger nutrition and health surveys, like the CCHS, the FNFNES, and the Manitoba First Nations Regional Longitudinal Health Survey (RHS) were reviewed and critiqued.

Step 3: critique tools for their development, validation, and reliability

The CCHS, as a major Statistics Canada survey, has been extensively evaluated and validated (Statistics Canada, 2014b). The CCHS was used as a guide for developing basic demographic questions and alcohol consumption and smoking questions. The FNFNES includes a 24-hour recall and traditional food intake questionnaire (Chan, 2012). The results of the most commonly consumed traditional foods were used as a guide for our FFQ. The RHS does not

include a comprehensive nutrition survey (AMC Health Information Research and Governance Commitee et al., 2006).

Furthermore, alcohol consumption tools were reviewed. For instance, the TWEAK (tolerance, eye-opener, amnesia, cut/down) five-item scale, developed to rapidly screen for risk drinking during pregnancy was tested with a subgroup of the target population and had criterion validity studies completed (Russell et al., 1994). However, this tool did not address actual alcohol consumption rates or prenatal nutrition. Overall, there was no tool that was focused on prenatal nutrition, alcohol consumption, and the associated factors among First Nations women.

Step 4: develop a construct for health measurement

The construct for *Nutrition for Two* was defined as: determinants of food insecurity and alcohol consumption like income, education, etc. (Part 1: basic demographics), food consumption patterns including macronutrient and food group assessment based on one time point in pregnancy (Part 2: eating habits, food choices, and 24 hour recall based on Part 4: due date nutrient status based on frequency and amount of consumption of specific foods (Part 2: FFQ), frequency and amount of alcohol consumption and smoking (Part 3), and complications during pregnancy (Part 4: morning sickness, bedrest).

Step 5: write the items, select items for the scale, and consult experts and a target group

During the process of writing the questions for *Nutrition for Two*, it was decided to have 4 parts so that each part includes a cohesive construct or category of questions and so that it allows the tool to be administered in a more acceptable format (i.e. the participant can take a break after each part and snacks are provided).

The 4 parts are as follows:

Part I: Who am I? (basic demographics)
Part II: How do I give myself and my baby energy during pregnancy? (food choices, food frequency, 24-hour food recall)
Part III: How is my health? (general health, alcohol, smoking)
Part IV: How has my pregnancy been? (past pregnancies, due date, morning sickness)

The description of the writing of the questions will be described in these 4 parts.

Write Items and select items for the scale

Part I: Who am I?

General Demographics

This section has 8 questions on age, Aboriginal status, education, employment, and amount of money available to spend on food. For education, income, and employment questions, wording and answer categories are based on the CCHS questionnaire (questions: EDU_Q01, EDU_Q02, EDU_Q04A; INC_Q5A) (Statistics Canada, 2014b) and average levels based on community profiles of a Manitoba reserve (Statistics Canada, 2007).

Part II: How do I give myself and my baby energy during pregnancy?

My Eating Habits and Cooking

This section has 7 questions on number of meals per day, snacks, eating breakfast, eating out, cooking, and food security. These questions were included for the purpose of the study. Questions were selected from routine survey questions developed in our research lab as part of undergraduate research course at the University of Manitoba.

How do I choose the foods I eat?

This section has an 8 item rating scale on food choice motives. Items such as "tastes good" or "is cheap" are rated as "not at all important, a little important, moderately important, or

"very important". Pertinent items were adapted from a food choice motives questionnaire developed by (Steptoe et al., 1995).

How frequently do I eat these foods?

This section is a 103 food item Food Frequency Questionnaire (FFQ). The FFQ method is a well-documented method of assessing dietary intake (Cade et al., 2002). The purpose of this section is to determine the level of intake of nutrients related to brain development, relevant to the signs and symptoms of FASD. We conducted an extensive review on what nutrients were important for fetal brain development and could play a role in reducing the severity of the effects of alcohol exposure *in utero* (Young et al., 2014). We also identified which nutrients were most important for healthy pregnancies in general. A total of 11 micronutrients have been well documented in prenatal nutrition, fetal brain development, and potential mitigation of the effects of alcohol on the developing fetal brain (calcium, iron, iodine, selenium, choline, zinc, vitamin E, vitamin C, vitamin A, folate, and docosahexanoic acid, an omega-3 fatty acid). Of these, 5 nutrients were determined important in all 3 topic areas (vitamin A, folate, docosahexanoic acid, choline, and zinc) (see Figure 3 and Young et al, 2014). These nutrients are the focus of the study.

The top 50-100 sources of all 11 nutrients were searched using the Canadian Nutrient File (Health Canada, 2010) and listed in order of higher to lower source. Some foods were eliminated if they were the same food but different cooking method (i.e. pan fried or baked chicken). The amount of each nutrient was listed and if multiple of similar foods were in a range (i.e. various cheese varieties have similar levels of calcium) then the average amount was listed. A total of over 500 food items were determined as high sources of the above 11 key nutrients. For an example of these lists, see Figure 2. Then the lists were narrowed down to top 5-15 sources of

each nutrient. These were narrowed down by eliminating repeated foods and uncommonly consumed or inaccessible foods in rural Manitoba. Accessible and commonly consumed market foods and traditional First Nations foods were determined using the Manitoban results from the FNFNES (Chan, 2012) Finally, 103 foods and beverages were selected, including 10 traditional food items and commonly consumed foods.

For each food item, participants were asked if they consumed the food during their current pregnancy (yes/no). If yes, they indicate how often they consume the food as follows: "rarely" (one to three times per month), "sometimes" (1-2 times a week), "often" (three to five times a week), "everyday" (one time a day), or "all the time" (two times or more a day). Then they indicate the typical or serving average size that they consume each time they consume that particular food: small, medium, or large. The medium serving size is based on Canada's Food Guide servings (i.e. ½ cup vegetables is 1 serving) and small is anything less than that and large is anything greater than that. To calculate the grams of food consumed per day, the frequency of consumption of food items can be multiplied by the portion size. The values used for each frequency option are the following: Never = 0; one to three times a month = 2/30; one to two times a week = 1.5/7; three to five times a week = 4/7; one time a day = 1; 2 times or more a day =2.5. The frequency categories and associated values are based on previously validated FFQs (Sauvageot et al., 2013; Sheehy et al., 2014a, b).

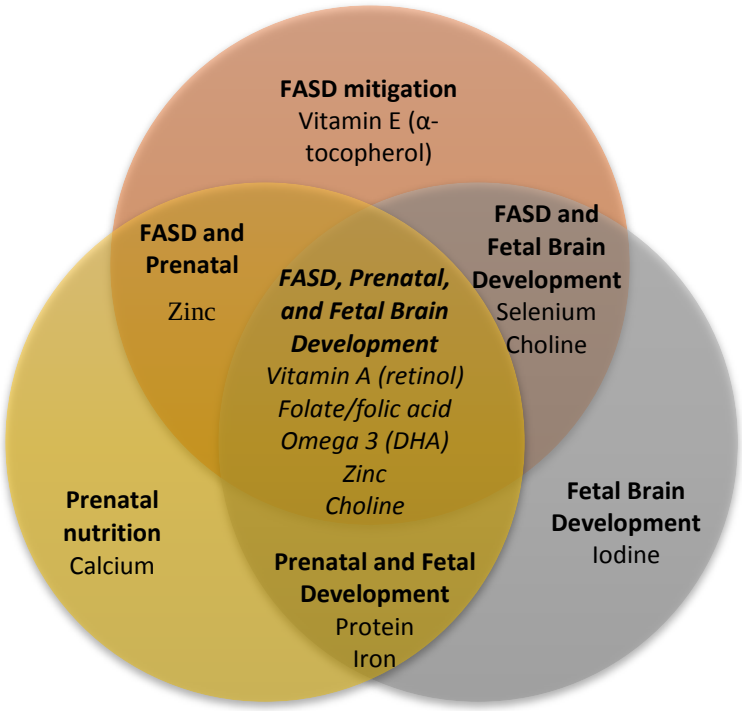

Figure 3: Venn diagram of nutrients associated with FASD mitigation, prenatal nutrition and fetal brain development

Source: Based on results from the following studies: Calcium (Health Canada, 2011), Choline (Thomas et al., 2009; Thomas et al., 2010), Folate (Craciunescu et al., 2004; Hewitt et al., 2011; Xu et al., 2006; Xu et al., 2008), Iodine (Georgieff, 2007), Iron (Georgieff, 2007; Health Canada, 2011), Omega 3 / DHA (Burdge, 1998), Protein (Georgieff, 2007; Health Canada, 2011), Selenium (Halmesmaki et al., 1986; Ojeda et al., 2009a; Ojeda et al., 2009b), Vitamin A (retinol) (Kot-Leibovich and Fainsod, 2009; Yelin et al., 2007), Vitamin E (Heaton et al., 2000; Mitchell et al., 1999a), Zinc (Carey et al., 2003)

Figure 4: Example of list of top sources – Omega 3 listed by food group and level of nutrient
Source: (Health Canada, 2010)

Omega 3 By Canada's Food Guide group AI in pregnancy = 1.4g/day				Omega 3 By Amount of Nutrient	
	Fatty acids, polyunsaturated, total omega n-3	Food	Amount g/CFG serving	Food	Amount g/CFG serving
Vegetables and Fruit	Vegetables and vegetable	mashed potato with 2% milk and marg	0.241	seeds, flaxseed, whole and ground	9.856
		mashed potato with 2% milk and butter	0.016	vegetable oil, flaxseed	5.602
	Fruits and fruit juices	none	0	seeds, chia, dried	5
Grain product	Cereals, Grains, and Pasta	wheat flour, whole wheat	0.015	mackerel, salted	3.863
		wheat flour, white, bread	0.01	salmon, king or chinook, smoked, brined	3.397
		wheat flour, white, all purpose	0.008	arctic char, skin, raw	3.307
	Breakfast cereals	none	0	fish oil, salmon	3.253
and alternat	Dairy products	cheese, fontina	0.395	animal fat, bearded seal, oil	2.854
		cream, table, 20%	0.368	burbot, eggs, raw	2.79
		cream, sour, 14%	0.316	nuts, walnuts, dried	2.694
		cheese, gouda	0.195	Shad, American, baked or broiled	2.528
		cheese, processed, cheddar	0.19	mackerel, atlantic, raw	2.385
		cheese, cheddar	0.18	roe, baked or broiled	2.331
t and alternat	Egg products	egg substitute, frozen, cooked	1.423	salmon, atlantic, farmed, raw	2.241
		egg, chicken, whole, fried	0.353	fish oil, sardine	2.218
		cheese omelet	0.251	salmon, atlantic, farmed or wild, baked or broiled	1.957
	Finfish and shellfish	mackerel, salted	3.863	salmon, king or chinook, canned	1.899
		salmon, king or chinook, smoked, brined	3.397	fish oil, cod liver	1.816
		arctic char, skin, raw	3.307	herring, pacific, baked or broiled	1.808
		burbot, eggs, raw	2.79	alewife, with bone, baked or broiled	1.725
		Shad, American, baked or broiled	2.528	burbot, liver, raw	1.71
		mackerel, atlantic, raw	2.385	sablefish, smoked	1.628
		roe, baked or broiled	2.331	salmon, sockeye, canned	1.59
		salmon, atlantic, farmed, raw	2.241	anchovy, canned with olive oil	1.575
		salmon, atlantic, farmed or wild, baked or broiled	1.957	whitefish, lake, native, baked	1.522
		salmon, king or chinook, canned	1.899	egg substitute, frozen, cooked	1.423
		herring, pacific, baked or broiled	1.808	sardine, canned in tomato sauce	1.26
		alewife, with bone, baked or broiled	1.725	tuna, bluefish, fresh, baked or broiled	1.245
		burbot, liver, raw	1.71	salad dressing, caesar dressing	1.15
		sablefish, smoked	1.628	duck, wild, native, cooked	1.136
		salmon, sockeye, canned	1.59	lamb, New Zealand, fat, cooked	1.13
		anchovy, canned with olive oil	1.575	cisco (lake herring), smoked	1.125
		whitefish, lake, native, baked	1.522	mollusk, oyster, boiled or steamed	1.102
		sardine, canned in tomato sauce	1.26	goose, wild, meat and skin, roasted	1.026
		tuna, bluefish, fresh, baked or broiled	1.245	trout, rainbow, wild, baked or broiled	0.996
		cisco (lake herring), smoked	1.125	vegetable oil, canola and soybean	0.905
		mollusk, oyster, boiled or steamed	1.102	nuts, simulated product, wheat-based	0.885
		trout, rainbow, wild, baked or broiled	0.996	smelt, dried	0.83
		smelt, dried	0.83	arctic char, native, meat, boiled	0.825
		arctic char, native, meat, boiled	0.825	margarine, tub, Healthy Attitude omega 3	0.712
	Lamb, Veal, and game	lamb, New Zealand, fat, cooked	1.13	margarin, tub, with olive oil, Becel	0.636
		lamb, New Zealand, rib, lean and fat	0.526	lamb, New Zealand, rib, lean and fat	0.526
		lamb, various	0.4	margarin, tub, regular	0.411
		veal, kidney, braised	0.195	lamb, various	0.4
		veal, heart, braised	0.128	quail, cooked	0.399
		veal, leg, lean and fat, pan fried	0.101	cheese, fontina	0.395
	Beef products	beef, chuck, short ribs, lean and fat, simmered	0.314	cream, table, 20%	0.368
		beef, loin, wing steak, boiled	0.28	egg, chicken, whole, fried	0.353
		beef, ground, well done	0.075	cream, sour, 14%	0.316
	Pork products	none	0	beef, chuck, short ribs, lean and fat, simmered	0.314
	Poultry Products	duck, wild, native, cooked	1.136	nuts, pecans	0.287
		goose, wild, meat and skin, roasted	1.026	beef, loin, wing steak, boiled	0.28
		quail, cooked	0.399	cheese omelet	0.251
		chicken, stewing, dark meat only, stewed	0.248	chicken, stewing, dark meat only, stewed	0.248
		ostrich, cooked	0.232	mashed potato with 2% milk and marg	0.241
	Nuts and seeds	seeds, flaxseed, whole and ground	9.856	ostrich, cooked	0.232
		seeds, chia, dried	5	cheese, gouda	0.195
		nuts, walnuts, dried	2.694	veal, kidney, braised	0.195
		nuts, simulated product, wheat-based	0.885	cheese, processed, cheddar	0.19
		nuts, pecans	0.287	cheese, cheddar	0.18
		nuts, almonds	0.157	nuts, almonds	0.157
		seeds, sesame, tahini	0.122	veal, heart, braised	0.128
		seeds, pumpkin, and squash,	0.011	seeds, sesame, tahini	0.122
Other	Baked products	none	0	veal, leg, lean and fat, pan fried	0.101
	Fast foods	none	0	beef, ground, well done	0.075
	Snacks	none	0	dessert, frozen yogurt	0.039
	Spices and herbs	none	0	mashed potato with 2% milk and butter	0.016
	Fats and Oils	vegetable oil, flaxseed	5.602	wheat flour, whole wheat	0.015
		fish oil, salmon	3.253	seeds, pumpkin, and squash,	0.011
		animal fat, bearded seal, oil	2.854	wheat flour, white, bread	0.01
		fish oil, sardine	2.218	wheat flour, white, all purpose	0.008

24-hour recall

This section asks participants to indicate what foods and beverages they consumed in the past 24 hours (i.e. from the time they got up in the morning to the time they went to bed yesterday). The 24 hour recall method has been well-documented as a valid and effective method of assessing dietary intake (Carter et al., 1981; Greger and Etnyre, 1978; Karvetti and Knuts, 1985). This will give us total calorie intake, calories from carbohydrate, protein, and fats as well as micronutrient intake status.

Part III: How is my health?

Height/Weight and General Health

This section asks about height, usual weight, current weight (as measured by the tool administrator), general health rating, time spent exercising, chronic illnesses (based on CCHS questions CCC_Q073B, CCC_Q10B, CCC_Q132), medications (based on CCHS questions CCC_Q073, CCC_Q105, CCC_Q106), and supplements (based on CCHS question DSU_Q1A) (Statistics Canada, 2014b).

How do I take energy away from my body?

This section asks about alcohol consumption and smoking (based on CCHS questions ALC_Q2, ALC_Q3, SMK_Q202, MXA_Q30, MXA_Q31) (Statistics Canada, 2014b). Questions related to partner's drinking habits are based on research that suggests that partner alcohol use increases maternal use (Public Health Agency of Canada, 2005).

Part IV: How has my pregnancy been?

This is a short section which aims to assess parity, gravidity, due dates, and any complications during pregnancy that influence food intake, such as nausea/vomiting or bedrest. These questions were included for the purpose of this study.

Consult experts and target group

The *Nutrition for Two* tool was reviewed at various stages by First Nation community coordinators of the Strengthening Families Maternal Child Health (SF-MCH) program, the Women's Advisory Committee at the Mothering Project, the program manager at the Mothering Project, and the target population.

Initial consultation was made at the quarterly SF-MCH meeting of community coordinators from 14 Manitoba First Nation reserves. A hard copy of the draft questionnaire was given to each attendee (n≈14), and each question was reviewed for clarity and appropriateness for the target population. Feedback on confidentiality, wording of questions, what foods to include or exclude from the FFQ was given. The tool was revised based on the feedback. Based on feedback received from the round-table discussion and other nutrition experts, it was determined that the tool should be in a more interactive format than just as a paper questionnaire considering the lengthy FFQ items and the literacy of potential participants. This led us to work with a software development firm, Function Four Ltd (Winnipeg, MB), to create a visually attractive and interactive tablet tool. With the final draft of *Nutrition for Two* in its tablet format, a review of the tool was conducted by the program manager and Women's Advisory Committee of the Mothering Project at Mount Carmel Clinic in Winnipeg, a program for women at risk for

alcohol and substance use. They gave verbal feedback on length, feasibility, acceptability, and appropriateness. The SF-MCH coordinators (n=2) reviewed the tool in its final version and commented on how it would be received by potential participants in their community. Finally the tool was reviewed by a sub-sample of our target population, pregnant First Nations women, in the form of a pre-test, as described in Step 7.

The target population for *Nutrition for Two* is pregnant First Nations women at risk for alcohol consumption during pregnancy. *Nutrition for Two* was pre-tested with pregnant women living in the Point Douglas area of Winnipeg, Manitoba, Canada, where 30% of the population is Aboriginal (City of Winnipeg, 2006). Although these women are not living on-reserve, which is where the major nutrition research gap exists, they have similar socioeconomic status, culture, and access to food. These women, most of whom are First Nations, attend programs for women who may be consuming alcohol and/or using drugs during pregnancy by providing support such as prenatal visits, healthy meals, and social support. Many of them live fairly transient lives and have experienced trauma and the effects of marginalization and colonization (Mothering Project program manager, personal communication, 2014).

Step 6: pretest items for readability

Nutrition for Two was pre-tested for readability and logical flow by 5 nutrition graduate students and 2 pregnant nutrition experts.

Step 7: pretest in a developmental sample

Nutrition for Two was pre-tested with 17 pregnant First Nations women who may or may not be drinking alcohol during pregnancy. Participants completed the questionnaire and then complete an evaluation form, providing written and verbal feedback on length, ease,

appropriateness, and overall rating. Participants were asked to rate whether they strongly agree, somewhat agree, somewhat disagree, or strongly disagree on 3 statements: (i) The questions are easy to understand; (ii) The format was interactive and fun; and (iii) I would recommend this to other pregnant women. They were asked how long it took them to complete the questionnaire (7 categories from less than 15 minutes to more than 40 minutes) and were given the opportunity to provide general comments.

Face and content validity

In Steps 5, 6, and 7, about 30 women reviewed on *Nutrition for Two.* All of this was done to detect any problems in a questionnaire, to make sure the questions made sense, that the questions were understood, and if the questions seemed to measure what they intended to measure and if they made sense. Questions were reviewed to make sure they were free of jargon and that the language was easy to understand by the reviewers and participants of the pre-test. Revisions were made on word choice, grammar, and order of questions as suggested by reviewers. These methods of reviewing tested face and content validity similar to the development and testing of an inflammatory bowel disease fatigue patient self-assessment scale (Czuber-Dochan et al., 2014).

Results

The tool

The result of these stages of developing *Nutrition for Two* is an interactive research tool that incorporates dietary assessment with alcohol and smoking assessment, pregnancy, and related determinants of health. The tool uses both a FFQ that focuses on brain development nutrients and commonly consumed foods in First Nations communities in Manitoba and a 24-

hour recall to assess dietary intake for total energy, macronutrient energy and micronutrient consumption. It also includes questions on basic demographics, food choices, general health, alcohol, smoking, past pregnancies, due date, morning sickness. These questions involve factors that influence dietary intake, and overall nutrition and health. Ultimately this tool will be used to assess dietary intake and determine which nutrients are sufficient and which are deficient based on Institute of Medicine Dietary Reference Intakes for pregnancy.

Review and Evaluation

This tool has been reviewed and evaluated by several groups: the SF-MCH community coordinators, the Women's Advisory Committee, the Mothering Project program manager, nutrition graduate students, pregnant nutrition experts, and pregnant First Nations women (sub-sample of our target population). Some of the key results of these reviewers are as follows.

Maternal Child Health Community Coordinators

Initially, 14 SF-MCH community coordinators reviewed tool in its draft form. They provided feedback on confidentiality, wording of questions, what foods to include or exclude from the FFQ was given. Confidentiality was stressed because it was noted that some potential participants may have had experiences with disclosing substance use during pregnancy and then had their children apprehended. The research tool does not have a name of the participant attached to it, only a participant code that is not linked to the name.

Later, when the tool was in its final form, five of those SF-MCH community coordinators, who showed an interest in our prenatal study, were contacted and two responded with feedback. The comment was that it was too long and there were too many food items in the

FFQ. They suggested that we could use categories instead of specific foods. For example use "vegetables" and then ask which ones they consume rather than listing specific types of vegetables. However, as mentioned the specific food items were chosen based on the content of the target nutrients in our study relating to fetal brain development. So to categorize the food items will limit the data available on these specific nutrients. Another comment was not to ask if participants are on social assistance, but to ask just about employment, because it could interpreted offensively as an assumption that they are on social assistance. It was also emphasized that we need to stress confidentiality during the consent process and that no one else will have access to their personal information.

Mothering Project Program Manager

The feedback from the Mothering Project program manager included that it was a *"pretty reasonable, clear, and easy (although long!) questionnaire"*. She had specific comments about the drug and alcohol sections since *"questions about mother's drinking […] bring up a ton of trauma history"*. She recommended that we have an interview guide about how to ask question about substance use in a way that is least invasive and judgemental. She suggested that we have some coaching on the trauma-informed approach and use the approach to guide the way we ask these sensitive questions. Another suggestion was that we include gender neutral identifiers when talking about the participant's partner since about 10% of the Mothering Project clients identify as LGBT (lesbian, gay, bisexual, and transgender). Finally, her recommendation was to include "stay at home parent" as an option under the employment section. This way we acknowledge that parenting and mothering is a full-time job for many and help participants feel okay about saying that their job is being a mom.

Women's Advisory Committee

Some women from the Women's Advisory Committee of the Mothering Project at Mount Carmel Clinic in Winnipeg, remarked that the tool was quite long, especially in the FFQ section. A few adjustments were made to condense the questionnaire based on their recommendation. They accepted the interactive tablet format as a good way to collect information in a way that is easy to understand and more enjoyable than filling out a questionnaire on paper. Since the tool is divided into 4 parts, we suggested that the questionnaire could be completed in stations so that participants could take a break or eat a snack in between. This was idea was supported by the committee.

Pregnant Nutrition Experts

Nutrition for Two was reviewed by 2 pregnant nutrition experts, a Registered Dietitian and a nutrition research scientist holding a PhD. They both indicated that they strongly agree or somewhat agree when asked if the questions are easy to understand, if the format was interactive and fun, and if they would recommend this to other pregnant women. One comment was that in the FFQ sometimes you can eat something less frequently than the "rarely" option of "1-3 times per month" but more frequently than "never". Another overall comment was it was *"easy to read and complete"* and *"I liked all of the pictures [of the food items]."*

Pre-test – Pregnant First Nations Women

The pre-test results indicate the tool is being well received by the sub-sample of the target population. Of the 17 participants 82.4 % indicated that they strongly agree that the questions are easy to understand, 82.4 % strongly agree that the format was interactive and fun, and 94.1 %

strongly agree they would recommend this to other pregnant women (Figure 5). Most of the women completed the questions in just over 40 minutes.

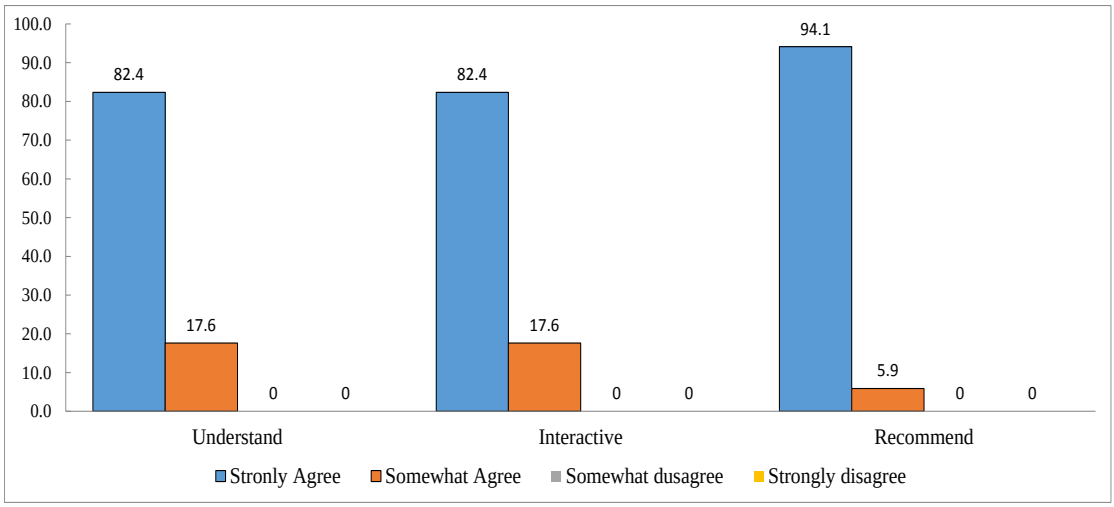

Figure 5: Participants responses from evaluation of *Nutrition for Two* (%)
Number in each category represents the percentage value. The data were compared using chi test: understand ($p<0.0001$); Interactive ($p<0.0001$); Recommend ($p<0.0001$)

The overall comments from pre-test participants were as follows:

"Awesome, good food"
"It was great!"
"Didn't feel much of a difference between paper and iPad - both ok"
"Comfortable. No problem with alcohol questions."
"Better than paper"
"It was fun and worth the $25"
"Fun looking at new food. Pretty good. Like the iPad"
"Like iPad - better than writing. It was much faster than writing it would been."
"Some of the food items like the oils are not clear."
"Technology makes things more fun.
"IPad was good. Could have been keeping 24 recall at home."
"Need better room to do questionnaire in. IPad was much faster than paper."
"Enjoyed iPad. Thought the questionnaire was fun. Will recommend to friends."

Discussion

It is critical to have an appropriate population-specific research tool to collect accurate data. This is the first research tool that includes a dietary assessment of important fetal brain development nutrients, alcohol consumption during pregnancy, and has a First Nations focus.

One of the major strengths of the *Nutrition for Two* research tool is that it is in the form of a tablet application. This makes the tool much more visually attractive and interactive than filling out a questionnaire on paper. Navigation through the questions, especially in the FFQ section, almost feels like a game. The FFQ section is full of colourful pictures and icons that make completing the questions intuitive, easy to understand, and fun. This is especially important and useful for the target population of this tool, as literacy levels among First Nations women have been reported as lower than non-Aboriginal women. In 2003 it was reported that of Aboriginal women living in urban Manitoba, 68.9% have lower literacy (levels 1-2[2]) and 31.1% have high literacy (level 3) whereas of non-Aboriginal women living in urban Manitoba, 41.2% have lower literacy (levels 1-2) and 58.8% have high literacy (level 3) (Statistics Canada, 2003), showing a 28% difference in both levels between the two groups. In a more recent study in 2013, the difference was narrowed to 14.5% but there still there is a gap as 38.9% of Aboriginal people (male and female) in Manitoba had high literacy (level 3 or higher) compared to 53.4% of non-Aboriginal people in Manitoba (Statistics Canada, 2013). The *Nutrition for Two* tool is easy to

[2] "Levels 1 and 2 typically have not yet mastered the minimum foundation of literacy skills needed to perform tasks generally viewed to be important for full participation in social and economic life…Level 3 performance is chosen as the benchmark because performance at or above that level is generally associated with a number of positive outcomes, such as increased civic participation, increased economic success and independence, and enhanced opportunities for lifelong learning" (Statistics Canada. 2003. Literacy profile of off-reserve First Nations and Métis people living in urban Manitoba and Saskatchewan: Results from the International Adult Literacy and Skills Survey 2003. Vol. 2015. Statistics Canada.).

understand and does not require high literacy levels to complete (rated as Grade 5 level according to the Flesch-Kincaid test). The intuitive nature of the tool is likely to increase the accuracy and reliability of the data.

To the researchers, a major benefit of the *Nutrition for Two* tool is that the tablet application allows the ability to automatically input the data into an Excel sheet. This gives the possibility of saving countless hours of data entry.

Another strength of this study is that it conducted several avenues of review and pre-testing of the *Nutrition for Two*. This is important considering the sensitive nature of the alcohol related questions and the vulnerable target population. The feedback from potential participants and support workers that work directly with the target population is invaluable to help ensure that it will be well received by future participants. However, these reviews and pre-tests only are able to test face and content validity and not able to provide external validity or reliability. Further testing of this tool may be able to achieve higher levels of validity and reliability, which is currently going on in our research group.

Finally, a major strength of this research tool is that it encompasses dietary assessment, food security, social determinants of health, alcohol and other substance use, and pregnancy. This means it is a sort of one-stop-shop for assessing pregnant women's risk for malnutrition, alcohol consumption, as well as several associated factors.

The *Nutrition for Two* research tool FFQ component has many strengths. It contains a thorough list of food items related to fetal brain development and prenatal nutrition. The list is a result of an intensive literature review and listing system based on data from the Canadian Nutrient File. The FFQ includes a serving size element as well, which is an addition to the

typical FFQ. This allows the data to be more accurately converted into amount (g) of nutrient consumed per day. However, there is a limitation to this element. The medium serving size is based on Canada's Food Guide servings, with the small size being anything smaller than, and the large size being anything larger than, that reference amount. This means that the small and large serving sizes are somewhat arbitrary and do not give an exact amount. This limitation may be partially addressed by the fact that more precise measurements of foods are given in the 24-hour recall component. Another limitation of this section is its lengthy list of foods as the reviewers pointed out. However, the ability to quickly move through the FFQ food items on the tablet may shorten the response time.

As with any FFQ or 24-hour recall, a major limitation of the *Nutrition for Two* tool is that it is reliant on the memory of the participant. For instance, in the FFQ, it may be difficult to remember exactly how often each food item was consumed during the period of pregnancy. Since this questionnaire is focused on the whole pregnancy, participants are tasked with remembering what they ate for up to 9 months prior to completing the questionnaire. One may of addressing this limitation would be to only ask for the frequency of consumption for one month prior to administration of the questionnaire. However, this reduces the breadth of the data and could add to the seasonal bias to the data collection. For instance, if the questionnaire is administered in the summertime, garden vegetables are more likely to be consumed than if the questionnaire is administered in the winter months. This is a limitation in itself, but asking participants the frequency of consumption over the whole pregnancy helps to minimize this.

As for the 24-hour recall, it is often difficult to remember what one has eating in the past 24 hours. Although the questionnaire administrators can ask prompting questions, accuracy is

again reliant on the participants' memory and patience to be thorough in describing the food items and amount consumed. However the validity of the 24 hour recall method increases when the sample size is large (Karvetti and Knuts, 1985).

Another limitation of the research tool is that the alcohol and smoking questions rely on the honesty of the participant. Alcohol and smoking during pregnancy have a certain stigma attached to them and many women in our target population may have had traumatic experiences of disclosing substance abuse and having their children apprehended, or having increased observation or investigation by social service, medical, and criminal justice authorities (Boyd and Roach, 1999). Given these realities, it is to be expected that some participants may be unwilling to truthfully answer these questions. However, this study has aimed to use methods to reduce the stigma of substance use during pregnancy and limit induction of further trauma for participants. This is done through trauma-informed, harm-reduction approaches that include, but are not limited to, building trusting relationships with participants before data collection, including support workers that work closely with participants in the administration of sensitive questions, providing opportunities for participants to express the ways they are helping themselves positively, and ensuring that participants are already enrolled in a program that is providing support. Simply put, these methods aim to create a safe place for participants where even sensitive questions can be answered in a non-judgemental and supportive space.

Implications

The *Nutrition for Two* research tool may be used by future studies that aim to determine food intake patterns, food choices, and nutrient status of pregnant First Nations women who may be consuming alcohol during pregnancy. In fact, this planned as a future extension of this study

conducted in our research group. . It could be used in conjunction with blood and urine samples which would add to the reliability of the nutrient data. The *Nutrition for Two* research tool can help address a critical research gap that exists in dietary assessment and nutrition status data in pregnant women. Nutrition for Two was designed for pregnant First Nations women living on or off-reserve in Manitoba, Canada. However, it could be easily adapted to other population that are at risk for FASD. The interactive tablet format is something that many other population could benefit from and the FFQ could be easily adapted to other cultures and populations.

Conclusion

The *Nutrition for Two* research tool is a novel tool and included several steps of development. It includes a fetal brain development focused FFQ, a 24-hour recall, and questions on social determinants of health and pregnancy – all factors that influence dietary intake. This study is unique and novel because no other studies to date have developed a tool that is First Nations-specific and captures nutrition, alcohol consumption, pregnancy, and the social determinants of health that influence access to food. The use of the *Nutrition for Two* tool will make data collection in this population a more efficient, effective, and will improve data management for researchers. The necessary revisions will be made with time as the research evolves. Data collected using this tool will provide a basis for future nutrition interventions that will target specific nutrients. This research will help to inform programs and policies which strive to improve food and nutrition security. Ultimately, this has potential to improve overall health and nutrition status of mothers and children and reduce the incidence of negative effects resulting from prenatal alcohol consumption and poor prenatal nutrition such as FASD.

CHAPTER 5: DISCUSSION AND CONCLUSION

Overall Discussion

This study aimed to develop an interactive dietary assessment tool that encompasses diet and nutrition, alcohol consumption, related factors such as socioeconomic status and access to foods, and pregnancy. To do this, it used a participatory approach to engaging with pregnant First Nations women and their communities to ensure that the tool is appropriate for the target population and to lay the ground work for future studies that involve dietary assessment among pregnant women at risk for substance use. All of this groundwork is essential to addressing a critical research gap that exists in FASD prevention. Prenatal nutrition research among First Nations women who may be drinking alcohol during pregnancy is one of the next obvious steps in FASD prevention research.

The methods and results of this study have been presented as two separate research papers (Chapter 3 and Chapter 4). Chapter 3 outlines the participatory approach that was employed in this study. It discusses the methods used to engage with pregnant women living on and off-reserve. To engage with women living on-reserve we connected with maternal and child health workers, health directors, and band councils in the community, as well as First Nations research ethics boards. This effort culminated in an information session with pregnant First Nations women in the community. Although the idea to study prenatal nutrition in connection with alcohol use was well-received by these potential participants, the study implementation did not move forward with the upper level leadership decision in the community. From here, we began engagement with pregnant women living off-reserve who are participating in programs that support at-risk pregnancies. This involved connecting with the program manager of the

Mothering Project and the Women's Advisory Committee at the Mount Carmel Clinic in Winnipeg, Manitoba. Furthermore, volunteering with pregnant women at a weekly drop-in occurred as a way of creating relationships with potential participants in a casual setting. These efforts developed a level of trust between the pregnant women and the researchers that allowed us to recruit participants for our study. Furthermore, this groundwork allowed our interactions with potential participants to be trauma-informed, non-judgemental, and respectful. Considering the difficulty of locating and approaching pregnant women who are at risk for substance use, without this participatory approach, the future of prenatal nutrition research among women who may be consuming alcohol during pregnancy would be compromised. Therefore, the methods discussed in Chapter 3 are a critical component to this study, as in the development of a research tool, but also to further research with this group of women, and as an example for future research with other women in other parts of Canada and around the world.

The experiences outlined in this study point to the fact that sometimes the scientific approach to research that emphasis an importance for research to be done in a timely manner or that biological samples much be obtained do not always align with the needs or goals of the community and the participants. To conduct respectful research on a vulnerable population such as pregnant First Nations women who use substances, some compromise is likely to be necessary. The engagement with communities and potential participants should be the first priority to build trusting relationships. The time it takes to develop these relationships is worth the wait and is critical to conducting respectful research and laying the groundwork for further study.

Chapter 4 outlines the methods used to develop a unique and interactive prenatal dietary and alcohol consumption assessment tool, called *Nutrition for Two*. The steps to develop such a tool are extensive. Writing the questions for the tool included a review of existing questionnaires related to pregnancy and nutrition, as well as an intensive literature review on the nutrients most important to fetal brain development and the potential mitigation of the effects of alcohol on the developing fetus. The tool was converted to a tablet application, making it an interactive tool that is intuitive and easy to use. Many levels of review and evaluation of the tool were conducted to ensure that the tool was going to be appropriate for the target population and answer the questions it set out to ask. Finally a pre-test was conducted with pregnant First Nations women who we had built trusting relationships with using the participatory approaches as outline above. These women completed the tool and an evaluation of it. They provided positive feedback on the tool. Testing out the tool also allowed us as researchers to evaluate the tool and the methods of administration so that it could be improved upon for further research with this population. The development of *Nutrition for Two* means that data can now be collected on prenatal nutrition, alcohol and tobacco use, and as well as the related social determinants of health, all in one questionnaire. The questionnaire takes about 45 minutes to complete and provides an extensive breadth and depth of informative data. Ultimately this tool could be used with other groups of First Nations pregnant women and could be adapted to other population who are at risk for FASD.

Strengths and Limitations

The participatory approaches used in this study and the development of the research tool, *Nutrition for Two*, both have several strengths and limitations. However, together, this study as a

whole presents strengths and limitations. Since this study comes at the beginnings stages of prenatal nutrition assessment research in relation to FASD prevention, the combination of a participatory approach and the development of an interactive research tool provides a unique set of experiences and data that is new to the world of FASD prevention research. Although participatory methods have been employed by past studies among First Nations women (Salmon, 2007; Salmon et al., 2010), this study is unique in that it involves First Nations women, prenatal nutrition, and risk for FASD (i.e. by assessing alcohol consumption levels and related factors). The research tool developed in this study is unique because it includes an overall assessment of prenatal nutrition and risk for FASD which has not been done before. Furthermore, its interactive format as a tablet application allows for more efficient and effective data collection. Together this study provides the essential groundwork that is necessary to complete further research among pregnant First Nations women.

This study has some limitations. As outlined in Chapters 1 and 3, the largest research gap in prenatal nutrition research exists among First Nations women living on-reserve. The *Nutrition for Two* research tool was developed with this in mind, including commonly consumed traditional foods and market foods available on-reserve. However, a pre-test was only conducted with women living off-reserve, in Winnipeg. Although the culture is the same and traditional foods are the same, the access to food is different in an urban centre than on-reserve. During this study we engaged with women living in reserve communities but were unable to complete a pre-test of the research tool in that location, so we moved on to engaging with women off-reserve. This was a practical decision that was made in order to get the pre-test completed in a timely manner. It led to further connections with women living in Winnipeg with whom data will be collected by upcoming studies. So although there is a limitation in the location that the pre-test

was conducted, the overall impact of engaging with women living off-reserve, was actually very positive.

For the full description of the strengths and limitations of the participatory approaches used in this study, please see Chapter 3, and for the strengths and limitations of the *Nutrition for Two* research tool, please see Chapter 4.

Research Implications

The present study has several implications. First, the participatory approach that was employed in this study not only lays the groundwork for further research with the target population, but also may provide an example of how to respectfully conduct research in a community setting. Second, the *Nutrition for Two* research tool will be used by future studies that aim to determine food intake patterns, food choices, and nutrient status of pregnant First Nations women who may be consuming alcohol during pregnancy. It could be used in conjunction with blood and urine samples which would add to the reliability of the nutrient data. *Nutrition for Two* was designed for pregnant First Nations women living on or off-reserve in Manitoba, Canada. However, it could be adapted to other population that are at risk for FASD. The interactive tablet format is something that many other population could benefit from and the FFQ could be easily adapted to other cultures and populations. Third, this study lays the groundwork for future studies that collect prenatal nutrition data on women at risk for alcohol consumption and at risk to have children with FASD. This research addresses a critical research gap in FASD prevention research. This study is the starting point for studies that will inform nutrition interventions, programs, and policies, and will ultimately be involved in reducing the severity of FASD.

Recommendations for Future Research

To complement the quantitative research as designed in this study, future research in the area of nutrition and FASD should include a qualitative component to answer questions about the root causes of FASD. For instance, a study that involves a narrative approach to create a space for women to share their stories would shed light on the lives that they live and why alcohol consumption is a part of it. Alcohol consumption is not in a bubble. It exists in connection to all aspects of life such as poverty, social supports, geographical environment, past trauma, mental health, etc. These factors must be explored in order to really address FASD in a holistic and sustainable way. For example, if poverty is what ultimately indicates a higher risk for alcohol consumption during pregnancy (Thanh et al., 2013), then poverty is what should be addressed. Job creation, improving access to education and affordable housing, just to name a few, are key interventions that could address poverty and ultimately health issues that afflict the poor like FASD.

Prevention of FASD is a complex challenge given the plethora of associated risk factors. Prenatal nutrition is one key factor that has often been overlooked and must be a key area of research in the next several years. The next steps should include collecting thorough dietary assessment data among women at risk for alcohol consumption around the world. This data should then be used to develop any necessary nutrition and food provisions. These interventions should not only provide specific nutrient recommendations for populations and individuals, but should also consider the broader aspects of nutrition such as food security and socioeconomic status and take the necessary steps to address these aspects. Although the task of improving

prenatal nutrition around the world is a daunting task, it ultimately will have an impact on many more health concerns than just FASD, such as diet-related cancer and diabetes.

In conclusion, optimal nutrition during pregnancy is vital to the health of both the mother and the developing infant. When alcohol is consumed during this stage it affects the proper development of the infant and can have teratogenic effects resulting in FASD. FASD is a health concern that is over represented among First Nations peoples. One potential intervention for FASD is improving prenatal nutrition. However, with a lack of prenatal nutrition assessment information among pregnant First Nations women, thorough data must be collected. To collect this data an interactive research tool that encompasses dietary assessment, alcohol consumption, and related factors is needed. This study developed this tool using a participatory approach to engage with pregnant women and their communities. The experiences and data outlined in this work lay the groundwork for further studies on prenatal nutrition related to FASD. Ultimately this study is the beginning stages of research which will make an impact on prenatal nutrition and the severity of FASD.

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APPENDIX A: COPY OF PARTICIPANT CONSENT FORM

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RESEARCH PARTICIAPNT INFORMATION and CONSENT FORM for Participants

Title of Study: Pilot study on food intake patterns and nutrition status among pregnant women living in Manitoba: Implications for Fetal Alcohol Spectrum Disorder

Principal Investigator: Dr. Miyoung Suh RD, PhD.
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Wanda Phillips-Beck
Assembly of Manitoba Chiefs

You are being asked to participate in a human research study. Please take your time to review this consent form and discuss any questions you may have with the study staff. You may take your time to make your decision about participating in this study and you may discuss it with your friends or family before you make your decision. This consent form may contain words that you do not understand. Please ask the study doctor or study staff to explain any words or information that you do not clearly understand.

Purpose of Study

The overall objective of this study is to identify food intake patterns and nutrition status of pregnant women.

The three specific objectives of the study are (i) to identify food group consumption patterns among pregnant women using a 24-hr food recall and food guide slide tool as well as a food frequency questionnaire, (ii) to identify nutrition status using blood and urine analysis, and (iii) to correlate food consumption patterns and nutrition status with prenatal alcohol intake patterns as well as other lifestyle parameters.

Study procedures

A total of approximately 160 pregnant women living in Manitoba will be recruited. Recruitment will involve community coordinators of the Strengthening Families Maternal Child Health

program and maternal and child health program in Winnipeg such as The Mothering Program at Mt Carmel Clinic and the Healthy Child Development Program Advisory Committee. Participants will either attend a 3-4 hour workshop that will include a brief prenatal nutrition lesson, a cooking demonstration and snack, and completion of the 4-part questionnaire or complete the questionnaire in a one-on-one visit. The questionnaire will be completed on paper or in an electronic format.

A small subgroup (10-15 participants) will be recruited to complete both formats of the questionnaire and an evaluation form. These participants will complete the study as all other participants (complete questionnaire plus blood and urine samples). The only change is that they will complete the questionnaire in 2 formats and submit an evaluation form. These participants may also participate in the follow-up stage if they are interested.

A subgroup of 60 participants will be followed at 1 to 4 time points throughout pregnancy. After the first time point, only the questionnaire and 24-hour recall will be administered. This subgroup will be followed till delivery, at which time birth parameters will be collected from the infant.

Workshop: In the workshop we will have some fun time together. The workshop will include a brief prenatal nutrition lesson, a cooking demonstration and snack/meal, completion of the 4-part questionnaire, and 24 hr food recall. Your height and weight will be measured and recorded in the questionnaire. The workshop will be facilitated by MSc student/study coordinators, Heather Giesbrecht/Karlee Dyck and student research assistants. This will take 3-4 hours to complete.

4-part questionnaire: The questionnaire will include (i) basic demographics and general health/lifestyle, (ii) eating pattern questions including a food frequency questionnaire, (iii) alcohol, smoking and drug use, and (iv) maternal health questions. Participants' responses will be assessed for meeting Canada's Food Guide serving requirements, consumption of nutrients important for prenatal nutrition and potential mitigation of alcohol affects, alcohol intake patterns, and other lifestyle parameters.

Blood and urine samples: In order to get a better idea of your nutrition status we would like to analyze your blood and urine for nutrient deficiencies. Fasting blood (20ml or a large tablespoon) and urine (15ml or a tablespoon) samples will be collected to determine nutritional deficiencies. Samples will be obtained from each participant during the week of the workshop with the help of local health centres and staff during the week of the workshop. The samples will be transported to our lab at the Richardson Centre for Functional Foods and Nutraceuticals.

> Blood analysis: Blood samples will be analyzed for specific nutrients (vitamins A, B3, B12, C, E, folate, zinc, calcium, iron, choline, iodine, omega 3 fatty acids (docosahexaenoic acid (DHA)), and carotenoids (lutein and zeaxanthin)), oxidative status, alcohol biomarkers (such as gamma glutamyltransferase and mean corpuscular volume), and other metabolites.
> Urine analysis: Urine samples will be analyzed for oxidative stress markers and other metabolites.

<u>Birth Parameters:</u>

Parameters will be taken of the newborn infant including low and normal birth weight, preterm or full term birth and stillbirth. Infant growth rates will be followed at time points of birth, 3 months, 6 months, and 12 months.

If participants are unwilling to provide blood and urine samples, they will be allowed to participate by completing the questionnaire only. They will be asked to fill out this consent form minus the 3rd check-box question (Do you understand why you are donating blood and urine samples?)

Risks and Discomfort
Although there are no direct risks by the study plan and procedures, there may be some emotional risks. For instance, participants may feel uncomfortable answering questions about alcohol, tobacco, and drug use. There may also be discomfort with blood and urine sample collection. Blood collection could lead to a mild bruise and there is a small risk of infection associated with drawing blood.

Benefits
Individual participant benefits: Individuals who participate in the study will benefit from the study in a variety of ways. First, by attending the nutrition workshop, participants will gain knowledge of nutrition and skills in improving nutrition. This could impact their overall health and the health of their family. Second, participants will be provided will the opportunity to connect with other pregnant mothers and gain support from their community and from the researchers. Third, individuals may gain awareness of the importance of reducing or stopping alcohol consumption during pregnancy. Fourth, participants will benefit from future nutrition interventions which could positively impact their health and the health of their families.
Community/program benefits: The proposed study has potential to benefit the participating communities/programs in a variety of ways. First, the study has potential to identify the specific points where a nutrition intervention could be useful. The communities/programs involved in future nutrition interventions could improve the availability, accessibility, and affordability of healthy market and traditional foods leading to increased food security, higher nutritional status, and improved overall health. Third, the communities/programs could benefit from community-university collaboration and research skills.

Costs
There are no costs to participating in this study.

Payment for participation
At the completion of the questionnaire and blood and urine donation, participants will receive a $25.00 gift certificate to a local retail store.

Alternatives
You do not have to participate in this study. The study coordinators, and principal investigator will answer any questions you have about the experimental group of this study.

Confidentiality:

Information obtained in this research may be published and presented in the scientific and/or dietetic community. The graduate student involved in conducting the study and/or analyses of the study results, will include data in her Masters thesis. Data will be scrubbed of any codes or linkages to subjects. You will receive the study results as the mean values obtained from the whole study population. However, you will not be able to have access to the individual results of other study participants.

Absolute confidentiality cannot be guaranteed, however we will do our utmost to keep all information confidential. Your name WILL NOT be used or revealed. When your sample is analyzed, your name will be coded throughout the study. Information collected will be stored on computer using the same code. Back up of electronic data and the hard copies will be stored in a locked cabinet (Dr. Suh's clinical research office, 209 RCFFN) for 5 years or until data are published. Research records will only be available to those directly involved in the study (Principal investigator(s), Research coordinator and a potential research student) and may be copied only for the purpose of this study. Despite efforts to keep your personal information confidential, absolute confidentiality cannot be guaranteed. Your personal information may be disclosed if required by law and/or by the University of Manitoba Health Research Ethics Board (HREB) for their auditing program. All data will be shredded after the time has expired.

Feedback /Debriefing:
Feedback on the research findings will be provided through a newsletter for each participating community or program.

Voluntary Participation/Withdrawal from the Study:
Your decision to take part in this study is voluntary. You may refuse to participate or you may withdraw from the study at any time. Your decision to not participate or to withdraw from the study will not affect your other medical care. You are free to withdraw from the study at any time, and /or refrain from answering any questions you prefer to omit, without prejudice or consequence.

Your participation in this study may be terminated without your consent by the study coordinators, or principal investigator. The study staff will withdraw you if she feels that participation is no longer in your best interest, or if you fail to follow the directions of the study staff.

If you decide to participate, you will agree to cooperate fully with the study visit schedule, and will follow the study staff's instructions. We will tell you about new information that may affect your health, welfare, or willingness to stay in this study.

Should you wish to withdraw your participation from the study, you must inform the study coordinators so that your file can be officially close.

Questions:
You are free to ask any questions that you may have about your rights as a research participant. If any questions come up during or after the study, contact the study investigator and the study coordinator.
Dr. Miyoung Suh, Principal Investigator: 204-474-8651

This research has been approved by the University of Manitoba Health Research Ethics Board (HREB) If you have any concerns or complaints about this project you may contact 204-789-3389.

A copy of this consent form will be given to you to keep for your records and reference.

DO NOT SIGN this form unless you have a chance to ask questions and have received satisfactory answers to all of your questions.

Please check your answers:

Do you understand the benefits and risks involved in taking part in this study? Yes ☐ No ☐

Have you had an opportunity to ask questions? Yes ☐ No ☐

Do you understand why you are donating blood and urine samples? Yes ☐ No ☐

Do you understand how your information is held confidential? Yes ☐ No ☐

Do you understand why you need to attend the workshop? Yes ☐ No ☐

Consent:

1. I have read and understood this Information and Consent Form, and I freely and voluntarily agree to take part in this research study) described above.

2. I understand that I will be given a copy of the signed and dated Information and Consent Form. I have received an explanation of the purpose and duration of the study, and the potential risks and benefits that I might expect. I was given sufficient time and opportunity to ask questions and to reflect back my understanding of the study to study personnel. My questions were answered to my satisfaction.

3. I am free to withdraw from the study at any time, for any reason, and without prejudice to my future medical treatment.

4. I have been assured that my name, address and telephone number will be kept confidential to the extent permitted by applicable laws and/or regulations.

5. By signing and dating this document, I am aware that none of my legal rights are being waived.

Signature:_____ Date/Time:_____

Printed name::_____

For research coordinator only:

I confirm that I have explained the purpose, duration and procedures of this study, as well as any potential risks and benefit, to the above participant. I believe that the participant has understood and has knowingly given their consent to participate by her personally dated signature.

Signature:_____ Date/Time:_____

Printed name:_____ Study Role:_____

All signatories must date your own signature

APPENDIX B: COPY OF CONSENT EXPLANATION DOCUMENT

Key Points on Consent Form

Why are we doing this?

- Learn how the nutrition balance works (see pictures of nutrition balance)
- See what you normally eat
- See where you are in the nutrition balance

What do we need from you?

- Fill out a questionnaire
- Give some brief feedback on your experience with the questionnaire

What will we do?

- Calculate amounts of vitamins and minerals in the food you eat
- Calculate the overall/average nutrition status of group of women

What WON'T we do?

- NOT share your personal results with ANYONE.
- NOT share this information with anyone who has any influence on your well-being or the well-being of your child and family
- NOT link your name to your personal results.

Are there any risks for you?

- You may feel uncomfortable answering quesitons about alcohol use.
- You may get a milk bruise from blood collection and there is a small risk of infection with drawing blood.

What if you decide to quit?

- Your decision to take part in this study is voluntary.
- You can refuse to answer questions you don't feel comfortable with.
- You can quit the study at any time, we won't judge.

What's in it for you?

- Free food - you will get breakfast and snacks
- Fun - the questionnaire should be as enjoyable as possible and we hope you have fun!
- Health - the information we get will help programs at Mount Carmel to know what can be done to improve your nutrition and health.