Methodological Examination of Screening Prenatal Exposure to Alcohol and Illicit Substances

By: Moumita Sarkar

A thesis submitted in conformity with the requirements for the degree of Doctor of Philosophy (PhD.)

Institute of Medical Sciences, University of Toronto.

© Copyright 2010 by Moumita Sarkar. All Rights Reserved. Unauthorized presentation, reproduction or publication is prohibited.
ABSTRACT

Fetal alcohol spectrum disorder (FASD) is the leading non-genetic cause of brain damage. In an effort to reduce alcohol-exposed pregnancies, steps are needed to identify at risk women as early as possible so that appropriate intervention can occur. The objective of this dissertation was to examine screening methods validated in identifying pregnant women at risk for consuming alcohol and illicit drugs during pregnancy. A systematic review identified three main approaches including maternal self-report, use of standardized questionnaires and detection via biological markers. Since most screening tools were developed in alcoholic women, it was important to examine performance in problem drinkers. Alcohol screening tools (ASQ), currently the best method of predicting prenatal problem drinking, were not effective in a cohort representative of problem drinkers. ASQ performance improved minimally, using higher thresholds, but not enough to be used alone. Provider’s knowledge of complexities inherent in women under their care is an important component in screening. As illicit drug use is an important predictor of problem drinking, identifying maternal risk factors associated with substance use was necessary. Increased
rates of STD’s, untreated psychiatric disorders, binge drinking and heavy smoking were all identified as predictors of prenatal methamphetamine (MA) use. These factors, combined with high rates of unplanned pregnancies have serious adverse implications for the fetus. The most widely used method to screen for illicit substance use is based on a practice-based approach that relies heavily on maternal self-report. Most providers do not ask about alcohol and substance use in the absence of a high index of suspicion due to the assumption that patient will deny use. But evidence suggests that maternal account can be accurate in a supportive environment. The last study examines the agreement between self-reported data, in comparison to illicit drug use based on positive hair test results. A reasonable agreement between the two approaches of identification demonstrates that maternal self-report can be reliable in women who are motivated enough to seek prenatal care. No single approach is sufficient to effectively identify at risk women. However, combining two or more methods will improve screening and help reduce the number of alcohol-exposed pregnancies.
ACKNOWLEDGEMENTS

I will start by thanking Dr. Gideon Koren for your continual encouragement and guidance as a mentor, and putting my best interest ahead. My heartfelt gratitude for presenting me with so many opportunities to develop as a researcher. To my advisors, Dr. Usoa Busto and Dr. Tom Einarson, I thank you for always taking the time to provide your invaluable feedback and guidance. I particularly want to acknowledge all the Motherisk counselors and fellow graduate students who have grown to become very close friends over the years and certainly set the standard for any future workplace environment. I feel privileged to have been part of this amazing team and hope to remain friends no matter where we are. My special thanks to Caroline Maltepe, Pina Bozzo, Sammy Gill, Ingrid Goh, Yvette Navioz, Eunji Kim and Lisa O’Brien for all the wonderful memories. My sincere gratitude goes to Adrienne Einarson, my “workplace mom” for her continual support and insight, as well as Dr. Irena Nulman for her valuable guidance over the years. I also want to thank The Institute of Medical Sciences and the entire Division of Clinical Pharmacology.

Most importantly, I want to acknowledge the most valuable aspect of my life, my amazing family. I will begin by thanking the most wonderful in-laws any girl can be blessed with: Papa, Mamma, Khushaal, Didi, Jij and our darling nieces, Amiya and Iyla. Thank you for your constant love, encouragement and understanding over the past three years. To my loving brother Debashis, thank you for never failing to put a smile on my face when I need it most. I dedicate this dissertation to my amazing parents, Ma and Baba. I am where I am due to your unconditional love, constant guidance and sacrifices over the years. Finally, to my loving husband, Sanjog, thank you for your unending devotion, encouragement and belief in me. The word “impossible” does not exist with you by my side - you are my everything.
# TABLE OF CONTENTS

Abstract ........................................................................................................................................... II
Acknowledgements ........................................................................................................................ IV
Table of contents ........................................................................................................................... V
List of tables ................................................................................................................................... VIII
List of figures ................................................................................................................................... VIII
List of appendices ........................................................................................................................ IX
List of abbreviations ..................................................................................................................... XI

1. Introduction ................................................................................................................................. 1

1.1 Overview of Research .................................................................................................................. 2

1.2 Scope of the Problem ................................................................................................................... 7

1.3 Study Rationale .......................................................................................................................... 9

1.4 Research Objectives .................................................................................................................. 13

1.5 Research Hypothesis .................................................................................................................. 14

2. Review of the Literature ............................................................................................................. 15

2.1 Classification of Prevention ....................................................................................................... 17

2.1.1 Universal Prevention.............................................................................................................. 17

2.1.2 Selective Prevention ............................................................................................................. 17

2.1.3 Indicated Prevention ............................................................................................................. 18

2.1.4 Alcohol ................................................................................................................................. 18

2.1.5 Definitions of Alcohol use ................................................................................................... 18

2.1.6 Drinking Patterns in Pregnancy ............................................................................................ 19

2.1.6.1 Binge drinking ................................................................................................................. 19

2.1.6.2 Risky or problem drinking ............................................................................................ 20

2.1.6.3 Alcohol abuse vs. Alcohol dependence ........................................................................... 20

2.1.7 Prevalence of Alcohol .......................................................................................................... 21

2.1.7.1 Use in women of childbearing age and pregnancy .......................................................... 21

2.1.8 Teratogenic Effects of Ethanol ............................................................................................. 22

2.1.8.1 Fetal exposure to ethanol ............................................................................................... 23

2.1.8.2 Fetal Alcohol Spectrum Disorder (FASD) ...................................................................... 23

2.1.8.3 Prevalence and Incidence of FASD ............................................................................... 24

2.1.8.4 Clinical Manifestations ................................................................................................. 25
Table 22: Common illicit substances in MA-exposed women………,…… 170

Table 23: Frequency of illicit drugs use by MA-exposed women…………… 174
<table>
<thead>
<tr>
<th><strong>Figure</strong></th>
<th><strong>Description</strong></th>
<th><strong>Page</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Figure 1</strong></td>
<td>The Spectrum of Alcohol Use</td>
<td>17</td>
</tr>
<tr>
<td><strong>Figure 2</strong></td>
<td>Chemical structure of amphetamine and methamphetamine</td>
<td>28</td>
</tr>
<tr>
<td><strong>Figure 3</strong></td>
<td>Metabolism of Amphetamine and Methamphetamine</td>
<td>30</td>
</tr>
<tr>
<td><strong>Figure 4</strong></td>
<td>Schematic drawing of a hair shaft</td>
<td>48</td>
</tr>
<tr>
<td><strong>Figure 5</strong></td>
<td>Timeline Follow-back Calender (TLFB)</td>
<td>76</td>
</tr>
<tr>
<td><strong>Figure 6</strong></td>
<td>Flow Chart of Level I and II</td>
<td>100</td>
</tr>
<tr>
<td><strong>Figure 7</strong></td>
<td>ROC Curve for TWEAK and T-ACE at various CP</td>
<td>136</td>
</tr>
</tbody>
</table>
LIST OF APPENDICES

Appendix A: The Motherisk Alcohol Intake Form………………………………………232

Appendix B: Script for Verbal Consent……………………………………………….236

Appendix C: The Motherisk Alcohol and Substance Use Questionnaire………..237

Appendix D: Ethics Approval……………………………………………………………240
**LIST OF ABBREVIATIONS**

<table>
<thead>
<tr>
<th>ABBREVIATION</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADHD</td>
<td>Attention-deficit hyperactivity disorder</td>
</tr>
<tr>
<td>ARND</td>
<td>Alcohol related neurobehavioural deficits</td>
</tr>
<tr>
<td>AUDIT</td>
<td>Alcohol use disorders identification test</td>
</tr>
<tr>
<td>CAGE</td>
<td>Cut-down, annoyed, guilty, eye-opener</td>
</tr>
<tr>
<td>CES-D</td>
<td>Center for Epidemiologic Studies Depression Scale</td>
</tr>
<tr>
<td>CI</td>
<td>Confidence Interval</td>
</tr>
<tr>
<td>CNS</td>
<td>Central Nervous System</td>
</tr>
<tr>
<td>DSM-IV</td>
<td>Diagnostic and Statistical Manual of Mental Disorders - Fourth Ed.</td>
</tr>
<tr>
<td>FAE</td>
<td>Fetal alcohol effect</td>
</tr>
<tr>
<td>FAEE</td>
<td>Fatty acid ethyl esters</td>
</tr>
<tr>
<td>FAS</td>
<td>Fetal alcohol syndrome</td>
</tr>
<tr>
<td>FASD</td>
<td>Fetal alcohol spectrum disorder</td>
</tr>
<tr>
<td>HIV</td>
<td>Human immunodeficiency virus</td>
</tr>
<tr>
<td>HSC</td>
<td>Hospital for Sick Children</td>
</tr>
<tr>
<td>IUGR</td>
<td>Interuterine Growth Retardation</td>
</tr>
<tr>
<td>MA</td>
<td>Methamphetamine</td>
</tr>
<tr>
<td>MAST</td>
<td>Michigan alcohol screening test</td>
</tr>
<tr>
<td>MRI</td>
<td>Magnetic Resonance Imaging</td>
</tr>
<tr>
<td>NPV</td>
<td>Negative predictive value</td>
</tr>
<tr>
<td>NTD</td>
<td>Neural tube defect</td>
</tr>
<tr>
<td>PAE</td>
<td>Prenatal alcohol exposure</td>
</tr>
<tr>
<td>PHAC</td>
<td>Public Health Agency of Canada</td>
</tr>
<tr>
<td>PIH</td>
<td>Pregnancy Induced Hypertension</td>
</tr>
<tr>
<td>PPV</td>
<td>Positive predictive value</td>
</tr>
<tr>
<td>PPD</td>
<td>Postpartum Depression</td>
</tr>
<tr>
<td>PRAMS</td>
<td>Pregnancy risk assessment monitoring system</td>
</tr>
<tr>
<td>PTSD</td>
<td>Post-Traumatic Stress Disorder</td>
</tr>
<tr>
<td>RR</td>
<td>Risk ratio</td>
</tr>
<tr>
<td>REB</td>
<td>Research Ethics Board</td>
</tr>
<tr>
<td>SAMHSA</td>
<td>Substance abuse and mental health services administration</td>
</tr>
<tr>
<td>SD</td>
<td>Standard Deviation</td>
</tr>
<tr>
<td>SSRI</td>
<td>Selective Serotonin Reuptake Inhibitor</td>
</tr>
<tr>
<td>T-ACE</td>
<td>Tolerance, amnesia, cut-down, eye-opener</td>
</tr>
<tr>
<td>TLFB</td>
<td>Timeline follow-back</td>
</tr>
<tr>
<td>TWEAK</td>
<td>Tolerance, worry, eye-opener, amnesia, cut-down</td>
</tr>
<tr>
<td>US</td>
<td>United States</td>
</tr>
</tbody>
</table>
CHAPTER ONE

INTRODUCTION
1.1 OVERVIEW OF RESEARCH

Alcohol and illicit substance misuse is a critical public health issue that can result in a wide range of physical, psychological, and social problems affecting mother, child, and society at large. An estimated one million children in the US are likely exposed to recreational drugs in utero each year, resulting in immense costs to society \(^1,2\). To combat this, focus needs to be directed at prevention strategies in an effort to reduce long-term medical, psychological and social consequences for both mother and child.

Screening pregnant women for alcohol and substance use aims to identify those at risk to allow subsequent prevention of in utero fetal exposure. Accurate identification of prenatal drinking and drug use is important not only to understand the nature and magnitude of the problem, but also to determine appropriate medical and psychosocial interventions. A large number of professional organizations recommend that primary care providers routinely screen all women of reproductive age, for risk of prenatal alcohol and/ or illicit drug use \(^3\)\(^\text{-}^6\). Screening in the clinical setting coupled with brief interventions or referral for treatment of alcohol abuse disorders, has been found to be an effective strategy against prevention of alcohol misuse related morbidity \(^7\). In spite of recent screening efforts, however, the incidence of fetal alcohol spectrum disorder (FASD) and substance related adverse effects have not substantially declined. One primary reason is failure to use appropriate screening methods to achieve effective identification of women who are most likely to consume alcohol in pregnancy.

In the past, prevention research focused on pregnant drinkers with heavy alcohol use or dependence problems, as it was thought that only heavy or binge drinking could harm the developing fetus \(^8,9\). However, findings indicate that most women who
continue to drink prenatally are not addicted to or dependent on alcohol, as defined by the DSM IV criteria. Rather, these women are referred to as problem drinkers as they generally engage in risky drinking behaviour. Health professionals have difficulty identifying problematic alcohol and substance using behaviour as women often under-report their exposures due to fear of societal stigma and legal ramifications. A Health Canada study revealed that women most likely to miss being identified by a healthcare provider include those who are Caucasian, well educated, employed, and of high socioeconomic status. Unfortunately, these demographics are also most representative of problem drinkers. Therefore, pregnant women who may be most likely to continue drinking are also those least likely to be asked about their alcohol use and hence, remain unidentified.

The Motherisk Alcohol and Substance Use Helpline is a national service that provides confidential evidence-based information regarding the effects of alcohol and illicit substances use during pregnancy. Women referred to the program are generally educated, employed and resourceful enough to seek medical help in order to define their risk. Since pregnant women themselves initiate contact and provide information about their exposures, “the Motherisk contact” presents an optimal opportunity to evaluate the effectiveness of individual screening tools. Over the years, a range of reliable strategies have been developed and refined to effectively identify at-risk women. Still, each screening method developed has particular strengths and weaknesses and varies in its applicability to clinical settings. Hence, in order to most effectively screen out at-risk women from the rest of the pregnant population, it is of utmost importance that health
professionals choose the most appropriate identification method, based on the type of drug and population being screened.

This dissertation focuses on selective prevention strategies and examines the different methodological approaches used in screening women who are at risk of consuming alcohol and illicit substances during pregnancy. For the first time, this research attempts to compare the effectiveness of different screening approaches in women who are representative of the problem drinking population, with methodology, which overcomes the under-reporting issue. The first step of my work was to critically review the existing literature in an effort to identify the most effective and feasible methods currently being used to identify high-risk pregnant women. This was an essential step as there is presently no set of consensus on guidelines available for health providers caring for these women. Using a consensus process, several evidence-based approaches were identified as effective ways of distinguishing prenatal alcohol and substance users when used alone, or in combination with other methods. The most widely used method in clinical settings was maternal self-reporting, where information regarding quantity and frequency (Q-F) of alcohol consumption and drug exposures are directly derived from pregnant patient herself. Since the issue of under-reporting is often linked to maternal history taking, standardized screening questionnaires were developed and employed.

The second step of my dissertation focuses on determining the effectiveness of several standardized questionnaires to screen for alcohol use in pregnant women. These tests have been validated as practical and effective methods of identifying pregnant women at risk, primarily because they focus on the consequences of drinking rather than
directly asking about alcohol use itself. Since test performance differs from one patient group to the next, it is critical to ensure the effectiveness of each questionnaire in the population in which it is being employed. For the first time, the effectiveness of TWEAK and T-ACE questionnaires will be compared head-to-head in a pregnant population, where under-reporting is minimized.

The third step focused on determining which cut-point thresholds are most suitable to detect problem drinking behaviour in the Motherisk cohort, by identifying scoring thresholds that maximize both sensitivity and specificity of the screening instruments studied.

As mentioned above, prevalence of substance use is high among problem drinkers. Given the context of this dissertation, the next step of my research focuses on methamphetamine (MA) use in reproductive women, which is important to address for a number of reasons. To start, the culture of using illicit substances such as MA in combination with alcohol has gained popularity as it not only provides a “relaxed high” but also offsets negative side effects experienced by users. In recent years, MA use has received considerable attention as the only illicit drug that does not have a lower rate of use in pregnant versus non-pregnant women. Gender-focused studies revealed MA was the only exception to the usual trend of males having higher rates of substance use, as well lower ages of substance use initiation versus females. Moreover, it is not surprising that problem drinking women would choose to use MA, in combination with alcohol, as it may serve as a “band-aid” or ‘quick fix’ for conditions such as anxiety, depression, ADHD and weight problems (issues all common amongst women of reproductive age).
In order to identify and improve the health of pregnant women and their infants, it is critical to understand the patterns of MA use during pregnancy, the demographics of pregnant users, and the circumstances of MA use. Hence, the fourth section of my dissertation characterizes pregnant women who use MA and investigates the risk factors inherent in this group. Knowledge of these predictors would place providers in a better position to identify pregnant MA users, who are likely drinking as well.

Finally, the last section of my thesis focuses on comparing the only two approaches presently available in screening chronic drug exposures during pregnancy. This work is the first attempt to assess the reliability of self-reported accounts of substance use, when compared to objective laboratory data provided by analysis of a validated biological marker (hair analysis). Given that self-reported information on drug exposures provided by pregnant women themselves is presently the most feasible and widely used identification method utilized by health professionals in the clinical setting, it is essential to gauge the validity of self-reported account in this group.

Ensuring confidentiality and addressing questions related to alcohol and illicit drugs in a sensitive and non-judgmental manner have been shown to influence truthful reporting. Routine inquiries about drug and alcohol use in all reproductive women further add to the validity of self-reporting as a method of identification, especially when combined with an additional screening approach. Identification of alcohol and illicit drug use in pregnancy continues to constitute the most significant barrier to successful prevention strategies aimed at eliminating FASD. This dissertation will examine the aforementioned screening approaches in an effort to improve the identification of at-risk pregnant women and allow for optimal maternal and fetal outcomes.
1.2 SCOPE OF THE PROBLEM

It has been almost 40 years since it was first discovered that alcohol consumption during pregnancy can cause the fetal alcohol spectrum disorders (FASDs), the leading preventable cause of birth defects and developmental disabilities. Although the majority of women drastically reduce or eliminate alcohol use once they become aware of their respective pregnancies, approximately one-fifth of all pregnant women continue to drink alcohol at some level \(^\text{19}\). It is estimated that the prevalence of FASD is 9.1 per 1000 live births in the United States \(^\text{12,20}\). Similarly, data from the Canadian Perinatal Health Report indicate that 14.6\% of children under the age of two years have mothers who admit to alcohol use during pregnancy \(^\text{21}\).

The critical need to screen all reproductive women and identify those who engage in problem drinking behaviour cannot be overstated, as this is the first step to reducing alcohol-exposed pregnancies. Children affected by prenatal alcohol exposure may present with prenatal or postnatal growth deficits but many can have normal growth. The most serious consequence of prenatal exposure to alcohol relates to the effect of alcohol on the developing brain, placing exposed children at risk for significant learning, behavioural and cognitive deficits \(^\text{20}\).

Adding to the predicament of screening for prenatal drinking is the significant overlap in the use of illicit substances and alcohol. Empirical evidence has demonstrated that illicit substance use is highly predictive of problem drinking, prompting researchers to also address the growing incidence of illicit drugs such as MA and their impact on society. A United Nation’s report predict MA to be the next drug epidemic of the 21\textsuperscript{st} century, with its use surpassing cocaine in various parts of the world. A large-scale
Canadian study found that in addition to alcohol, 75% of participating youths reported crystal MA use. Knowledge and awareness of the high prevalence of poly-substance use among problem drinkers need to improve so that providers can routinely screen for all drugs used during pregnancy.

Finally, research indicates that children exposed to alcohol or MA have significantly lower health and quality of life outcomes versus children and youth from the general Canadian population. Children with FASD struggle with depression and anxiety; experience difficulties in social interactions and relationships; and are often seen as “bad children”. Moreover, the economic burden of FASD is substantial. Lifetime direct tangible costs per individual with FASD, related to health care, education and social services in Canada has been estimated as high as $1.4 million. Stade et al report the societal costs associated with FASD include: direct costs (i.e. medical, education, social services), out-of-pocket costs, and indirect costs (i.e. productivity losses). The total adjusted expenditure per child with FASD is estimated to be $14,342 per year. The severity of a child’s condition, the age of a child, and geographical setting are important determinants of costs. It is estimated that the combined cost of FASD annually to Canadians for affected children from one to twenty-one years of age is $344,208,000.

Despite the wealth of knowledge available, there are presently no consistent guidelines on screening and identifying at-risk pregnant women or for the implementation of screening into routine health care practices.
1.3 STUDY RATIONALE

As the deleterious effects of prenatal exposure to alcohol and illicit substances are 100% preventable, successful prevention strategies including screening and intervention are essential. Early identification of alcohol-exposed pregnancies can lead to long-term reductions in morbidity for mother and child as well as health care costs to society\textsuperscript{23,26}. Healthcare professionals play a pivotal role in reducing the number of exposed infants by influencing the health behaviours of women under their care\textsuperscript{27,28}. Several screening approaches currently exist to help them in their task of identifying problem drinking. However, the complexities surrounding these methods of screening make it challenging for providers to effectively identify pregnant women at risk of alcohol and substance use. A major roadblock to effectively screening for alcohol use and related problems is limited reliability of currently available screening methods\textsuperscript{29}. In order to overcome this challenge and improve identification of at risk pregnant women, methodological weaknesses inherent in each type of screening approach need to be examined and addressed. In particular:

1. Healthcare professionals are often unsure of the appropriate methods used in screening pregnant women at risk for problem drinking. Survey findings suggest that many providers fail to inquire about alcohol use or even make use of indirect methods such as standardized tools, which have been found to be most effective in clinical settings. Moreover, even when screening is performed, its validity is comprised due to inappropriate use of tools that are not validated in pregnancy. It is essential to critically review the literature and identify the most
effective methods of screening that have been validated for screening alcohol use in pregnant women.

2. The issue of under-reporting is strongly associated with maternal self-report. Questionable reliability of self-report is of concern for the following reasons: 1) it is the most widely used method of screening in prenatal settings and b) validation of standardized tools relies heavily on maternal self-reported data from population it has been studied. These issues, combined with the knowledge that the effectiveness of screening tools is population specific, highlights the need to examine the effectiveness of tools in groups less severely addicted to alcohol and from higher socio-economic backgrounds. The Motherisk cohort not only share characteristics similar to those with risky drinking behaviour, but also tend to be motivated enough to seek medical care upon pregnancy recognition. This provides the best opportunity to examine the effectiveness of screening tools in a cohort where under-reporting is minimal and study subjects are more representative of problem drinkers.

3. Performance of standardized screening tools depends on the cut-point threshold at which the test most effectively screens problem drinking. Since these thresholds vary based on the population, it is important to determine the threshold most appropriate for use in screening at-risk women in the Motherisk cohort.
4. Given the worldwide popularity of MA amongst reproductive-aged women and its co-morbidity with alcohol misuse, examining different approaches in identifying MA use is also important. Currently, limited knowledge exists regarding pregnant women who use MA and their associated risk factors and demographics. Previous screening findings are from retrospective chart reviews of pregnant women enrolled in treatment programs for severe addiction or dependence on MA\textsuperscript{30,31}, in which recall bias and incomplete documentations were prominent issues\textsuperscript{32}. Hence, women who are not addicted to MA may be less likely to be identified by their respective healthcare providers. It may be helpful to providers to have a better understanding of the women at risk via research conclusions derived from the study of women from a diverse cohort of MA users, where under-reporting is less likely.

5. Although poly-drug use is a common culture among MA users, focus has been limited to concurrent use of alcohol, nicotine and THC\textsuperscript{33}. To our knowledge, there is no data available on other types of synthetic drugs generally co-used by pregnant MA users. There is a need to identify these substances as it has important implications for both screening and fetal outcome.

6. Since maternal self-report is considered unreliable, many providers fail to inquire about substance use in pregnancy under the assumption that women will deny use. However, formally assessing the reliability of this widely used approach is essential as it is presently the most practical method for use in identifying chronic
MA use in the clinical setting. This study is the first attempt to test the validity of maternal self-reported account of MA use in comparison to a validated MA-use biomarker (hair analysis).

Addressing above methodological/practical issues may improve screening and allow more pregnant women who are at risk for alcohol and MA use to be readily identified. This in turn may help reduce the number of maternal and fetal complications related to alcohol and illicit drug use.
1.4 RESEARCH OBJECTIVES

Objective 1:
To critically evaluate all available screening tools validated for the identification of problem drinking in pregnancy

Objective 2:
To compare the effectiveness of TWEAK and T-ACE tool in the Motherisk cohort using different thresholds

Objective 3:
To characterize pregnant women using methamphetamine, and determine potential reproductive risk factors

Objective 4:
To assess agreement between self-report as a method of data collection in comparison to a biological marker in women using methamphetamine
1.5 RESEARCH HYPOTHESES

Hypothesis #1:
There will be several types of approaches that can be used to identify problem drinking during pregnancy.

Hypothesis #2:
There is a difference in the performance of the TWEAK and T-ACE tools. Due to the nature of the study cohort, the TWEAK and T-ACE is less likely to perform effectively using traditional thresholds.

Hypothesis #3:
Some risk factors associated with pregnant women addicted to MA are a concern in less severe users of MA. Alcohol consumption will be a risk predictor of moderate MA use as well, but may not be problematic.

Hypothesis #4:
Maternal self-report is a valid method of identifying pregnant women using MA in the Motherisk cohort.
CHAPTER TWO

REVIEW OF THE LITERATURE
2. CLASSIFICATION OF PREVENTION STRATEGIES

2.1.1 Universal Prevention

Prevention strategies are classified as universal, selective and indicated forms. Universal prevention is a broad-based strategy directed at the general population or a particular group and utilizes a range of popular approaches from public awareness campaigns, to less popular and controversial policy initiatives such as increasing taxation on alcoholic beverages and mandating warning labels on alcoholic beverage containers. It often relies on mass media, educational materials and campaigns to raise awareness of the general public or women of childbearing age about the dangers of drinking during pregnancy 19, 34.

2.1.2 Selective Prevention

This prevention class targets specific populations who might be at greater risk for a particular outcome compared to the general population. An example of selective prevention is screening in populations known to engage in higher alcohol and substance use. This type of prevention is key for a subgroup where women are able to stop using alcohol once they know they are pregnant or when planning pregnancy. The potential of selective prevention is further highlighted given that majority of women significantly cut back their alcohol consumption upon recognizing their pregnancy 35, 36.

2.1.3 Indicated Prevention

This classification of prevention strategy involves individuals who exhibit early signs of problems related to their condition. This level of prevention includes treatment
for alcohol dependence among pregnant or planning women and also addresses other issues usually inherent in women’s lives.  

2.1.4 Alcohol

A standard drink is defined as one 341 mL (12 oz.) bottle of beer (5% alcohol), one 142 mL (5 oz.) glass of table wine (12% alcohol), one 43 mL (1.5 oz.) serving of spirits (40% alcohol) or one 85 mL (3 oz.) serving of fortified wine, such as sherry or port (18% alcohol).

2.1.5 Definitions of Alcohol Use

There is ample empirical evidence that alcoholism encompasses several patterns of drinking. Consumption of no more than one drink per day is considered moderate drinking, while an average of one or more standard drinks daily qualifies as heavy drinking. Binge drinking is a pattern that corresponds to having four or more drinks in one occasion over two hours. For screening purposes, it is also essential to characterize different types of drinkers based on their patterns of alcohol use. The following are some common classifications of female drinkers as per the NIAAA (Figure 1):

**Abstainers:** Do not consume alcohol at all or have less than 1 drink per month.

**Low-risk drinkers:** Consume 1–2 standard drinks per day, less than four times a wk.

**At-risk drinkers or problem drinkers:** Consume 7 or more standard drinks per week; OR consume more than 3 standards drinks at one sitting.

**Alcohol-dependent drinkers:** There is no specified amount of alcohol to classify these drinkers (as per DSM IV criteria).
Figure 1: The Spectrum of Alcohol Use

Saitz R. N Engl J Med. 2005; 352:596-607. The Spectrum of Alcohol Use. The spectrum of alcohol use extends from abstinence and low-risk use (the most common patterns of alcohol use) to risky use, problem drinking, harmful use and alcohol abuse, and the less common but more severe alcoholism and alcohol dependence. Consumption and the severity of consequences increase from low-risk use through dependence. The areas of the pyramid reflect the approximate prevalence of each category.
2.1.6 Drinking Patterns in Pregnancy

In the context of pregnancy, alcohol use patterns can range from mild social drinking (e.g. one drink during dinner) to episodic binge drinking, to more prevalent trend of risky or problematic drinking, to less common pattern of alcohol abuse and dependency.

2.1.6.1 Binge Drinking

In 2005, the definition of binge drinking for women was five or more drinks on any one occasion. However, this was developed for the general population and not specifically for women. Binge drinking for women has since been redefined as more than three drinks on any one occasion. Over the past decade, there has been a significant rise in the rate of binge drinking among women of childbearing age. It is estimated that binge drinking prevalence among childbearing aged women, aged 18–44 years, is presently around 13.0% and rising. Additionally, younger women are more likely to engage in binge drinking than are their older counterparts, placing them at risk for unplanned pregnancies and a host of other adverse consequences.

2.1.6.2 Risky or Problem Drinking

“Risk drinking” is commonly used to describe non-dependent drinking, which may or may not be severe enough to meet the criteria for alcohol abuse disorder, but can result in adverse consequences for the drinker. Sokol et al originally defined risk drinking in pregnancy as an average of two or more drinks daily. However, the current criterion for at risk drinking emerged from research suggesting adverse outcomes may be associated with much lower levels of alcohol consumption. Defining at risk prenatal
consumption levels is critical given that these levels are more representative of the
population at large and less commonly identified compared to alcohol abuse/dependency
This is because problem drinkers are characterized as Caucasian, employed, educated,
have higher incomes and generally seek medical care\textsuperscript{12, 45, 46}.

Unfortunately, although women with risky drinking behaviour are cared for by
physicians, they often remain unrecognized and untreated as external signs of this type of
intake may not present with stereotypical symptoms seen in alcoholic subjects. Addiction
experts estimate that up to 90\% of people who use drugs or alcohol are able to maintain
normal lifestyles\textsuperscript{47}. Similarly, pregnant women who are problem drinkers are no more
likely than non-problem or non-drinking pregnant patients to miss appointments, start
prenatal care late, or appear intoxicated. Not recognizing this fact makes it very difficult
for healthcare practitioners, who often rely on appearance, to identify women at risk of
using alcohol and other substances in pregnancy.

2.1.6.3 Alcohol Abuse versus Alcohol Dependence

According to the DSM-IV criteria, alcohol \textit{dependence} is characterized by
multiple symptoms, including tolerance, withdrawal, diminished control over drinking, as
well as cognitive, behavioral and/or physiological symptoms that suggest the individual
continues to drink despite experiencing significant alcohol-related problems. Alcohol
\textit{abuse}, on the other hand, is considered a maladaptive pattern of drinking that leads to
clinically significant impairment or distress. A diagnosed alcohol abuser continues to
drink despite alcohol-related physical, social, psychological, or occupational problems\textsuperscript{48}.

- 20 -
Over the years, most research on alcohol related interventions have focused on the population that abuse and/or are dependent on alcohol.

2.1.7 Prevalence of Alcohol Use

2.1.7.1 Use in Women of Childbearing Age and in Pregnancy

Research indicates that although the prevalence of alcohol misuse in females has been steadily rising toward the rate in men, more women than men are hidden drinkers. In the US, prevalence data to determine the potential number of women (aged 18-44) at risk for an alcohol-exposed pregnancy are collected using the Behavioral Risk Factor Surveillance System (BRFSS), which is the world’s largest, ongoing, random-digit-dialed telephone survey. Recent data indicate that 54.9% of women who might become pregnant reported using alcohol and 12.4% of these women reported binge drinking. Moreover, these young women also appeared to have initiated and developed dependence at much younger ages. Babor and colleagues found as many as 74% of women over the age of 15 years consumed alcohol, many of who were sexually active and often failed to use contraception. These women were at high risk for an alcohol-exposed pregnancy (AEP), as they generally continued drinking early in pregnancy at levels that were harmful to the fetus.

In Canada, an informal evaluation by the Edmonton First Steps Fetal Alcohol Spectrum Disorder program, offering mentorship for women who are pregnant or who have recently given birth and used drugs or alcohol prenatally, found that of the 96 female clients interviewed, all had begun to use alcohol and/or drugs prior to age 13. Canadian national surveys indicate incidence of alcohol use in previous pregnancy...
ranges from 17% to 25%, with up to 9% continuing it throughout the pregnancy. In more recently published data, prevalence of women’s use of alcohol during pregnancy obtained from the Report on Maternal and Child Health in Canada indicated “roughly 14% of mothers reported drinking alcohol (any amount) during pregnancy”.

From a global perspective, countries that have high rates of alcohol consumption also have high rates of FASD. South Africa, for example, has the highest reported birth prevalence for FAS with reports of 41 to 46 cases per 1,000 live births, particularly in the rural areas where many workers are involved in wine production.

2.1.8 Teratogenic Effects

Human and animal studies have clearly demonstrated that prenatal exposure to alcohol is harmful to the fetus, resulting in physical malformations, growth problems, or abnormal functioning of the central nervous system (CNS). These adverse effects are lifelong and serious; numerous mechanisms have been proposed to explain the damaging effects of prenatal alcohol exposure, with no single consensus. Since effects on the fetus are exhibited through a spectrum of disorders, each individual may exhibit a different combination and severity of the spectrum of alcohol effects. It is important to recognize that the prenatal environment may be important to fetal developmental outcome since it may act to intensify the effect of alcohol teratogenicity. Therefore, each individual’s predetermined genetic vulnerability to alcohol, amount and frequency of alcohol intake and timing of alcohol exposure in pregnancy may play a role. External factors such as mother’s nutritional intake (e.g. adequate folic acid intake), access to medical care, amount of stress she undergoes and presence of substances such as recreational substances in her system also needs to be accounted for.
2.1.8.1 Fetal Exposure to Alcohol

Although the adverse mechanisms of prenatal alcohol exposure are not completely understood, the harmful effects are evident. As a pregnant woman consumes alcohol and her blood alcohol level rises, the alcohol readily crosses the placenta, and typically the fetus is exposed to similar blood alcohol levels as the mother. Gender-specific studies demonstrated that, given the same amount of alcohol consumption under standardized conditions, women attain consistently greater blood alcohol concentrations than men following equivalent amounts of alcohol consumption. This is due to two factors: 1) women’s body water (the compartment in which the alcohol distributes) is significantly smaller than that of men and 2) women have a higher rate of alcohol absorption from the stomach than do men.

2.1.8.2 Fetal Alcohol Spectrum Disorder (FASD)

The association between alcohol use in pregnancy and associated constellation of physical abnormalities was first published when Paul Lemoine described the effects of prenatal alcohol exposure in the medical literature in 1968. However, it was not until 1973 that the term Fetal Alcohol Syndrome (FAS) was first coined to describe the discrepancies in facial characteristics, growth and neurobehavioural function in children exposed prenatally to alcohol. In 1981, the U.S. Surgeon General issued a public health advisory warning that alcohol use during pregnancy could cause birth defects. The warning was subsequently reissued by the Surgeon General in 2005. The severity of these long-term core deficits is independent of the presence of facial anomalies, meaning a diagnosis of alcohol-related neuro-developmental disorder can be as debilitating as full fetal alcohol syndrome. In fact, in many cases, it can be even worse,
because the person may appear superficially healthy and will be expected to perform to a level of maturity and abilities.

Ninety per cent of individuals afflicted by FASD have been shown to have some form of diagnosable mental disorder\textsuperscript{60, 61}. These can range from ADHD (attention deficit hyperactivity disorder), social and communicatory impairments, personality disorder, addiction and depression\textsuperscript{62}. Fifty per cent may get into trouble with the law and 50\% some form of sexually inappropriate behaviour\textsuperscript{63}. Much of this may be related to their inability to control and maintain their behaviour as a result of damage to their executive function combined with receptive language difficulties.

\textbf{2.1.8.3 Prevalence and Incidence of FASD}

In the US, CDC reports FAS prevalence rates between 0.2 to 1.5 cases per 1,000 births across various populations in the United States\textsuperscript{64, 65}. The task of estimating the number of Canadian children with FASD is difficult, as the ability to perform diagnosis varies across the nation significantly. However, in Health Canada’s Framework for Action on FASD, the incidence is estimated to be nine in 1,000 live births\textsuperscript{28}. This translates to about 4,000 alcohol-affected births annually in Canada.
2.1.8.4 Clinical Manifestations

Physical Manifestations:

- Abnormal facial features, such as a smooth ridge between the nose and upper lip
  (this ridge is called the philtrum)
- Small head size
- Shorter-than-average height
- Low body weight

Common Psychological Deficits:

- Hyperactivity
- Attention deficits
- Sustained attention
- Focused attention
- Cognitive problems
- Planning difficulties
- Learning/memory problems
- Lower IQ
- Arithmetic difficulties
- Receptive language difficulties
- Verbal processing problems
- Social understanding difficulties
Common Secondary Difficulties:

- Psychiatric problem
- Disrupted school experience
- Trouble with the law
- Confinement
- Inappropriate sexual behaviour
- Alcohol/drug problems

The relationship between prenatal alcohol exposure and growth deficiency appears to be linear, with effects documented even at relatively low levels of exposure. Although the facial dysmorphology and growth retardation associated with prenatal alcohol exposure are perhaps more easily identified, the most damaging effects are abnormalities of the central nervous system (CNS), which affect neurocognitive and behavioural functioning. One study found that the average IQ of 178 individuals diagnosed with FAS was 79 (range 20–120), which is below the general population range of 85–115.

2.1.9 Guidelines and Recommendations for Perinatal Alcohol Use

Recommendations of the U.S. Surgeon General, ACOG, AAP, and PHAC advise counseling all women who are pregnant or planning pregnancy that drinking can be harmful to the fetus and that abstinence is the safest policy. This is primarily because alcohol exposure has no apparent benefit for the developing fetus and is not necessary for the health and wellbeing of the mother.

With new research, adverse consequences attributed to low and moderate drinking (less than 7 drinks per week) have emerged. But possible under-reporting by heavy
drinkers and confounding effects of other important factors (nutrition, environment, etc.) make it difficult to prove or disprove a direct effect. In light of this, several organizations have redifined recommendations about "safe" levels of alcohol consumption for non-pregnant women of reproductive age.

According to the NIAAA and the dietary guidelines from the U.S. Department of Health and Human Services, sensible alcohol limits for women include:

- Not drinking more than one standard drink per day
- Not drinking more than three drinks per drinking occasion
- Not drinking alcohol at all if you are pregnant, breastfeeding, or planning
- Not drinking alcohol if you are sexually active and not using contraception.
2.2  METHAMPHETAMINE (MA)

2.2.1  History and Use of MA

MA (C10H15N) was first synthesized in Japan in 1919, patented in 1920 to be marketed as an anorectic. Currently in North America, oral MA is approved for the treatment of attention-deficit hyperactive disorder and short-term treatment of obesity. Unfortunately, due to its high abuse potential and easy accessibility, this potent central nervous system stimulant has grown to become the most widely available and used synthetic drug globally. In the 1960’s, it became a common street drug known as "speed" usually taken in pill form, while in the late 1980s, a crystal form that easily dissolves in water or alcohol was created and continues to gain popularity. Crystal MA, also known as ‘ice’ or ‘crystal’, is a crystalline form of higher purity MA. Compared to other forms, the increased demand for crystal MA can be attributed to its quick onset of action and significantly higher levels of dependence.

2.2.2  Pharmacology of MA

MA is a highly addictive stimulant that is a chemical variant of amphetamines. At comparable doses, MA penetrates into the brain to produce much stronger CNS effects through the release of higher levels of dopamine than amphetamines. The methyl group is thought to be responsible for increasing the stability of the substance against enzymatic degradation by MAO and for alleviating transport across the blood brain barrier through greater lipid solubility.
The primary action of MA is by elevating the levels of extra-cellular monoamine neurotransmitters (dopamine, serotonin, norepinephrine) by promoting their release from the nerve endings and subsequently activates both the cardiovascular and CNS systems.\textsuperscript{81}

MA is primarily metabolized in the liver by CYP 2D6 via 1) N-demethylation to produce amphetamine 2) aromatic hydroxylation resulting in 4-hydroxymethamphetamine and 3) \(\beta\)-hydroxylation to produce norephedrine.\textsuperscript{82} The mean elimination half-life, thought to be independent of route of administration, is around 10 h (oral), 11 h (smoking), or 12 h (IV injection). In contrast to cocaine, MA has a much longer duration of action and much of it remains unchanged in the brain, leading to prolonged stimulant effects. While the excretion of MA and metabolites is carried out via the kidneys, in the context of abuse (repeated daily dosing or “tweaking”), MA can be detected in the urine up to 7 days due to its long-term half-life.\textsuperscript{83}

Knowledge on dopamine’s role in MA-induced neurotoxicity originated from experiments suggesting that reduction of dopamine production or blockage of dopamine release led to a decrease in toxic effects upon MA administration.\textsuperscript{84} Since reactive oxygen species (e.g. hydrogen peroxide) is produced from dopamine breakdown, it was subsequently hypothesized...
that resulting oxidative stress from MA use is most likely responsible for neuro-toxic effects. Moreover, the physical sensation produced from an MA “rush” most likely results from the release of dopamine in the pleasure center of the brain. Figure 3 demonstrates the metabolism of MA.

**Figure 3**  **Metabolisms of Amphetamine and Methamphetamine**

![Diagram showing the metabolism of amphetamine and methamphetamine]
2.2.2.1 Pharmacological Actions of MA

The typical acute behavioral effects of MA include feelings of increased energy, alertness, wellbeing, appetite suppression and at high doses, euphoria. Short-term effects upon MA use can include:

- Increased attention and concentration
- Increased wakefulness and activity
- Decreased appetite
- Decreased fatigue and increased energy
- Experience of euphoria and rush
- Increased respiration (tachypnea)
- Rapid / irregular heartbeat (high blood pressure, tachycardia, arrhythmia)
- Hyperthermia (increased body temperature, flushing)

Long-term effects from chronic use:

- Addiction
- Psychosis (including paranoia, hallucinations, repetitive motor activity)
- Memory loss
- Aggression / violent behavioural tendencies
- Mood disturbances (anxiety, irritability, insomnia etc)
- Weight Loss (Anorexia)

In situations of chronic and/or high dosages, seizures, strokes, heart attacks and even death can occur. Depression accompanied by anxiety is commonly seen in the withdrawal period.
2.2.2.2 Route of Exposure

The intensity of a MA “high” experienced by an individual is largely dependent on their pattern of use and route of exposure. MA can be injected, smoked, snorted, or ingested orally. Although smoking and snorting are most common methods for first time use of MA, recent stats suggest injection MA use is on the rise, particularly among the youth. Onset of effects is rapid following intravenous use and smoking, while effects onset more slowly following oral use. Typically, effects are less intense after oral ingestion than following smoked or intravenous use. Overall effects typically last 4-8 hours; residual effects can last up to 12 hours. Table 1 outlines the different routes of administration and a summary of pharmacological parameters including bioavailability, half-life and the average time it would take to peak effect post dose.

### Table 1. Pharmacological Parameter for Routes of MA Exposure

<table>
<thead>
<tr>
<th>Route</th>
<th>Dose (mg)</th>
<th>Bioavailability (%)</th>
<th>Half-life (hour)</th>
<th>Time to Peak effect (mins)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral (^b)</td>
<td>30</td>
<td>62</td>
<td>3-17</td>
<td>180</td>
</tr>
<tr>
<td>Intra-nasal (^a)</td>
<td>50</td>
<td>79</td>
<td>11</td>
<td>≤ 15</td>
</tr>
<tr>
<td>Smoking (^c)</td>
<td>30</td>
<td>67 (^a) – 90</td>
<td>8-17</td>
<td>18</td>
</tr>
<tr>
<td>Intravenous (^d)</td>
<td>30</td>
<td>100</td>
<td>8-16</td>
<td>&lt; 15</td>
</tr>
</tbody>
</table>

Half-life: Methamphetamine plasma half-life; data is presented as a range where appropriate.
(Adapted from Logan BK, Forensic Science Review. 2002; 14(1/2): 133)

2.2.2.3 Stages of MA Use

Among regular MA users, dosing pattern may vary from one individual to the next. Self-reported data indicates that a typical pattern of use appears to consist of four doses daily, often in binges that can last for up to four days. MA abuse typically has three patterns:
**Low intensity abuser** describes a casual user who swallows or snorts MA but is not psychologically addicted and fails to experience any rush. These users typically function normally in society but want the extra stimulation that MA provides to either stay awake long enough (e.g. students, workers, truck drivers) or suppress appetite to lose weight (e.g. young girls, housewives).

**Binge and high-intensity abusers** are psychologically addicted and prefer to smoke or inject MA to achieve a faster and stronger high. This initial response to MA results in faster heartbeat, increased blood pressure and metabolism and can continue for approximately 5-30 mins (in contrast to cocaine which lasts for 2-5 minutes.) The rush is followed by a high that can last 4-16 hours, maintained each time by smoking or injecting more MA until finally, there is no rush and no high. This binge pattern can last 3-15 days and renders the abuser hyperactive, both mentally and physically.

**Tweaking** is the most dangerous stage of the MA abuse cycle and occurs at the end of the binge when nothing fails to take away the feeling of emptiness and dysphoria, including taking more MA. Since this stage is very uncomfortable, the abuser often takes a depressant to ease the bad feelings. The most popular choice of depressant is alcohol, followed by opiates such as heroin. Japanese researchers discovered that chronic maternal administration of this drug changes the mRNA expression pattern in rat fetal and neonatal hearts, leading to abnormal development, plasma hormone levels, and myocardial damage.

**Withdrawal:** There is no acute, immediate symptoms of physical distress are evident with MA withdrawal. Often 30-90 days must pass after the last drug use before the
abuser realizes they are in withdrawal. The individual becomes depressed, lethargic and loses the ability to experience pleasure.

### 2.2.3 Epidemiology of MA use

Use of illicit drugs is widespread among Canadian teenagers and young adults and has increased in recent years. The source of these drugs is often linked to nightclubs and all-night raves, venues frequented by young people, including young women of childbearing age. In Canada, current use of illicit drugs is almost entirely a young people’s concern (ages 15-24 years old). Popularity in the use of club drugs can be attributed to their low costs and easy access, since they are not difficult to produce in “underground” labs. In turn, users of these drugs can achieve intoxicating “highs.” Crystal MA, for example, is easily produced in small, clandestine labs or even at home by mixing a cocktail of about 15 substances, primarily pseudoephedrine (a cold remedy), red phosphorous and iodine as well as other household chemicals such as Ammonia, paint thinner, Drano and lithium from batteries. Unlike other drugs, MA is most often manufactured in the country of consumption. This eliminates the need for elaborate trafficking and smuggling at the border and subsequently makes it more widely available and a cheaper substitute than cocaine. In 2005, DAWN estimated that about 10% of all visits to the emergency department (ED) for drug misuse were by MA users. This was followed by cocaine, marijuana and heroin. In terms of cost, one gram of ‘ice’ (crystal MA) decreased from a range of $120-$700 (in 2002) to $30 - $700 (by 2005) in the US, while the average purity increased from 49% to 69%, respectively.

Off-label use of MA is quite prevalent among women due to effects such as appetite suppression, weight control and increased energy levels, all of which are
appealing to young women of childbearing age. Women generally begin using MA at an earlier age and become more dependent and committed to it than men. Moreover, very high co-morbidity of depression and depression-related symptoms are present in female MA users, suggesting the drug may serve as a type of self-medication for their depression. MA and sexual relationships are integrally linked, where users frequently engage in multiple sexual risk behaviours, drink alcohol daily, use other drugs and have unprotected sex with multiple partners. A study in Tijuana reveals MA as a primary drug of choice among female sex workers.

### 2.2.4 MA Use in Pregnancy

The undisputed concern inherent to all women of childbearing age using MA is the culture of risky sexual behaviour, particularly unprotected sexual activity. Consequently, MA use in pregnant women is also a reality making exposure to the developing fetus inevitable.

A few studies have attempted to examine the prevalence of MA use during pregnancy. For example, data from Arria and colleague’s longitudinal study addressed the prevalence of MA use in pregnancy and found rate of prenatal use to be greater than 5% and growing, partially due to the ample accessibility of MA. Among pregnant women routinely screened via urinalysis (at time of delivery), at least 6% were positive for MA use, while other studies have quoted rates of up to 8% through meconium and hair. Since 2003, MA has been the primary drug of abuse among pregnant women admitted to treatment centers in the US, accounting for 40% of all admissions for drug addiction. Moreover, poly-drug use is also a common phenomenon in this population,
with over 70%-85% of pregnant women admitting to additional drug use concurrently\(^{30}\), most common being alcohol and nicotine\(^{32}\). Finally, withdrawal syndrome is not well established in MA-exposed infants, with data indicating that only 4% of neonates show evidence of withdrawal symptoms requiring any pharmacologic intervention\(^{113}\).

### 2.2.4.1 Fetal and Neonatal Implications

Ample evidence demonstrates that not only does MA cross the placenta\(^{114,115}\), but MA levels in the fetus were found to equal maternal levels\(^{116}\). Levels of MA and crystal MA have also been found in infant blood and several organs including brain, liver, kidneys and lungs\(^{117}\). When pregnant women use MA, the foremost concern is the potential adverse effect of this substance on fetal development. Unfortunately, although animal studies suggest various types of negative ramifications associated with prenatal MA exposure\(^{78,118}\), the full effect of maternal MA use needs further investigation in humans. Isolated cases of fetal malformations (e.g. cleft lip, cardiac defects, intestinal, microcephaly) have been reported, but due to confounding effects of poly-substance use, there is no way to clearly establish a direct link between fetal abnormalities and maternal MA use\(^{109,119}\). Some clinical studies have demonstrated decreased weight, length, and head circumference of neonates born to mothers, who abused MA during pregnancy\(^{120-122}\). Other reports of adverse maternal and fetal outcomes of prenatal MA use include increased risk of placental abruption, preterm delivery, fetal distress, intrauterine growth restriction and low birth weight\(^{113,123}\). However, among these potential complications, low birth weight has been the most consistent association in human studies\(^{113,124}\). A large-scale study in 1,618 women from four medical centers in different parts of the United States found pregnant women who use MA are 3.5 times more likely than other
mothers to have underweight babies. Moreover, a recent study demonstrated that 4% MA exposed infants needed treatment for experiencing withdrawal symptoms including irregular sleep patterns, poor feeding, tremors and increased muscle tone. Finally, infants exposed in utero may also be at increased risk for SIDS, hepatitis (such as Hepatitis B and C), and HIV.

2.2.4.2 Neurotoxic Implications

Substantial animal data suggest that repeated prenatal exposure of MA can cause long-term sequelae in offspring, dependent on factors such as dose and time of MA administration. Preclinical studies found that MA (5 or 10 mg/kg) administered to pregnant female mice or rats results in fetal brain drug concentrations, which approximate those reported in human infants, whose mothers abused MA. Moreover, MA administered prenatally increases offspring mortality, decreases growth rate, and delays development of physical characters, eye opening and functional reflexes. Clinical studies in humans have found that exposure to MA during brain development can cause neurobehavioral abnormalities, such as aggressive behavior, learning problems, and poor social adaptation. It can also result in reduced alertness, both visual and motor difficulties as well as altered neurobehavioral patterns in children characterized by abnormal sleep patterns, poor feeding, tremors, and hypertonia. In addressing long-term implications, exposed children born underweight are more likely to develop type 2 diabetes, cardiac risk factors (such as high blood pressure and obesity) and face higher risk of behavior problems, such as hyperactivity, short attention span, and/or learning difficulties.
2.3 SCREENING, IDENTIFICATION AND INTERVENTION

2.3.1 Screening During Pregnancy

The term “screening” refers to the testing of members of a certain population (e.g. women of childbearing age at a physician’s office) to estimate the likelihood that they have a specific disorder, such as risky or problem drinking behaviour \(^{132}\). It is not a diagnostic test, which establishes a definite diagnosis of a disorder. Rather, screening is used to identify people who are likely to have a disorder (that is determined by their responses).

Half of all pregnancies are unplanned \(^{50,133}\). This, combined with the knowledge that women who consume alcohol at risky levels often present asymptptomatically, or with problems that are not recognized as being alcohol-related, makes it critical to screen women of reproductive age. Pregnancy is a unique time when intervention for harmful drinking can be more effective than at other times in a woman’s life. The health of her unborn child serves as a major motivator when a woman can no longer deny that her alcohol use is harming anyone else but herself. Effective screening can lead to successful identification of at risk women and subsequently get one step closer to reducing the number of alcohol-exposed pregnancies, either by initiating a brief intervention or by referring the patient to treatment \(^{134}\). The current recommendation by most professional organizations is to routinely screen all pregnant women \(^{3-5}\). Several methods of screening currently exist to help providers in their task of identifying at risk pregnant women: 1) obtaining a descriptive account of frequency and quantity of use 2) use of standardized tools that screen for the presence of drug and alcohol misuse and 3)
objective measures such as biomarkers and biochemical tests. The choice of which method to use is dependent on the following considerations:

- The target population
- The purpose of assessment
- Clinical usefulness of the assessment
- Length of time to administer and score
- Availability and costs involved

2.3.1.1 Role of the Provider

Health care professionals are in a position of responsibility to identify, influence and assist women who may be consuming alcohol or illicit substances. Pregnant women often describe their health care providers as the best source of information and generally follow their advice. When faced with the choice of selecting the most appropriate method of screening, health care professionals should consider factors such as the goals of the screening process, characteristics of the target population (age, pregnancy, ethnicity, literacy rates, etc.), and feasibility of implementation.

Presently, the commonly practiced approach to screening in a clinical setting is to simply ask about her alcohol use. However, a high index of suspicion is generally necessary in order to prompt screening detect alcohol dependent women, as providers have often reported their discomfort in addressing the topic of alcohol or drugs. Unfortunately, relying on suspect behaviour or appearance alone can result in many risky drinkers who fail to present as addicts not being identified. In addition, evidence suggests that physicians are less likely to identify alcohol problems among female patients than
among male patients\textsuperscript{10}. Although many practitioners state that they routinely screen for alcohol use\textsuperscript{137,138}, the actual screening rates are low\textsuperscript{139,140}. Patients themselves report that they rarely get asked about alcohol, even in the case of excessive use\textsuperscript{141}. This was evident in a study on alcohol-exposed pregnancies revealing 73\% of cases had no record of alcohol use, despite knowledge of high-risk nature of the women\textsuperscript{142}. The reasons most cited by providers are lack of time, inadequate training, concern about antagonizing patients, lack of interventional services and belief that those who drink at harmful levels do not respond to interventions\textsuperscript{143}. Since most patients with problem drinking behaviour are unknown to their providers\textsuperscript{139,144}, routine screening should be implemented into clinical setting. This also provides an opportunity to educate women of childbearing age under their care about the risks of drinking during pregnancy.

2.3.2 Maternal Report

It is important to distinguish between maternal report that was obtained through an indirect approach (based on structured questionnaires) and data obtained from directly inquiring about her use (based on maternal self-report), as the latter is considered less reliable. The main drawback associated with the self-reported method of screening is the commonly held view that problem drinkers will under report their alcohol use as either a defence mechanism or to avoid the repercussions of admitting use (e.g. fear of child welfare involvement)\textsuperscript{145}.

Evidence of self-reporting problem drinkers minimizing their alcohol use has been established in the literature\textsuperscript{146}. On the other hand, several studies assessing the validity of self-reported alcohol use have also found some degree of agreement between
problem drinkers and other informational sources, such as family members or spouses. However, in spite of the concerns related to under-reporting, maternal self-report remains the most commonly used method of screening in prenatal settings due to its ease of administration. Accuracy of self-report data has been shown to improve in the context of a respectful, non-judgmental and trusting relationship between the woman and her provider. Presently, much of the information collected on alcohol use in pregnancy is based on self-report data, gathered through interviews, self-administered questionnaires and intake histories. Aside from the ease of administration, the main advantage of this direct method of screening is that it obtains information on how much women drink (quantity) and how often they drink (frequency). The Timeline Follow back Method (TLFB) is another technique developed to assist women in their recollection of alcohol and substance use retrospectively. This method of self-reported screening is considered highly reliable when administered in person or over the phone, and has been validated for collecting information on other recreational drug use, in addition to alcohol consumption. Knowledge of amount and frequency of alcohol use is valuable as it allows providers to distinguish between women with risky drinking behaviour and non-problem drinkers.

2.3.2.1 Motivational Interviewing Techniques

An essential first step in increasing the accuracy and reliability of maternal account obtained from clinical interviewing is to develop the relation between the pregnant patient and her provider. Although there are several ways of establishing this, a wealth of research suggests that utilizing Motivational Interviewing Techniques (MIT) during the clinical interview can significantly decrease risks of under-reporting.
Motivational interviewing is a well-known, scientifically tested method of counselling developed by Miller and Rollnick. They defined this process as a “patient-centered, directive method for enhancing intrinsic motivation to change by exploring and resolving ambivalence”. The goal is to steer the patient towards motivation for change by obtaining reasons for change from the patient, hence, an amicable relationship between the clinician and pregnant patient is important. Table 2 outlines some of the attributes inherent in this method of counseling. An interviewer who is confrontational, authoritative and challenging is less likely to obtain accurate information regarding alcohol use than one who is empathic and non-threatening. Hence, empathy is a key element of motivational interviewing.

**Table 2. Characteristics of Motivational Interviewing Techniques**

<table>
<thead>
<tr>
<th>Characteristics of Motivational Interviewing Techniques</th>
</tr>
</thead>
<tbody>
<tr>
<td>- A directive, client-centered counseling style.</td>
</tr>
<tr>
<td>- It elicits behavior change by helping clients explore and resolve ambivalence.</td>
</tr>
<tr>
<td>- It helps resolve ambivalence by increasing discrepancy between client’s current behaviors and desired goals while minimizing resistance.</td>
</tr>
<tr>
<td>- During MI empathic listening is essential to minimizing resistance.</td>
</tr>
<tr>
<td>- Communicates respect for clients and their feelings</td>
</tr>
<tr>
<td>- Encourages a nonjudgmental, collaborative relationship</td>
</tr>
<tr>
<td>- Establishes a safe and open environment for the client that is conducive to examining issues and eliciting personal reasons and methods for change</td>
</tr>
<tr>
<td>- Allows clinician to be supportive and a knowledgeable consultant Compliments rather than criticize</td>
</tr>
<tr>
<td>- Gently persuades, with the understanding that change is up to the client</td>
</tr>
<tr>
<td>- Provides support throughout the process of recovery</td>
</tr>
<tr>
<td>- Understands each individual client’s unique perspective, feelings, and values</td>
</tr>
</tbody>
</table>

2.3.3 Standardized Questionnaire

Designed to detect the presence or absence of at risk behavior such as problem drinking in pregnancy, use of standardized alcohol screening questionnaire (ASQ) is a less direct method of screening. This approach was developed to overcome the concerns of under-reporting often inherent in maternal report by focusing on the consequences of drinking, rather than directly questioning women about their use. Since they are quick, practical and cheap, ASQ’s are considered the best available method for detecting problem drinking in a clinical setting.\textsuperscript{156, 157} Rather than providing a diagnosis, these tools help identify patients who may benefit from a more thorough assessment of their drinking behaviour through subsequent follow-ups. The disadvantage of this approach however, is its inability to determine the range of use (i.e., amount and frequency). Therefore, these tools are most suitable solely screening and detecting the presence of possible misuse of alcohol and illicit drugs. In general, a positive screen on ASQ is not useful for alcoholism diagnosis, but rather an indication for prenatal risk drinking. This is in contrast to approaches such as quantity/frequency and biochemical tests that can provide measures of drug and alcohol use that can be helpful for planning interventions.

2.3.3.1 Validation of ASQ

A central issue surrounding any screening method, including ASQ, is the validity of the instrument. The term validity describes how accurately an instrument measures what it is supposed. ASQ are population-specific, meaning they are only as good as the population they were tested on. Therefore, the performance of each ASQ varies from one subgroup of women to the next. Effectiveness of a tool is related to measures such as sensitivity, specificity, positive predictive value and negative predictive value. The
characteristics of individual ASQ including the TWEAK and T-ACE are further discussed in detail in section 3.6.2.

### 2.3.4 Biological Markers

Optimally, women exposed to drugs during pregnancy should be identified soon after birth so that appropriate intervention and follow-up can be done on both mother and child. The commonly used methods to screen women for illicit drug use such as MA include: 1) maternal self-reported drug history (information may be unreliable) and 2) maternal urinalysis (high risk of false-negative results due to short elimination half-life of drugs). Additionally, analysis of amniotic fluid or urine of the baby at the time of delivery can also be conducted; however, there is a high risk of false-negative results if mom chose to abstain from the drug a few days prior to delivery. Due to the limitations associated with maternal report and biochemical measures, they are not considered suitable methods of detecting chronic exposures to drugs on their own, especially in the context of pregnancy.

Over the past two decades, biological markers such as hair and meconium levels have garnered a lot of attention due to their ability to capture prolonged drug exposures in both mother and her neonate. Use of this method to identify at risk women has been documented for a growing list of illicit drugs including cocaine, MA, opioids and cannabinoids\(^{110}\). Meconium is obtained from the first bowel movement of the neonate. Although meconium collection is an easy and non-invasive process, it allows for detecting drugs only in the second and third trimester\(^{145}\). This is because meconium formation begins around the 12\(^{th}\) and 14\(^{th}\) week of gestation. Its inability to detect drug exposures during organogenesis is an important limitation since in utero exposure during
this period can have a severe impact on fetal development and future implications for the child.

The analysis of drugs in hair samples has become very popular in recent years with possible applications in forensic and in clinical toxicology as well as in work-place drug testing procedures. Aside from the ease and non invasive nature of the collection process, the main advantage over meconium in using maternal hair as a biomarker is that window of drug detection is dramatically extended to weeks, months or even years. Although hair analysis makes it possible to confirm a fetal drug exposure, use of biomarker data to identify women is not routinely done in Canada\textsuperscript{158}.

2.3.4.1 Hair as a Biological Marker

Use of hair analysis as a chronic state biological marker has been the subject of considerable study. Although the first reports of hair analysis for the detection of drug exposure date back to the mid-nineteenth century\textsuperscript{159}, the last 20 years have seen hair analysis emerge as a valid tool for the detection of chronic xenobiotic exposure. As a result, hair analysis has become a valid screening tool for exposure to a number of xenobiotics and is accepted as evidence in most judicial proceedings\textsuperscript{160-162}. A variety of drugs and endogenous substances have been accurately measured in hair, including: opiates, barbiturates, benzodiazepines, anabolic steroids, cocaine, nicotine and recently, MA\textsuperscript{163, 163, 164}. In clinical settings, hair drug levels have been used to assist in therapeutic drug monitoring\textsuperscript{165}. 

- 45 -
Hair fibers are structurally complex consisting of three main layers: the cuticle, the cortex and the medulla. The hair shaft is surrounded by a root sheath that is continuous with the scalp epidermis (Figure 4). The precise mechanisms by which drugs are incorporated into the hair shaft are complex. Studies examining drug incorporation into hair suggest four possible sources of drug deposition in hair that include contact with blood, sweat, sebum and/or adsorption through environmental exposure. While the relative degree of drug deposition from each of these sources is presently unclear, most studies suggest that hair follicle contact with blood from the systemic circulation is the primary method of drug incorporation. Adult hair typically grows at an average rate of approximately 1 cm per month. Segmentation of maternal hair can reveal information about patterns of drug use and identify periods of drug use and abstinence.

2.3.4.2 Validation of Hair Analysis

Validating a biomarker means to ensure that it correctly identifies exposure without false positives or false negatives. Markers of exposure must be validated according to their ability to assess the true exposure (i.e. sensitivity) and lack of exposure (i.e. specificity). A number of factors can affect the validity and feasibility of biomarkers. These can pertain to analytic procedures including time between exposure
and hair collection, amount of hair sample required, storage, contamination and standardization of the procedure. It can also vary based on intrinsic characteristics of the biomarker e.g. its ability to distinguish populations with different exposure levels (sensitivity), its inter and intra-individual variability or other confounders affecting the marker (such as dyeing or bleaching the hair) \(^{168}\). Hence, interpretation of hair results is not as straightforward as that of other specimen’s such as blood given that the relationship between actual amount of drug used and the quantitative hair results can be complex \(^{169}\). The use of hair analysis in detecting MA and other amphetamines have been validated in adults \(^{111,169}\). For the first time, Garcia-Bournissen and colleagues demonstrated trans-placental transfer of MA in humans as evidenced by accumulation in neonates’ hair at levels similar to those of their mothers \(^{111}\).

### 2.3.5 Brief Intervention in the Clinical Setting

Brief interventions (BI) are a critical part of the screening and prevention process. This type of intervention refers to 10 to 15 minutes of counseling, with feedback about drinking, advice and goal setting, and follow-up contact with a clinician. A review of numerous trials have suggested that brief interventions for problem drinking: (1) are significantly more effective than no intervention at all; (2) can have as much impact as more extensive interventions; and (3) can improve the effectiveness of subsequent specialized treatment \(^{170}\). Project CHOICES (Changing High-risk alcohol use and Increasing Contraception Effectiveness Study) was a large interventional study using motivational interviewing and aimed at preventing alcohol-exposed pregnancies among high-risk women. Study focused on providing women two alternatives: reducing risk drinking levels or instituting effective contraception. At the end of a 6-month follow-up,
68.5% of women had lowered their risk of having an alcohol-exposed pregnancy: 13% reduced their drinking only; 23.1% reported using effective contraception only; and 32.9% reported doing both. Screening for risky drinking in combination with BI should be incorporated into routine clinical practice to achieve maximal reductions in AEP.
2.4 BARRIERS TO SCREENING AND IDENTIFYING AT-RISK WOMEN

Since many pregnant women see physicians as their principle source of prenatal care, the primary care setting provides an optimal environment for screening pregnant women as part of routine prenatal health care\textsuperscript{171}. However, accurate assessment for alcohol or drug use is complicated by several factors posing as challenges for health care providers attempting to screen during the routine clinical encounter.

2.4.1 Limitations of Existing Methods

Initiating discussions about difficult issues takes time and skills, as well as adequate knowledge about current alcohol guidelines and risks in pregnancy. For example, the diagnostic standard for alcohol dependence or abuse (as per DSM-IV) requires a detailed interview and is not feasible for routine screening. As a result most clinicians, being under strict time constraints may have time to inquire only about one screening question pertaining to patient’s quantity and frequency (QF) of alcohol consumption.

Although it is an essential component of assessing drinking problems, the QF method is probably not sufficiently sensitive or specific for screening on its own. In one study, drinking 12 or more drinks a week was specific (92%) but insensitive (50%) for patients meeting DSM criteria for an active drinking disorder\textsuperscript{172}. At present time, routine screening of pregnant women for alcohol use disorders is a recommended practice, but not implemented into Canadian practice\textsuperscript{20}. A national study on a sample of Canadian health providers (pediatricians, psychiatrists, obstetricians and gynecologists, midwives
and family physicians) asked pregnant women about their alcohol use, but only 62% report using a standardized screening tool \textsuperscript{173}.

Providers caring for pregnant women are concerned about deterring women from seeking future prenatal care as a consequence of having to report use, and as a result, fail to ask about alcohol or drug use routinely. Several studies have indicated that less than half of self-reported problem drinkers are asked by their primary care provider about their alcohol consumption \textsuperscript{140, 174, 175}. Moreover, D’Amico and colleagues found that only 21.1% of patients had received any type of subsequent advice (e.g., told to stop, referred, or 5 minutes spent on counseling) afterward \textsuperscript{176}. Aside from time constraints, poor reimbursement for procedures such as screening further decreases physician’s motivation to spend the additional time to identify and subsequently refer women to treatment resources \textsuperscript{177}.

Inconsistent guidelines pertaining to the safety of low and moderate prenatal alcohol use can lead to more confusion for women. Although most North American guidelines recommend complete abstinence from alcohol during pregnancy, British and Australian guidelines are much more lenient. The National Institute for Health and Clinical Excellence (NICE) from the United Kingdom (UK) presently recommends that “pregnant women should limit their alcohol intake to less than one standard drink (1.5 UK units or 12 g of alcohol) per day and if possible avoid alcohol in the first three months of pregnancy. Women should be informed that binge drinking (defined as 5 standard drinks on a single occasion) may be more problematic during pregnancy.” In addition, the NICE draft guidance stated that drinking no more than 1.5 units daily does not appear to be associated with harm to the developing fetus \textsuperscript{178}. The current Australian
guidelines advise pregnant women “not to have” more than seven standard drinks a week and no more than two standard drinks within two hours at one sitting. They go on to state that an abstinence-based approach is not recommended, in part because it could result in “disproportionate anxiety” and "precipitous decisions to terminate a pregnancy". 179

2.4.2 Misperception of Risks

As a legal and culturally accepted recreational drug around the world, it is not surprising that teratogenic risks associated with prenatal alcohol consumption, continue to be underestimated. Kesmodel et al. studied a group of pregnant Danish women. The majority (74%) felt that drinking in pregnancy was acceptable; 65% reported they had received little or no information from their midwife about possible dangers. This is consistent with data collected by the UK government in their alcohol reduction strategy that 61% of women drank during pregnancy to some level. 178

In the US, MacKinnion’s study on a group of teenagers found that although 97% had heard of alcohol causing problems during pregnancy, 48% considered it to be a condition related to the baby being addicted to alcohol and just over 50% felt the condition could be resolved. 181 Perception of risk associated with using illegal drugs such as cocaine and heroin is often much greater than a legal drug like alcohol in pregnancy. Hence if cocaine use is suspected, it may become the focus of concern, while others (e.g. alcohol) remain unreported. Along these lines, the woman herself may have a misguided perception of risk as to what is most harmful to the fetus and seek help only for the drugs she considers a risk. This can subsequently result in unintentionally failing to report her alcohol use, if she is not specifically asked about it. Provider’s personal bias can also contribute to at-risk women’s failure to be identified. This is evident from
Canadian national survey findings that 10% of all health care professionals are still advising low to moderate drinking (one glass of wine or bottle of beer) is acceptable in pregnancy 55.

2.4.3 Under-reporting or Denial of Use

Reliability of maternal report is highly variable and dependent on the patient, the health care provider, and individual circumstances. During pregnancy, the stigma attached to drinking and using illicit drugs is usually accompanied by guilt, shame and fear that their children will be apprehended by child protection services. Hence, many women may choose to deny or disclose lesser levels of consumption than true levels. In a study of 361 mothers, 53% of women who initially disclosed alcohol consumption of more than 1.3 drinks per week during pregnancy reported much higher levels of drinking when interviewed retrospectively 44. Evidence over the years indicate that the greater the dependency, the higher the amount of under-reporting in pregnancy 182, 183.

2.4.4 Knowledge Gaps and Resource Limitations

Physicians have previously acknowledged gaps in their knowledge regarding risk factors, impact of gender differences and up to date alcohol definitions and guidelines (i.e. the equivalency of 1.5 oz of distilled spirits to 5 oz of wine) 184. For example, in one survey study, doctors defined “light drinking” as an average of 1.2 drinks per day, an amount that exceeds the current (NIAAA) guidelines for at-risk drinking for women 185. Moreover, while majority of Canadian providers agree that prenatal alcohol exposure is a significant risk factor for brain damage, about 25% still say that the effects of alcohol on fetus are unclear 21. Given the clear evidence of alcohol as a teratogen, combined with
redefinition of drinking criteria based on emerging research, addressing these gaps are essential for effective screening. In countries like the US, these knowledge gaps are further compounded by state laws designed to criminalize drug use during pregnancy due to women’s fears of losing custody of their children $^{186}$.

Primary care settings provide a unique opportunity to detect, treat, and refer patients to appropriate services, yet consistent formal training for residency programs in initial diagnosis and management of alcohol use disorders is lacking $^{187}$. Research shows that trained clinicians typically intervene with more than 70% of patients $^{188}$. At present, the commonly practiced intervention is for frontline providers to refer problem drinkers to specialized treatment facilities. This option is appealing to most professionals for a number of reasons: 1) time is no longer an issue, 2) they may feel ill-prepared to intervene due to inadequate training in the realm of addictive behaviours or 3) have a preconceived perception that this subgroup of women may be chronically unmotivated, dishonest and unwilling to change their recreational drug using behaviour. Finally, screening for pregnant women who consume alcohol, presupposes that intervention resources are readily available to support women who are identified. Unfortunately, experts generally agree that resources to care for and treat pregnant women with substance use issues are quite insufficient in this country, making this a major barrier in the incentive to screen.
2.5 ALCOHOL AND SUBSTANCE USE – A MULTIFACTORIAL ISSUE

Women who are at risk of giving birth to children with FASD are a diverse and complex group of individuals whose behaviors and lifestyles are often resistant to change. The variability in clinical manifestation of children born to alcohol using women (symptomatic 3-40%) also suggests that other factors (e.g. genetic, nutritional, metabolic, or temporal) may influence the expression of FASD. For many women, alcohol and/or illicit substance use helps them contend with difficult life circumstances such as history of trauma, mental health problems, partner substance abuse, poverty, feelings of guilt, shame and inadequacy. Failure to understand and address the complexity of their lives in a clinical setting will lead to lack of proper identification of women that are actually in need of help in pregnancy for their alcohol use.

2.5.1 Psychiatric Disorders During Pregnancy

Women experiencing mental health problems may use substances to self medicate, with ongoing self-medication being a typical response pattern. In turn, presence of psychological disorders may also impact on the pregnant patient’s ability to discontinue her alcohol and substance use, if remained undiagnosed. The co-existing presence of alcohol/drug dependencies and mental health disorders as two distinct disorders is usually termed “dual disorder.” Mental health problems found to be common among substance/alcohol abusing women include depression, anxiety, and PTSD (Post Traumatic Stress Disorder).
There is growing recognition that dual disorder is a common phenomenon, that is, many people with drug or alcohol problems also experience a range of other psychiatric and psychological problems. These conditions can vary greatly, from undetected major psychiatric illnesses to less defined feelings of low mood and anxiety that do not meet diagnostic criteria but nevertheless impact on her sense of wellbeing and affect her quality of life \(^{194}\). In fact, there is evidence for a continuum in the magnitude of co-morbidity as a function of alcohol use level \(^{195}\).

2.5.2 History of Trauma and Volatile Lifestyle

A prevalent risk factor common to almost all women dependent on alcohol is the experience of trauma at some point in their lives. Over 50% of women report having experienced physical, sexual, and/or emotional abuse and neglect \(^{196}\). Not surprisingly, many of these young women turn to alcohol in an effort to numb their emotional pain and cope with the uncertainty and instability of their lives. Berenson and colleagues found that battered women were more likely to use alcohol, drugs and smoke \(^{197}\). Another study examining the profiles of 80 children with FASD found that at-risk women have commonly experienced abuse and mental health problems, both of which are known to co-occur with substance abuse. Unfortunately, risks for adverse fetal outcome are also the highest risk in this group due to their frequent binge drinking patterns \(^{198}\).

Many of these women develop low self-esteem, and often get involved in abusive relationships. Experiences of intimate partner violence (IPV) have been documented and were found to be prevalent mostly among women using alcohol and other substances to cope with the abuse \(^{304}\). Also, since at risk women tend to have unprotected sex, they are at greater risk of developing STI’s. Reports show that 60% of college women who
developed a sexually transmitted infection (such as genital herpes or AIDS) were under the influence of alcohol at the time they had intercourse \(^\text{305}\).
CHAPTER THREE

CRITICAL EVALUATION OF ALCOHOL SCREENING TOOLS AND PROCESSES USED TO IDENTIFY HIGH RISK PREGNANT WOMEN

3.1 ABSTRACT

Alcohol use during pregnancy is amongst the most preventable causes of birth defects and developmental disabilities that are known. Perinatal alcohol use, in sufficient quantities and at critical time periods of development may result in the fetal alcohol spectrum disorders (FASD), the social and economic burden of which are substantial. This systematic review proposes three levels of screening to be carried out on all consenting women of child bearing age: Level I screening involves practice-based approaches that can be used by health care providers when talking to women about alcohol use, such as motivational interviewing and supportive dialogue; Level II screening includes a number of structured questionnaires that can be used with direct questioning (TLFB) or indirect /masked screening (AUDIT, BMAST / SMAST, CAGE, CRAFFT, T-ACE, TWEAK); and Level III screening includes laboratory-based tools that can be used to confirm the presence of a drug, its level of exposure and determine the presence of multiple drugs. There are challenges and limitations associated with the use of most available screening and assessment tools. Currently, no consensus on the appropriate screening tools or regimens exists in Canada, owing to a multitude of different health systems, each of which is under the jurisdiction of an individual provincial/territorial government. Practice-based questions (single question method) are most feasible to implement at the prenatal setting, however, TWEAK and T-ACE tools appear to be the most effective validated tools to screen pregnant women at risk for alcohol use.
3.2 PROJECT OVERVIEW

3.2.1 Project Rationale

Lifetime direct tangible costs per individual related to health care, education and social services in Canada have been estimated to be $1.4 million\(^{25}\). Screening women of childbearing age and pregnant women and recording their alcohol consumption is a practical process to identify and evaluate women alcohol-exposed infants at risk for adverse health outcomes.

Within the framework of a project funded by the Public Health Agency of Canada, a FASD Advisory Workgroup was established. The task of this group was to analyze current screening tools and available recording systems and make recommendations on the most appropriate screening and recording processes for implementation in the clinical setting. This initiative is an important component of the multi-faceted approach implemented by the Public Health Agency of Canada to decrease the incidence of FASD.

We conducted a search of all existing screening tools and processes that have been validated for use in women of childbearing age. All original articles using RCT, case-control, or cohort studies were included. Articles were searched using the terms “screening tools,” “screening tests,” “women,” “pregnancy” and “risk/problem drinking” in Medline (January 1966-September 2007), Pubmed (1950-September 2007), EMBASE (January 1980-September 2007) and Cochrane database in all languages. Articles that
failed to focus on pregnant women or women of childbearing age, review articles and letters to editors were excluded.

There are challenges and limitations in the use of the screening and assessment tools. For example, the single question about alcohol use and the various questionnaires rely on a woman to provide details about her alcohol use. There are presently no guidelines or consensus on the appropriate approach to screening across Canada and as a result, each provincial / territorial jurisdiction, health care organization and health care provider uses a variety of formal and informal screening tools. In addition, there are inconsistent processes across Canada for the recording of alcohol use in a woman’s chart and the transfer of the information to the infant and the child’s health records.

This consensus report aims to support health care professionals in their role for the screening and recording of alcohol use in all women of childbearing age and pregnant women. From this document, health care providers will recognize the importance of routinely asking women about alcohol consumption, understand the need for, and the effectiveness of using a screening tool to ask women about alcohol use; recognize the importance of recording information about a woman’s alcohol consumption before, during and after pregnancy; offer brief interventions to a woman who is identified as drinking alcohol during pregnancy or while planning a pregnancy; and ensure appropriate documentation in a newborn record and a child’s health record.
3.3 INTRODUCTION

Women’s use of alcohol is an important public health and social issue in Canada as alcohol use during pregnancy is one of the leading preventable causes of birth defects and developmental delays in Canadian children. The adverse effects of alcohol exposure during pregnancy include fetal alcohol syndrome (FAS), partial FAS, alcohol-related birth defects (ARBD) and alcohol-related neuro-developmental disorders (ARND). These are diagnostic terms used to describe conditions along this spectrum. Fetal alcohol spectrum disorder is an umbrella term used to describe all of the above conditions\textsuperscript{20}. The diagnosis of FASD is complex. Since the condition carries lifelong consequences, early recognition of FASD can result in a better outcome for the baby who receives a diagnosis. It is therefore of utmost importance to raise awareness of the impact of alcohol use and to encourage the use of effective screening tools and recording processes in order to reduce the incidence of FASD.

In 1979, the Canadian Task Force on the Periodic Health Examination found there was fair justification for recommending the inclusion of counseling to reduce the alcohol intake of pregnant women in the periodic health examination. This was based on evidence that counseling proved effective in reducing the amount of drinking in pregnant women and the rate of morbidity in their offspring\textsuperscript{199}. The evidence compiled since 1979 supports this original recommendation.

In order to provide prevention and intervention programs and strategies to reduce the incidence of FASD, maternal alcohol consumption must be identified. Asking questions about alcohol use during pregnancy is necessary for gathering accurate and
reliable information that will initiate an appropriate intervention program, as well as early diagnosis of babies affected by prenatal alcohol exposure.

Health care professionals play a critical role in screening women for alcohol use during pregnancy. There is general agreement that improvements in the use and implementation of screening tools for alcohol use among women will have a significant impact in decreasing the incidence of FASD. However, there are currently no standard screening approaches or tools available in the clinical setting in Canada and there are no processes in place to ensure consistency in the recording of this information. In a study that collected information from Canadian health care professionals, the majority of health care professionals (93.6%) reported that they routinely discussed current drinking patterns with pregnant patients. However, only 62% reported using a standardized screening tool. The aim of this report was to provide an overview of the tools and processes available for the screening and recording of alcohol use in women of childbearing age and pregnant women.
3.4 SCREENING PROCESS

Pregnant women should be informed that no safe level of alcohol consumption during pregnancy has been established. The Public Health Agency of Canada recommends abstaining from alcohol use during pregnancy. Women who have consumed small amounts of alcohol before they knew they were pregnant can be reassured that the risk to their baby is small if they abstain from further alcohol consumption, eat a balanced and nutritional diet, and adopt a healthy lifestyle, throughout the course of their pregnancy.

Some groups and health professionals still maintain that there are safe guidelines for drinking while pregnant, but the safety of mild drinking cannot be proven. While a systematic review of the effects of pre-natal exposure to low levels of alcohol indicated no significant effects on physical development pre- or postnatally, a meta-analytical review of the research literature by Testa et al indicated significant effects on mental development at age 12 months. Therefore, abstaining from alcohol use is the only responsible approach for women who are, or may become pregnant.

While the importance of the health care provider as an effective information resource for harm reduction is recognized, it is essential that adequate community resources also be made available for women who require interventions beyond this primary interaction.

Screening for alcohol use in childbearing women should be part of a comprehensive psychosocial assessment. Psychosocial risk factors for substance use may be part of many Canadian women’s life experiences. The ALPHA form (Antenatal Psychological Health Assessment) is a validated ante-natal psychosocial assessment form.
available at http://dfcm19.med.utoronto.ca/research/alpha. The ALPHA form contains questions relating to family factors (social support, recent stressful life events, the relationship of the couple, etc.), maternal factors (self-esteem, mood disorders, relationship with parents, etc.), substance abuse issues (including partner’s substance use, poly-drug use, etc.), and family violence (childhood experience of family violence, childhood sexual abuse, intimate partner violence, etc.). The form is available as either a self-completing or provider-completing version for each use. By asking a woman about the totality of her psychosocial health, a provider can better understand the issues that may lead to alcohol use. Additionally, by using a standardized psychosocial assessment instrument, which includes a section on substance use, the woman may feel less vulnerable responding to personal questions.

3.4.1 **Maternal Alcohol Screening**

The Canadian guidelines for diagnosis of fetal alcohol spectrum disorder recommends the screening of all pregnant and post-partum women for alcohol use.

**What?** A process to identify and evaluate alcohol use that might put the mother-child well-being at risk.

**Who?** Women who are pregnant or of child-bearing age.

**Why?** Improved maternal-child health outcomes through:

- Early identification and reduction of problem maternal drinking
- Recording of maternal alcohol history on a newborn’s birth record
- Early identification of exposed infants
- Earlier diagnosis of FASD
Maternal alcohol screening and recording by health care providers could lead to a reduction of primary FASD disabilities as well as reduction of secondary disabilities often related to FASD in the absence of diagnosis and appropriate interventions. The take home message remains that the earlier in pregnancy a woman can stop drinking, the better the outcome; the younger the age at which the affected child is identified, the lower the frequency of secondary disabilities ²⁰².

3.4.2 Benefits of Identifying Maternal Alcohol Consumption

There are several advantages of identifying problem drinking during pregnancy. These include:

• Identification of women who would benefit from information about Health Canada’s recommendations regarding safe drinking levels pre-pregnancy and abstinence during pregnancy.

• Identification of pregnant women who could benefit from information about FASD and the possible effects of pre-natal alcohol exposure.

• Identification of pregnant women or women of child-bearing age who should be referred for varying levels of drug and alcohol services – assessment, counseling, detoxification or inpatient treatment.

• Referral of women who’s drinking might be related to depression, abuse or other mental health issues to the appropriate mental health service.
3.5 LEVEL 1: PRACTICE-BASED SCREENING

Recent surveys of health professionals indicate that some clinicians feel uncomfortable asking about alcohol use. They may avoid the subject of alcohol use entirely because they do not know how to identify women who engage in at-risk drinking without embarrassing or offending their clients who are not consuming alcohol. Others lack knowledge of the alcohol treatment and counseling services that are available or reside in areas that simply lack adequate services. Still others may hesitate to screen because they are pressed for time and screening for alcohol use may seem to be beyond the scope of their practice.

Screening for alcohol use need not be complicated, time consuming, or difficult. One or two interview questions concerning alcohol use have been shown to be an effective way to screen women by identifying those who are drinking and in need of education or intervention. Most pregnant women appreciate their practitioner’s concern for their health and the health of their unborn baby. Women are especially open to changing their lifestyle when they are pregnant if they know that it will help their baby. This offers practitioners an opportunity in terms of motivating women to change at-risk behaviours. Practitioners should inquire about a woman’s alcohol consumption and provide information about the effects of alcohol on the unborn baby at the very first pre-natal visit or at a preconception counseling visit. Many women do not know that alcohol could affect their unborn child. They may have been told in the past by friends, relatives, or even other health providers that drinking moderately during pregnancy was acceptable. Many people are not aware of recent research studies of large population samples of pregnant women that prove a dose-response effect of pre-natal alcohol
exposure. The children of mothers who drank at low levels (less than one drink a day) were shown to be at significant risk for problem behaviour. This does not mean that a woman who is drinking at low levels will necessarily have a child with behavioural problems, but it does mean that they increase the probability of a problem.

There are several approaches that health care providers can use when talking to women about alcohol use during pregnancy. The initial inquiry can be included as part of routine pre-natal questioning regarding a healthy lifestyle during pregnancy in terms of nutrition, exercise, and the avoidance of environmental toxins such as nicotine and second-hand smoke. Some physicians choose to have women fill out written questionnaires while they are waiting in the office. Health providers may include one or more questions regarding alcohol or they may embed standardized alcohol screeners in their questionnaires.

For the practitioner who chooses to use the single question method, the following are questions identified as being effective for establishing a rapport and introducing a discussion about alcohol use:

```
“When was the last time you had a drink?”
“Do you ever enjoy a drink or two?”
“Do you sometimes drink beer, wine or other alcoholic beverages?”
“Do you ever use alcohol?”
“In the past month or two have you ever enjoyed a drink or two?”
```

If a woman indicates she does not consume alcohol, then positive reinforcement of her lifestyle choice is beneficial. Research shows that it is helpful to provide brochures and
other information about a healthy lifestyle during pregnancy that includes details about alcohol abstinence and the effects of alcohol on the fetus. Any written information should be provided in a way that is linguistically and culturally sensitive.

If a woman indicates that she does consume alcohol, then a second stage of screening is necessary. This can be done using standardized screening questionnaires such as the T-ACE or TWEAK. Practitioners can also use this opportunity to help a pregnant woman who is using alcohol with a brief intervention (BI) in the office. Research has shown that BIs can be very useful in helping a pregnant woman who drinks mild-to-moderate amounts of alcohol to reduce their alcohol intake during pregnancy. BIs are cost effective and can be implemented in a variety of clinical settings. BIs normally include four components: (1) assessment and direct feedback after assessment; (2) goal setting through establishing contracts; (3) positive reinforcement; and (4) education through pamphlets and hand-outs for self-help.

3.5.1 Use of Supportive Dialogue

A woman-centered approach has been found to be effective in engaging a woman in the decision to change behaviours. As discussed in Section 2.3.2.1, motivational interviewing is a relational model that is based on collaboration between the health professional and a woman seeking care (Table 2). Research shows it to be especially effective in an office setting when health providers are helping women who are drinking when pregnant, but not addicted to alcohol. A woman who is alcohol dependent can be more resistant to change and should be referred to counsellors who can devote the time it takes to establish a collaborative relationship. A non-judgmental approach is especially helpful for a woman who drinks heavily and may have other problematic substance use.
issues. Engaging a woman in the decision-making process concerning her own care can increase her will to change while minimizing resistance. Open-ended questions allow a woman to expand on her life circumstances. Practitioners can begin by simply asking a woman what she has heard about using alcohol during pregnancy. They can use this as an opportunity to provide information as well as to correct any misinformation. This can be followed by questions such as:

“Can you tell me a bit about your drinking patterns before you knew you were pregnant?”

“Have you been able to stop or cut down since you found out?”

“Do you have any concerns about your drinking?”

A woman may have concerns about drinking before she knew she was pregnant and it is at this time that the practitioner can reassure her that if she cuts down or stops, she can help her baby. It is also at this time that the practitioner can offer help on how to cut down or to stop drinking.

3.5.2 Interview Techniques for Effective Engagement - “Do’s and Don’ts”

Due to concerns surrounding fear, guilt and stigma, it is essential to utilize effective interview techniques to engage a woman of childbearing age in order to obtain an accurate alcohol use report. These include empathetic listening, and non-judgmental, non-confrontational questions that are woman-centered. The following examples suggest interview techniques for effective engagement 206
• An example of an introductory statement that can be used in a woman of child-bearing age: “I want to ask you a series of questions today about your lifestyle. I ask all my patients these questions because it helps me to get a better understanding of what your day-to-day life is like (in terms of diet, exercise and other lifestyle issues). It will help me to know you, and that will help me to provide better care.”

• The following is an example of an introductory statement for a pregnant woman: “I ask all my patients these questions because it is important to their health and the health of their babies.”

• Unless otherwise reported, assume use of alcohol by all women. Try to pose questions in the past tense to avoid triggers associated with the stigma of alcohol use during pregnancy: “In a typical week, how many occasions did you usually have something to drink?”

• Avoid questions such as: “Do you drink often?” or “How much are you drinking?”

• To encourage more accurate reporting, one can suggest high levels of alcohol consumption: “And on those days, would it be something like 3 to 4 drinks or about 8 to 10 drinks?”

• It is important to avoid questions that require a “yes” or “no” response. It is preferable to ask open-ended questions to open a dialogue, such as: “What do you know about the effects of drinking in pregnancy?”
• In cases of confirmed or suspected history of past alcohol dependency / abuse, the following questions are suggested\textsuperscript{203}: “Have you ever had a drinking problem?” followed by “When was your last drink?”

• Avoid statements that increase guilt in a woman who admits to continued alcohol use: “You can have a healthier baby if you stop drinking for the rest of the pregnancy.” or “You may have already hurt your baby.”
3.6  LEVEL II SCREENING – STRUCTURED QUESTIONNAIRES

3.6.1  Direct Questioning

3.6.1.1 Time Line Follow Back Tool (TLFB)

The timeline follow-back method (TLFB) is an assessment interview developed to assist individuals in their recollection of alcohol consumption\textsuperscript{18}. As risky (high-volume / binge) drinking can occur in the absence of any alcohol problems, direct questions regarding the quantity and frequency (QF) of alcohol intake in the TLFB method aim to identify risky drinkers. This interview can assist in identifying a woman who would be otherwise missed by indirect questions focusing on the consequences of heavy drinking. The TLFB provides information on various characteristics of a given patient’s drinking habits – the average number of drinking days at higher levels of alcohol consumption, the number of abstinent days, the mean number of drinks per drinking day, the maximum number of alcoholic beverages consumed, and temporal patterns such as weekend versus weekday drinking. From this information, alcohol exposure can be examined, based on the dose of daily exposure and the period of fetal development during which the exposure occurred\textsuperscript{207}. The TLFB is considered a useful and accurate retrospective assessment of drinking and has been shown to be both highly reliable and valid when individually administered by an interviewer over the telephone\textsuperscript{208,209}. Sacks et al also reliably assessed substance use in psychiatric populations using the TLFB method\textsuperscript{210}. Moreover, this method is quite reliable when administered to various patient groups cross-culturally and with abuse of recreational drugs, other than alcohol\textsuperscript{209}. 
Figure 5. Timeline Follow-back Calendar (TLFB)

A Standard Drink is Equal to

<table>
<thead>
<tr>
<th>1 Standard Drink</th>
<th>Equivalent Quantities</th>
</tr>
</thead>
<tbody>
<tr>
<td>One 5 oz glass of regular (12%) wine</td>
<td>1 (\frac{1}{8}) oz of hard liquor (e.g. rum, vodka, whiskey)</td>
</tr>
<tr>
<td>1 mixed or straight drink with 1 (\frac{1}{8}) oz hard liquor</td>
<td></td>
</tr>
</tbody>
</table>

Complete the Following

**Start Date** (Day 1): ____________________________  **End Date** (yesterday): ____________________________

What is your typical pattern of drinking?

- Use on weekdays (i.e. Mon-Thurs)? ________________________________

- Use on weekends (i.e. Fri-Sun)? ____________________________________________________________________________

<table>
<thead>
<tr>
<th>2008</th>
<th>SUN</th>
<th>MON</th>
<th>TUES</th>
<th>WED</th>
<th>THURS</th>
<th>FRI</th>
<th>SAT</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>J A N</td>
<td>6</td>
<td>7</td>
<td>8</td>
<td>9</td>
<td>10</td>
<td>11</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>13</td>
<td>14</td>
<td>15</td>
<td>16</td>
<td>17</td>
<td>18</td>
<td>19</td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>21</td>
<td>22</td>
<td>23</td>
<td>24</td>
<td>25</td>
<td>26</td>
</tr>
<tr>
<td></td>
<td>27</td>
<td>28</td>
<td>29</td>
<td>30</td>
<td>31</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>F E B</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
<td>Ash Wednesday</td>
<td>7</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>11</td>
<td>12</td>
<td>13</td>
<td>Valentine Day</td>
<td>14</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td>17</td>
<td>18</td>
<td>19</td>
<td>20</td>
<td>21</td>
<td>22</td>
<td>23</td>
</tr>
<tr>
<td></td>
<td>24</td>
<td>25</td>
<td>26</td>
<td>27</td>
<td>28</td>
<td>29</td>
<td>1</td>
</tr>
<tr>
<td>M A R</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
<td>7</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>9</td>
<td>10</td>
<td>11</td>
<td>12</td>
<td>13</td>
<td>14</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td>16</td>
<td>17</td>
<td>18</td>
<td>19</td>
<td>20</td>
<td>21</td>
<td>Good Friday</td>
</tr>
<tr>
<td></td>
<td>23</td>
<td>24</td>
<td>25</td>
<td>26</td>
<td>27</td>
<td>28</td>
<td>29</td>
</tr>
<tr>
<td></td>
<td>30</td>
<td>31</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>
3.6.2 Indirect/Masked Screening

Direct questions about quantity and frequency may pose challenges to the pregnant patient due to the stigma associated with alcohol use. In order to overcome issues of possible under-reporting and denial of alcohol exposure in early pregnancy, brief screening instruments that include masked questions regarding alcohol intake have been developed and are outlined in this section.

3.6.2.1 The AUDIT Tool

The Alcohol Use Disorders Identification Test (AUDIT) includes 10 questions that may be used to obtain more qualitative information about a patient’s alcohol consumption. Validated in 6 countries, the AUDIT is useful for identifying hazardous and dependent drinking as it asks about quantity and frequency of alcohol use, drinking behaviour (i.e. binge drinking), and alcohol-related problems or reactions. An important limitation is the lack of a cut-off point indicating harmful use. A score of 8 is associated with problem drinking, while 13 or more is indicative of alcohol dependence.
Table 3: AUDIT TOOL (Alcohol Use Disorders Identification Test)

<table>
<thead>
<tr>
<th>QUESTIONS</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>How often do you have a drink containing alcohol (Score)</td>
<td>Never (0) Monthly or less (1)</td>
</tr>
<tr>
<td></td>
<td>Two to four times a month (2)</td>
</tr>
<tr>
<td></td>
<td>Two to three times a week (3)</td>
</tr>
<tr>
<td></td>
<td>Four or more times a week (4)</td>
</tr>
<tr>
<td>How many drinks containing alcohol do you have on a typical day when you</td>
<td>1 or 2 (0)</td>
</tr>
<tr>
<td>are drinking?</td>
<td>3 or 4 (1)</td>
</tr>
<tr>
<td></td>
<td>5 or 6 (2)</td>
</tr>
<tr>
<td></td>
<td>7 to 9 (3)</td>
</tr>
<tr>
<td></td>
<td>10 or more (4)</td>
</tr>
<tr>
<td>How often do you have six or more drinks on one occasion?</td>
<td>Never (0)</td>
</tr>
<tr>
<td></td>
<td>Less than monthly (1)</td>
</tr>
<tr>
<td></td>
<td>Monthly (2)</td>
</tr>
<tr>
<td></td>
<td>Weekly (3)</td>
</tr>
<tr>
<td></td>
<td>Daily or almost daily (4)</td>
</tr>
<tr>
<td>How often during the last year have you found that you were not able to</td>
<td>Never (0)</td>
</tr>
<tr>
<td>stop drinking once you had started?</td>
<td>Less than monthly (1)</td>
</tr>
<tr>
<td></td>
<td>Monthly (2)</td>
</tr>
<tr>
<td></td>
<td>Weekly (3)</td>
</tr>
<tr>
<td></td>
<td>Daily or almost daily (4)</td>
</tr>
<tr>
<td>How often during the last year have you failed to do what was normally</td>
<td>Never (0)</td>
</tr>
<tr>
<td>expected from you because of drinking?</td>
<td>Less than monthly (1)</td>
</tr>
<tr>
<td></td>
<td>Monthly (2)</td>
</tr>
<tr>
<td></td>
<td>Weekly (3)</td>
</tr>
<tr>
<td></td>
<td>Daily or almost daily (4)</td>
</tr>
<tr>
<td>How often during the last year have you needed a first drink in the</td>
<td>Never (0)</td>
</tr>
<tr>
<td>morning to get yourself going after a heavy</td>
<td>Less than monthly (1)</td>
</tr>
<tr>
<td></td>
<td>Monthly (2)</td>
</tr>
<tr>
<td>Question</td>
<td>Weekly (3)</td>
</tr>
<tr>
<td>-------------------------------------------------------------------------</td>
<td>---------------------------------------------------------------------------</td>
</tr>
<tr>
<td>How often during the last year have you had a feeling of guilt or remorse after drinking?</td>
<td>Never (0)</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>How often during the last year have you been unable to remember what happened the night before because you had been drinking?</td>
<td>Never (0)</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Have you or someone else been injured as a result of your drinking?</td>
<td>No (0)</td>
</tr>
<tr>
<td>Has a relative or friend, or a doctor or other health worker been concerned about your drinking, or suggested you cut down?</td>
<td>No (0)</td>
</tr>
</tbody>
</table>

**Scoring:** The number for each response is equal to the number of points. Scores for each question range from 0 to 4. There is no set cut-off point indicating harmful use but a score of 8 or more indicates problem use.


**Relevant Research**

- The AUDIT tool was found to be somewhat less sensitive to female alcohol abuse and dependence than the TWEAK (sensitivity of 65% and specificity of 94% for alcohol dependence and a very low sensitivity of 42% and specificity of 97% for any type of alcohol use)\(^\text{211}\).
• As a self-administered questionnaire completed by a woman waiting for her appointment, the AUDIT offers the advantage of obtaining specific information regarding her alcohol consumption and any presence of dependence symptoms.

• Compared to T-ACE, the AUDIT tool was found to be slightly less sensitive to pre-natal alcohol consumption in a sample of pregnant women.

• Given that the AUDIT questionnaire has been well-validated in the male population, Torres and colleagues investigated its usefulness in female patients to determine the test cut-off point for the diagnosis of alcohol problems in women. From the 414 women recruited, the AUDIT tool was determined to be a questionnaire with good psychometrics properties and valid for detecting dependence and risk alcohol consumption in women.

3.6.2.2 The BMAST Tool / SMAST Tool

The Michigan Alcoholism Screening Test (MAST) is a long questionnaire of 25 questions about drinking behaviour and alcohol-related problems that was originally developed for use with men. There are several variations of MAST, including modified versions such as brief MAST (BMAST) and short MAST (SMAST). The main disadvantage of these tests is their focus on the lifetime use of alcohol rather than recent use, which subsequently limits their ability to detect problem drinking at an early stage.
Table 4: BMAST TOOL (Brief Michigan Alcoholism Screening Test)

<table>
<thead>
<tr>
<th>QUESTIONS</th>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Do you feel you are a normal drinker?</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Do friends or relatives think you are a normal drinker?</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Have you ever attended a meeting of Alcoholics Anonymous (AA)?</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Have you ever lost friends or girlfriends/boyfriends because of your drinking?</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Have you ever gotten into trouble at work because of drinking?</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Have you ever neglected your obligations, your family, or your work for two or more days in a row because you were drinking?</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Have you ever had delirium tremens DTs, severe shaking, after heavy drinking?</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Have you ever gone to anyone for help about your drinking?</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Have you ever been in a hospital because of your drinking?</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Have you ever been arrested for drunk driving or driving after drinking?</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>

**Scoring:** Less than 3 points indicates not a problem drinker

4 points suggest possible problem drinker

5 or more is indicative of problem drinking

(Adapted from Pokorny AD et al. American Journal of Psychiatry 1972; 129(3): 342-5)
Table 5  THE SMAST TOOL *(Short Michigan Alcoholism Screening Test)*

<table>
<thead>
<tr>
<th>QUESTIONS</th>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Do you feel you are a normal drinker?</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Do your spouse or parents worry or complain about your drinking?</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Do you ever feel bad about your drinking?</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Are you always able to stop drinking when you want to?</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Have you ever attended a meeting of Alcoholics Anonymous?</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Has drinking ever created problems between you and your spouse?</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Have you ever gotten into trouble at work because of drinking?</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Have you ever neglected your obligations, your family, or your work for 2 or more days in a row because you were drinking?</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Have you ever gone to anyone for help about your drinking?</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Have you ever been arrested even for a few hours because of drinking?</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Have you ever been in a hospital because of your drinking?</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Have you ever been arrested for drunk driving or driving after drinking?</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

**Scoring (1 point for each of answers in bold):**

2 points = possible problem drinker  
3 points or more= probable problem drinker

(Adapted from Seltzer, M.A. et al. *Journal of Studies on Alcohol* 1975; 36: 117-126)
Relevant Research

- The BMAST was shown to be relatively less sensitive in detecting alcohol problems in female drinkers compared to men using a cut-off point of 6, in the non-Caucasian American population\textsuperscript{214}.

- Both CAGE and the brief MAST questionnaires performed effectively in screening for significant alcohol problems in a high-risk sample composed of relatives of alcoholic subjects and also in a community sample consisting of families not selected for alcohol dependence disorder\textsuperscript{215}.

- As serious mental illnesses are frequently diagnosed along with alcohol dependence (“dual diagnosis”), it is important for clinicians to be able to recognize the presence of alcohol dependence in people with mental illnesses. Breakey et al utilized the CAGE and the SMAST, and a clinical DSM-III-R diagnosis of alcohol use disorder and found that both had good sensitivity. The addition of either screener enhanced the clinicians’ ability to detect alcohol use disorders\textsuperscript{216}.

- The T-ACE, the AUDIT and the SMAST tools were completed by 350 women initiating pre-natal care at a Boston hospital to compare their accuracy with clinical predictors in the identification of prenatal alcohol use. The T-ACE, the AUDIT and clinical predictors alone correctly identified 65 to 70\% of current drinkers, whereas the SMAST alone performed only slightly better than chance. The predictive ability of the T-ACE was further improved with the addition of clinical predictors\textsuperscript{217}.
• The standardized evaluation of alcoholism and other psychopathologies in (non-pregnant) minority populations, particularly American Indians, has long been questioned. This study investigated the validity of SMAST in two distinct American Indian tribal groups from large community representative samples of 456 South Western and 214 Plains Indians. The SMAST cut-off score of greater than or equal to 3 had a sensitivity of 86% to 95%, but had lower specificity (23%-47%). Authors concluded that the SMAST is not a valid tool for the screening of alcohol use in these two tribal populations due to the highly elevated and different thresholds required from one population to the next 218.

3.6.2.3 The CAGE Tool

One of the oldest brief screening instruments, the CAGE (Cut-down, Annoy, Guilty, Eye-Opener) questionnaire has been widely used in a range of cultures worldwide and is popular for screening in the primary care setting 219. This 4-item screening instrument is designed to identify and assess potential alcohol abuse and dependence. However, it primarily focuses on the consequences of drinking rather than the quantity or frequency of alcohol use, levels of consumption, or episodes of binge drinking - all factors that help identify patients in the early stages of problem drinking. An affirmative response to 2 or more questions is an indication that a more thorough assessment is warranted.
Table 6: CAGE TOOL (Cut-down, Annoy, Guilty, Eye-opener)

<table>
<thead>
<tr>
<th>QUESTIONS</th>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Have you ever felt you should <strong>Cut</strong> own on your drinking?</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Have people <strong>Annoyed</strong> you by criticizing your drinking?</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Have you ever felt bad or <strong>Guilty</strong> about your drinking?</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Have you had an <strong>Eye opener</strong> first thing in the morning to steady nerves or get rid of a hangover?</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

(Adapted from Ewing JA et al. *JAMA* 1984; 252(14):1905-7)

**Relevant Research**

- The mode of administration for the CAGE tool (as a self-report, or as part of a clinical medical interview) was not shown to have an influence on accuracy of the outcome\(^{220}\).

- Two large studies of disadvantaged, minority, obstetric patients reported that the calculated sensitivity and specificity of the T-ACE and TWEAK were superior to the CAGE in identifying risk drinking (defined as 1 ounce or more of alcohol consumption per day)\(^{221}\).

- The CAGE tool shows less sensitivity for assessing dependence or harmful drinking in non-Caucasian women\(^{214}\).

- Due to its lack of ability in distinguishing between heavy and non-heavy drinkers in the general population, clinical use of the CAGE tool is recommended amongst
individuals previously identified as alcohol users rather than screening individuals in the general population \(^2^{22}\).

- The CAGE tool outperformed both the BMAST and the AUDIT in predicting lifetime alcohol dependence (highest sensitivity at 84%; specificity at 90%) in trauma center populations. It should be used in combination with alcohol testing to identify patients at risk of alcohol use problems \(^2^{23}\).

3.6.2.4 The CRAFFT Tool

Researchers at the Children's Hospital in Boston refined a brief questionnaire, called CRAFFT (Car, Relax, Alcohol, Forget, Friends, Trouble) that primary care physicians can use to screen for alcohol or substance abuse problems in adolescents. By drawing on situations that are more suitable to this age group, the purpose of this tool is to identify which teens require more time for comprehensive evaluation such as a diagnostic interview. This test can be administered by any health care professional who can maintain confidentiality and can refer the teen to appropriate resources. A score of two or more positive items usually indicates the need for further assessment. The CRAFFT screening tool is included in a policy statement issued by the American Academy of Paediatrics, and has been part of a national case-based training curriculum in some paediatric residency programs \(^2^{24},^{225}\).
Table 7: The Craft Tool
(CAR, RELAX, ALONE, FRIENDS, FORGET, TROUBLE)

<table>
<thead>
<tr>
<th>QUESTIONS</th>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Have you ever ridden in a CAR driven by someone (including yourself) who was high or had been using alcohol or drugs?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Do you ever use alcohol or drugs to RELAX, feel better about yourself, or fit in?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Do you ever use ALCOHOL or drugs while you are by yourself Alone?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Do you ever FORGET things you did while using alcohol or drugs?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Does your family or FRIENDS ever tell you that you should cut down on your drinking or drug use?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Have you ever gotten into TROUBLE while you were using alcohol or drugs?</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Scoring: A score of 2 or more indicates the need for further assessment

Relevant Research

- To validate the CRAFFT instrument, project investigators interviewed and screened 538 adolescents at a Boston outpatient adolescent clinic and compared their CRAFFT scores with scores on 2 longer questionnaires that previously had been shown to reliably identify adolescents with substance abuse problems or diagnoses. Findings: A score of 2 or more proved to be the optimal cut-off for identifying adolescents with alcohol or drug problems (sensitivity at 0.76; specificity at 0.94), while a score of 4 or higher indicated that the adolescent may be dependent on drugs or alcohol (sensitivity at 0.92; specificity at 0.80). The
investigators concluded that the CRAFFT screening tool offers primary care providers a valid and practical means of quickly identifying adolescent patients who need more comprehensive assessment or referral to substance abuse treatment.

- A second study by the same authors compared the validity of the CRAFFT questionnaire, the AUDIT tool, the Problem Oriented Screening Instrument for Teenagers substance use/abuse scale (POSIT), and the CAGE tool among adolescents from a hospital-based adolescent clinic. **Findings:** Sensitivities (95% confidence intervals) were AUDIT 0.88 (0.83-0.93), POSIT 0.84 (0.79-0.90), CAGE 0.37 (0.29-0.44), and CRAFFT 0.92 (0.88-0.96); specificities were AUDIT 0.81 (0.77-0.85), POSIT 0.89 (0.86-0.92), CAGE 0.96 (0.94-0.98), and CRAFFT 0.64 (0.59-0.69). Authors concluded the AUDIT, POSIT, and CRAFFT have acceptable sensitivity for identifying alcohol problems or disorders in this age group but the CAGE is not recommended for use among adolescents.

3.6.2.5 The T-ACE Tool

As the first validated screening questionnaire for risk drinking developed for pregnant women, the T-ACE (Tolerance, Annoyed, Cut down, Eye-Opener) has been established as a highly effective screening tool, and is regularly used by practitioners as part of routine care. A woman who answers “more than two drinks” on the tolerance question, “how many drinks does it take to make you feel high?” is scored 2 points. Each “yes” to the additional 3 questions scores 1. A score of 2 or more out of 5 indicates risk of a drinking problem, and a woman should be referred for further assessment.
Table 8. The T-ACE Tool

<table>
<thead>
<tr>
<th>T-ACE</th>
<th>QUESTIONS</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tolerance</td>
<td>How many drinks does it take to make you feel the first effect (before pregnancy)? _________</td>
<td>(3 or more = 2 points)</td>
</tr>
<tr>
<td>Annoyed</td>
<td>Have people ever annoyed you by criticizing you about your drinking?</td>
<td>(yes = 1 point)</td>
</tr>
<tr>
<td>Cut down</td>
<td>Do you sometimes feel the need to cut down on your drinking?</td>
<td>(yes = 1 point)</td>
</tr>
<tr>
<td>Eye-opener</td>
<td>Do you sometimes take a drink in the morning when you first get up?</td>
<td>(yes = 1 point)</td>
</tr>
</tbody>
</table>


**Relevant Research**

- The first study looked at a population of African-American inner-city women and found T-ACE (76% sensitivity and 79% specificity) to be superior to both MAST (76% sensitivity and 76% specificity) and CAGE (59% sensitivity and 82% specificity) in identifying pre-natal risk drinking.\(^{42}\).
- Chang et al subsequently tested the T-ACE as a self-administered, independent screening tool embedded in a health-habits survey with questions about smoking, stress, weight, and dietary habits. This was tested in a more socially and ethnically diverse obstetric population initiating pre-natal care at the Women's Hospital in Boston.\(^{226}\). They compared the sensitivity and specificity of the T-ACE with the sensitivity and specificity of three other popular methods of screening for alcohol...
use in other clinical settings, including the AUDIT and the SMAST\textsuperscript{227} and a review of the patient’s medical record. Researchers gave each participant the AUDIT and SMAST independently as well as reviewed the participant’s medical record. T-ACE was found to be more accurate than AUDIT in detecting current risk drinking behaviour, as well as a past history of alcoholism\textsuperscript{226}.

- The T-ACE was more effective in identifying at-risk women for pre-natal alcohol use than medical records\textsuperscript{228}.

- The “hold” version of the tolerance question was examined by Russell et al who gave it a positive scoring when women reported being able to consume more than 5 drinks without passing out. The T-ACE performed even better with increased sensitivity (91%) and specificity (81%). More recent studies using a cut-off point of $\geq 2$ for T-ACE very clearly distinguished the women at risk of pre-natal alcohol use from those who are not (88% sensitivity and 79% specificity)\textsuperscript{229}.

3.6.2.6 The TWEAK Tool

The TWEAK (Tolerance, Worry, Eye-opener, Amnesia, Cut down) is a 5-item screening tool that combines questions from other tests including MAST, CAGE, and T-ACE, which were found to be effective in identifying at-risk drinkers\textsuperscript{230}. These questions address tolerance, feeling the need to cut down on drinking, and having close friends or relatives worry or complain about the drinking\textsuperscript{231}. On tolerance, 2 points are given if a woman reports that she can consume more than 5 drinks without falling asleep or passing out (“hold version”) or reports that she needs 3 or more drinks to feel the effect of alcohol (“high version”). A positive response to the worry question yields 2 points, and
to the last 3 questions yields 1 each. Scored on a 7-point scale, a woman scoring 2 or more points is likely an at-risk drinker.

Table 9. The TWEAK Tool

<table>
<thead>
<tr>
<th>TWEAK</th>
<th>QUESTIONS</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tolerance</td>
<td>How many drinks does it take to make you feel the first effect (before pregnancy)? ________ (3 or more = 2 points)</td>
<td></td>
</tr>
<tr>
<td>Worry</td>
<td>Have close friends worried or complained about your drinking in the past year? (yes = 2 points)</td>
<td></td>
</tr>
<tr>
<td>Eye-opener</td>
<td>Do you sometimes take a drink in the morning when you first get up? (yes = 1 points)</td>
<td></td>
</tr>
<tr>
<td>Amnesia</td>
<td>Has a friend or family member ever told you about things you said or did while you were drinking that you could not remember? (yes = 1 point)</td>
<td></td>
</tr>
<tr>
<td>Cut Down</td>
<td>Do you sometimes feel the need to cut down on your drinking? (yes = 1 point)</td>
<td></td>
</tr>
</tbody>
</table>

(Adapted from Russell M et al., Alcohol Health and Research World 1994; 18 (1):55-61)

Relevant Research

- The TWEAK was first tested in three male and female samples randomly selected from three groups: (1) alcoholics in treatment at a county medical center; (2) patients at two primary health care centers; and (3) the general population of the Buffalo, New York, metropolitan area. Subsequent evaluation of the TWEAK has revealed its promise as a screening tool for identifying pregnant women who are at-risk drinkers, defined as those consuming 1 ounce of alcohol or more daily.

- In a study of 4,743 African-American women of low socioeconomic status who were also given the MAST, the CAGE, and the T-ACE tolerance question, the
calculated sensitivity and specificity of the TWEAK were 79% and 83%, respectively, in contrast to the calculated 70% sensitivity and 85% specificity of the T-ACE 229.

- The utility of items included in the TWEAK was demonstrated in studies of obstetric and gynecologic outpatients, the general household population, hospital in-patients and in emergency room settings. Chang et al assessed the efficacy of TWEAK to identify alcohol use in pregnant patients 205. They found that TWEAK performed similar to T-ACE in detecting a range of drinking patterns from moderate to high-risk drinking, but performed better than T-ACE in predicting lifetime alcohol diagnosis and risk drinking. It is well-documented that the TWEAK questionnaire has an approximately 90% sensitivity and 78% specificity to detect a woman who is a problem drinker and is therefore considered to be more appropriate for use during pregnancy.

- Subsequent research suggests that TWEAK is well-established as a sensitive instrument for detecting alcohol problems not only among pregnant women, but in the general population as well using different cut-off points 214.

It is important to note that many of the studies investigating the TWEAK’s performance have relied on the older definition of risk drinking (≥1 ounce alcohol daily) rather than the current definition (≥0.5 ounce alcohol daily). Nonetheless, it offers another option for clinicians. The TWEAK screening tool is currently recommended for use with pregnant women by L’Institut national de santé publique du Québec, Alberta Health Services (formerly Alberta Alcohol and Drug Abuse Commission (AADAC)) and the United States National Institute on Alcohol Abuse and Alcoholism.
### 3.6.2.7 A Comparison of Structured Questionnaires

#### Table 10. Advantages and Disadvantages of Structured Questionnaires

<table>
<thead>
<tr>
<th>Tool</th>
<th>Advantages</th>
<th>Limitations</th>
<th>Validation</th>
</tr>
</thead>
</table>
| **AUDIT** | • 10 item questions (2 minutes)  
• Easy to administer  
• Detects problem drinking; dependence / abuse  
• Validated for cross-cultural applicability and ability to identify people who have problems with alcohol but who may not be dependent  
• Shown to be especially useful when screening women, minorities and adolescents  
157, 234 | • Not well examined in prenatal settings  
• Less sensitive to female alcohol abuse and dependence than the TWEAK 214  
• Definition of a positive score on the AUDIT for drinking pregnant women remains to be established  
• Developed for use in men and therefore less effective in identifying drinking problems among women  
• Fails to distinguish between problem drinking and dependence | Validated for use in women |
| **BMAST** | • 10 item questions (2 minutes)  
• Detects harmful use of alcohol | • Focuses on lifetime rather than current drinking | Validated for use in women |
<p>| <strong>CAGE</strong> | • Routinely incorporated into clinical assessments as it is short and very easily administered (takes ≤1 min) | • No cut-off point to differentiate dependence and abuse | Validated in women of childbearing age, including pregnant |</p>
<table>
<thead>
<tr>
<th>Tool</th>
<th>Advantages</th>
<th>Limitations</th>
<th>Validation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Validated for use in general population (primary setting), minority ethnic groups, and adolescents</td>
<td>• Focuses on lifetime rather than current drinking</td>
<td>women</td>
</tr>
<tr>
<td></td>
<td>• Detects alcohol dependence / abuse</td>
<td>• Developed for use in men and therefore less effective in identifying drinking problems among women</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Has been proven effective for detecting a range of alcohol problems</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CRAFFT</td>
<td>• Validated as the most sensitive tool for detecting a range of alcohol problems among adolescents</td>
<td>• Limited research conducted specifically in pregnancy</td>
<td>Validated for use in adolescents</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T-ACE</td>
<td>• Instrument developed specifically for use with pregnant women</td>
<td>• Emerging research suggests TWEAK outperforms the T-ACE</td>
<td>Validated for use in pregnant women</td>
</tr>
<tr>
<td></td>
<td>• Questions are easy to remember and score and can be asked by an obstetrician or a nurse (1 min)</td>
<td>• Validity of the tool varies across different ethnic populations</td>
<td></td>
</tr>
<tr>
<td>TWEAK</td>
<td>• Developed specifically for use with pregnant women</td>
<td></td>
<td>Validated for use in pregnant women</td>
</tr>
<tr>
<td></td>
<td>• Short and very easily administered (takes ≤1 min)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Optimal for racially diverse groups, superior in sensitivity versus other tools as it has been extensively validated in different obstetric populations²¹¹</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Emerging research suggests TWEAK outperforms the T-ACE</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
3.6.3 **Inconsistent Use of Structured Questionnaires**

Use of these tools and their implementation in the prenatal setting is recommended. But as previously mentioned, health professionals fail to use it routinely. Table 11 summarizes the findings related to how many provincial prenatal records include questions about alcohol and/or make use of a structured questionnaire in Canada.

**Table 11. Summary of Provincial Prenatal Records in Canada**

<table>
<thead>
<tr>
<th>Summary of Drinking Patterns</th>
<th>NWT</th>
<th>BC</th>
<th>AB</th>
<th>SK</th>
<th>MN</th>
<th>ON</th>
<th>QC</th>
<th>NB</th>
<th>NS</th>
<th>PEI</th>
<th>NFLD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Drinking Patterns</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>“Amount”</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>“Frequency”</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td># drinks/day</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td># drinks/wk</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td># drinking days/wk</td>
<td></td>
<td></td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Max # per occasion</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Quit Date</strong></td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>T-ACE Score</strong></td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td><strong>TWEAK Score</strong></td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Internationally, use of screening tools and processes are also complex and varied based on the population type. The following countries have national guidelines and recommendations on the type and combination of tools to use as summarized in Table 12.
Table 12  Use of Tools in the International Environment

<table>
<thead>
<tr>
<th>Countries</th>
<th>General Population Screening</th>
<th>Special Population Screening (Pregnancy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>United Kingdom</td>
<td>CAGE</td>
<td></td>
</tr>
<tr>
<td>Scotland</td>
<td>AUDIT</td>
<td>TWEAK</td>
</tr>
<tr>
<td>Australia</td>
<td>CAGE followed by TLFB or QF;</td>
<td>TWEAK followed by AUDIT</td>
</tr>
<tr>
<td></td>
<td>AUDIT; TWEAK</td>
<td></td>
</tr>
<tr>
<td>Indigenous</td>
<td>AUDIT</td>
<td>AUDIT</td>
</tr>
<tr>
<td>Australians</td>
<td>CAGE</td>
<td>CAGE</td>
</tr>
<tr>
<td>United States</td>
<td>CAGE</td>
<td>T-ACE, TWEAK, CAGE in combination with TLFB and QF</td>
</tr>
<tr>
<td></td>
<td>AUDIT</td>
<td></td>
</tr>
<tr>
<td></td>
<td>BMAST</td>
<td></td>
</tr>
</tbody>
</table>

3.6.4 Summary: An Overview of Findings

• The T-ACE and TWEAK tools were developed specifically to identify at-risk drinking in a pregnant woman. Common to both, the tolerance question appears to be most sensitive for indicating problem drinking in a woman as it places less emphasis on issues of guilt related to drinking. There are two different versions of the tolerance question, with one focusing on the number of drinks to feel “high**”：“How many drinks does it take to make you feel the first effect of alcohol?” while the second focuses on the number of drinks one can “hold”:

** The high question works well for women who often have 3 or 4 drinks at most but never to the point of passing out. On the other hand, the hold question detects binge drinking patterns where large amounts of alcohol are consumed.
• Overall, the TWEAK questionnaire appears to be superior for identifying heavy drinking patterns, alcohol dependence or abuse across a range of socio-economically and ethnically diverse populations. A cut-off point of 2 or more was found to have optimal sensitivity and specificity for detecting alcohol problems in women with sensitivities ranging from 89%-91% and specificity ranging from 77%-87% \(^{235}\).

• However, since both of these tools fail to provide a picture of a woman’s pattern of consumption, a positive screen may be supplemented by the TLFB tool which includes quantity-frequency questions.

3.6.5 Knowledge Gaps and Challenges of Structured Questionnaires

• There is no consensus on the appropriate questionnaire to use across Canada as each provincial/territorial jurisdiction, health care organization and health care provider uses a variety of formal and informal screening questionnaires. It is interesting to note that only 6 of the 11 provinces have a screening tool (Table 11); however, some provinces use tools that do not ask specific questions in the screening process.

• There are inconsistent recording processes across Canada. The information collected in the clinical setting by the health care professional is not consistently noted in all records of the women and not necessarily connected to the records of the child.

• Health care professionals are not trained in motivational interviewing techniques. Motivational interviewing is a scientifically tested method of
counselling people in the treatment of lifestyle problems and motivates them to change their behaviour without evoking resistance.

- Health care professionals may not be motivated to screen for alcohol use if there are no facilities or programs available to refer a woman for intervention and / or counselling on alcohol use.
3.7 LEVEL III SCREENING – LABORATORY-BASED SCREENING TOOLS

3.7.1 Biological Markers

Unlike brief questionnaires, biochemical markers address concerns shared by many researchers who feel that self-reporting underestimates alcohol consumption. In a pregnant patient, current alcohol use can be detected by urine toxicology, blood, saliva or breath, to follow-up a positive interview screen. Gamma-glutamyl transferase (GGT) and carbohydrate-deficient trans-ferin (CDT) have been used as biochemical measures of detecting long-term heavy drinking\(^2^{35-237}\). However, they are not specific and may reflect liver damage due to other causes.

Among the benefits of toxicology tests is their ability to confirm the presence of a drug and determine multiple drug use, while disadvantages include the high costs associated with lab analysis. There are limitations to lab testing. For example, alcohol being the most widely used substance with severe adverse impact on the fetus is very hard to detect due to its short time in the blood streams. Hence, negative results do not rule out alcohol / substance use; a positive test fails to reveal information regarding pattern of drug use; urine toxicology is also limited by the short window of appearance. Fatty acid ethyl esters (FAEEs) are metabolic products that result from the interaction between alcohol and fatty acids. FAEEs can be detected in blood, hair, placenta, cord blood, and meconium (i.e. first stool of newborns). Over the last few years, a revolutionary test using adult hair has been developed and validated to measure FAEEs. The test can accurately separate chronic alcohol abuse from moderate and non-
drinking status. Six centimetres of hair are needed, representing 6 months of growth of hair (hence, the recent 6 months in the life of the individual) \(^{236}\).

The following are the cut-offs for the test:

- FAEE levels above 1 ng/mg are 100% specific for regular, excessive alcohol consumption. At this level 25% of chronic alcohol abusers will test below (i.e. 75% sensitivity).
- FAEE levels between 0.5-0.99 ng/ml are 90% specific for regular, excessive alcohol consumption. At this level 10% of chronic alcohol abusers will be missed, and 10% of moderate drinkers will show results in this range.
- FAEE levels below 0.49 ng/mg indicate no evidence of excessive alcohol consumption (up to 2 drinks per day)
- FAEE levels between 0.2-0.4ng/mg mean no evidence of alcohol consumption \(^{110}\).

3.7.2 Knowledge Gaps and Challenges of Laboratory-Based Screening Tools

- Traditional methods of measuring alcohol in blood or through breath test reflect only drinking in the last few hours, and hence do not assist in defining problem drinking.
- There are limitations of laboratory testing as negative results do not rule out alcohol use. The hair test overcomes this shortcoming, as a level above 0.5 ng/mg would not miss excessive drinkers, and levels below 0.49 ng/mg indicate no evidence of excessive alcohol drinking. These characteristics make the test very relevant in the context of drinking patterns associated with FASD.
• While positive test results provide separation between excessive alcohol consumption and milder intake, information regarding pattern of alcohol use (e.g. binge vs. chronic continuous use) is not revealed.

• Laboratory tests of liver function usually only identify those patients with long-term use in whom secondary symptoms have occurred, e.g. liver function tests.

• Urine toxicology has no value in identifying teratogenic effects that occur early in pregnancy.

• The hair test has been found to accurately separate chronic alcohol abuse from moderate to non drinkers and is likely to become gold standard of corroborating alcohol use.

• Ethical considerations: as with any other test, respect to the autonomy of the woman, to her rights for confidentiality and for refusal, must be strictly adhered to.
3.8 CHALLENGES OF IMPLEMENTATION OF SCREENING AND ASSESSMENT TOOLS

The task of identifying and managing health issues in a pregnant woman who uses alcohol during pregnancy can be difficult. Universal screening would mean that all childbearing women are asked about the amount of alcohol they consume. A positive response to the screening question(s) should be followed by further in-depth assessment.

3.8.1 Level 1: Screening with Interviewing Techniques

Asking a woman a single question about alcohol use is the first step in the screening process. A woman may admit to drinking on occasion or deny any use of alcohol. Any denial of use should be sieved through the provider’s impressions of the woman, ascertained by a non-judgmental observation of her body language, general deportment, and eye contact, as well as through past interactions with her. Asking about alcohol use at other times during the pregnancy would be prudent.

3.8.2 Level II: Screening/Assessment with Standardized Questionnaires

The least challenging (Level II) screening strategy would be the use of open-ended interviewing techniques (the Timeline Follow Back Method and Quantity-Frequency Tool), wherein the provider asks a woman to provide details about her recent consumption of alcohol. If the provider is respectful and non-judgmental, a woman will often respond positively. However, a woman may not accurately recall the amount or frequency of their alcohol consumption. A woman may also underestimate, minimize or deny their alcohol intake. The provider must also clarify the amount of alcohol in a standard drink and ask for details on amounts consumed (e.g. a bottle of wine can vary in
size). Consequently, a screening interview may not elicit an accurate record of alcohol consumption and medical records may not be accurate.

Standardized questionnaires (AUDIT, BMAST, CAGE, TWEAK, T-ACE, CRAFFT) are sometimes used as screening tools and can also be used for further in-depth assessment of alcohol consumption. However, the questionnaires have limitations because they do not perform equally well in heterogeneous populations. They do provide a structured way to elicit alcohol consumption, yet require that providers know their individual components and also know the scoring system.

Some providers include a questionnaire for completion by a woman in the waiting room. There are difficulties with this approach; for example, if a woman is not literate, speaks English as a second language, is accompanied by her spouse, or is lacking privacy. The responses on these “pen and paper” versions need to be reviewed carefully with a woman during a pre-natal visit, wherein the provider can observe a woman’s responses. The questionnaires also need to be used in a respectful and non-judgmental manner in order to engage a pregnant woman. Some questionnaires, e.g. the T-ACE, have been validated in pregnant populations but the overlay of cultural, ethnic and socio-economic factors may interfere with their accuracy. The ideal screening test should be both highly sensitive and highly specific. However, there is often a trade-off between sensitivity and specificity for any given test. A tool with high sensitivity will identify all pregnant women with problematic alcohol consumption (a positive result) while a tool with high specificity will exclude all women who are not consuming risky levels of alcohol, (a negative test result) $^{167}$. Typically, given the importance of identifying problematic
alcohol use, priority is placed on high sensitivity. In communities with a paucity of
resources for follow-up, a tool with high specificity may prove more cost-effective, as
false positive scores are reduced. In the absence of a “gold standard”, clinicians are
limited by the characteristics of a particular tool. The challenge for providers is the
variability in screening instruments to detect women at-risk and to eliminate false
positives, especially in different subpopulations of women, e.g., immigrant or refugee
women\textsuperscript{238}. In addition, providers need to ask the questions with cultural competency and
sensitivity to each woman’s circumstance.

3.8.3 Level III: Assessment for Biological Markers

In-depth biomedical assessment with a laboratory-based test, such as maternal
hair testing for FAEE (fatty acid ethyl esters), provides quantifiable results that can
inform the clinician about a woman’s alcohol consumption. However this test can be
invasive for a woman. Full and informed consent must be obtained before this test is
conducted. Although hair-testing offers a more accurate understanding of a woman’s
alcohol use, it is not available in all centres and its clinical use is not yet wide-spread.
Currently hair testing is usually ordered for legal reasons. Additionally, some providers
may be disinclined to use such tests because of a woman-centered philosophy towards
caring for a pregnant woman, which advocates belief in a woman and acceptance of her
reports of alcohol use as the truth.

3.8.4 Project Summary

The task of identifying and managing a pregnant woman who uses alcohol during
pregnancy can be difficult. Each level of screening or assessment presents some
challenges and limitations. A negative response to screening questions does not warrant further investigation, although it is prudent to ask about alcohol use during each trimester. A positive response to screening for alcohol consumption should be followed by further assessment and recording as well as providing assistance and resources as required.

As recommended by the Public Health Agency of Canada, and as reflected in the goal of this project, there is a need for the development and validation of screening tools that are specific and sensitive to pre-natal alcohol exposure. These tools should be adaptable for use in various contexts, they should be culturally appropriate and they should lead to further assessment. Additionally, providers must be trained to accurately record the alcohol history of the mother, which can facilitate diagnostic referral of the infant if necessary.
3.9 RECORDING ALCOHOL USE

Specific recommendations for documentation of alcohol and other substance use during pregnancy on the maternal, newborn and child health records are crucial. Primary health care providers (family doctors, nurse practitioners, midwives, family practice nurses, public health nurses, physician assistants, etc.) are encouraged to include questions about alcohol and other substance use a routine part of well-woman visits (Pap smears, birth control renewals, annual checkups, etc.). Ideally this information is gathered in contexts before, during and after pregnancy.

The answers to screening questions regarding alcohol use should always be documented in the chart for future reference. Recording alcohol use in pregnancy is important for a woman, her developing fetus, a newborn infant and a child who may have fetal alcohol spectrum disorder. It is useful to ask these questions at multiple visits so that they become part of the standard of care. In this way, a pregnant woman will not feel stigmatized by questions that are only linked to her pregnancy. Documentation should be on the Standardized Antenatal Record so that obstetrical providers and hospital labour and delivery staff are able to access the information.

Equally important is the recording of important risk factors present during the pregnancy on the chart of a newborn infant. Contents of the newborn’s hospital or midwifery care chart should be easily and routinely available to the family physician or paediatrician caring for the infant. Subsequently, the relevant information about maternal alcohol and substance use is available to be transferred to the child’s health record.

It is important to note that there is some sensitivity surrounding a woman’s consent to the recording of this information in her and her child’s health records, as a
woman may be concerned of the potential discriminatory actions of hospital staff and others in response to her use of alcohol use during pregnancy.

The diagnosis of FASD is challenging and not always possible in the immediate newborn period. Many children do not have the typical facial features of FASD. Some children will present with developmental delays in the toddler period, behavioral issues in the preschool period or learning difficulties in the childhood years. Health care practitioners providing care for children and adolescents must consider FASD in the differential diagnosis of any cognitive or emotional problem.

3.9.1 Benefits of Recording Maternal Alcohol History on Infant Birth Records

- Identification of infants who might be at-risk for FASD through the recording of specific information regarding maternal drinking.
- Earlier and more accurate FASD diagnosis in terms of ARND and PFAS.
- Earlier implementation of appropriate interventions.
- Decreased levels of secondary disabilities related to in utero exposure to alcohol.
3.10 RECOMMENDATIONS

The implementation of a consistent and effective screening process for the assessment of pre-natal alcohol exposure is an important measure and allows the establishment of a blueprint for early intervention. The following recommendations are intended to improve the screening process and recording process for alcohol use in women of child-bearing age and pregnant women, thereby improving diagnosis and intervention for all women and their families.

3.10.1 General Recommendations

1. Recognizing the importance of the health care provider as an effective resource for harm reduction, it is essential that adequate community resources be made available for women who require interventions beyond a primary interaction.

2. That research on the effects of alcohol use be expanded to ensure there is sufficient comparative evidence showing the effectiveness of screening tools with particular cultural groups.

3. That a public education / awareness program be initiated to inform women they should expect to be asked about the frequency and amount of alcohol use and ensure this information is transmitted to all health care providers involved in their care.

3.10.2 Recommendations Relative to Screening for Alcohol Use:

4. That health care providers use a standardized, universal set of questions routinely during regular health exams that will include at least Level I screening.
5. That Level II screening be adopted as the standard screening process to identify alcohol use in all women of child-bearing age and pregnant women (Figure 13).

6. That health care provider is aware of the risk factors that may inform their clinical impression in combination with other psychosocial assessment.

7. That health care providers access on-line training tools for screening of FASD offered by Best Start, Ontario’s maternal, newborn and early child development resource centre (www.beststart.org), and other resources offered by programs such as PRIMA (www.addictionpregnancy.ca) and Motherisk (www.motherisk.org). Resources are also available from Healthy Choices in Pregnancy program in British Columbia (www.hcip-bc.org/resources_for_practice/default.htm) and from the Canadian Centre for Substance Abuse (www.ccsa.ca/toolkit/introduction.htm).

8. That health care providers use Level III screening methods when there is discordance between Level I and Level II screening results (e.g. frequency, perception of risk), or when there are doubts unresolved by Levels I and II.

3.10.3 Recommendations Relative to Recording Alcohol Use:

9. That the frequency and amount of alcohol use be recorded in a woman’s chart on a routine basis and not only in relation to pregnancy.

10. That the information relative to frequency and amount of alcohol use be recorded in a woman’s chart and that this information be transferred to appropriate health care providers and health records to ensure a continuum of care.
11. That information relative to frequency and amount of a woman’s alcohol use be routinely recorded in her newborn’s chart and in her child’s health record.

Figure 6. Flow chart of Level I and II

Practice-based Screening

Single Question Method  Motivational Interviewing  Supportive Dialogue

STRUCTURED QUESTIONNAIRE

Direct Questioning  Indirect / Masked Screening

Time Line Follow Back Tool  CAGE AUDIT MAST AND BMAST CRAFFT T-ACE TWEAK
CHAPTER FOUR

PART I

COMPARING TWEAK AND T-ACE IN PREDICTING PROBLEM DRINKING
4.1 ABSTRACT

The TWEAK and T-ACE screening tools are validated methods of identifying problem drinking in pregnant women. The study objective was to compare the performance of both screening tools in identifying problem drinking at various cut-point (CP) thresholds. 

**Methods:** Study participants consisted of women calling the Motherisk Alcohol Helpline for information regarding their alcohol use in pregnancy. In this cohort, concerns surrounding under-reporting are not likely as women self-report their alcohol consumption. Participant’s self-identification, confirmed by her self-reported amount of alcohol use, determined whether or not the participant was classified as a problem drinker. This was the standard against which screener performance was assessed. The TWEAK and T-ACE tools were administered on both groups and subsequent analysis was done using chi-square test, student t-test, operational characteristic calculations and ROC analysis, where appropriate. **Results:** The study consisted of 75 problem and 100 non-problem drinkers. Both TWEAK and T-ACE tools poorly identified potential at-risk women (PPV=0.54) using traditional CPs, with high sensitivity (100%-99% and 100-93%, respectively) but low specificity (36 - 43% and 19 - 34%, respectively). However, performance of both tools improved using higher CP, where TWEAK was significantly better than T-ACE at CP of 4 or more. **Conclusion:** Neither the TWEAK nor T-ACE tests were able to identify problem drinkers effectively in this cohort using the current recommended thresholds. These results provide further evidence that screening tools are population-dependent. If either tool is used, providers should use additional screening tests for further follow-up regarding antenatal alcohol use.
4.2 INTRODUCTION

Approximately 14 to 22 percent of women have reported drinking some alcohol during pregnancy\textsuperscript{3, 19, 192}. This perinatal alcohol use underscores the reason that Fetal Alcohol Spectrum Disorder (FASD), a condition that is 100% preventable, remains the number one cause of mental retardation in the world today.

With new evidence suggesting even low to moderate level of alcohol consumption may have negative long-term implications for children exposed to alcohol \textit{in utero}\textsuperscript{43, 69, 239, 240}, identification of non-abusive but still risky alcohol consumption in pregnant women becomes critical. The TWEAK and T-ACE questionnaires are considered to be most effective screeners in pregnancy, as both were developed and validated for use in identifying alcohol use in obstetric populations\textsuperscript{241}. Easy to administer and score, both instruments were initially adapted from CAGE and MAST tools to specifically identify at-risk drinking in pregnancy\textsuperscript{42, 229}. The TWEAK tool has been validated using cut-points of either two or three, depending on the population on which it is administered. Through similar studies, a cut point score of two has been shown to be most effective for use with T-ACE. These two tools are apart from other similar instruments, in terms of their efficacy, as they place a \textit{decreased} emphasis on issues of guilt related to drinking. Studies have consistently found them to be superior instruments to either the CAGE or the MAST in samples attending prenatal clinics, although the TWEAK appears to be the more frequently used and validated instrument of the two\textsuperscript{211, 212}. 
Given that screening questionnaires often do not perform well across varying populations and given that health care practitioners often rely on appearance to identify women at risk of using alcohol in pregnancy, more research is necessary to determine the effectiveness and validity of screening tools amongst various population sub-groups.

Validation research on both tools to date has been conducted in primarily minority women, from low SES, with a history of dependence and/or abuse to alcohol. As this may not represent the majority of potential at-risk pregnant women for whom clinicians routinely care (and generally fail to screen), it is important to determine the effectiveness of these tools in a more diverse population. The women who call the Motherisk Alcohol and Substance Use Helpline for information are representative of this target population, as they are educated, employed and come from various socio-economic strata. To our knowledge, these two screeners have not been compared head to head in the type of pregnant population found via Motherisk. The primary objective of our study was to ascertain the effectiveness of the TWEAK and T-ACE at identifying at-risk drinkers in a diverse population of pregnant women calling this helpline of their own volition. Secondly, a comparison was done to determine if one test performed better than the other at recommended thresholds.
4.3 METHODS

4.3.1 Study Setting and Subjects

Pregnant women calling the Motherisk Alcohol and Substance Use Helpline who reported any alcohol consumption during pregnancy and at least two months prior were invited to participate in our study. As part of the inclusion criteria, women had to provide all relevant information as required on the standardized intake form (Appendix A) and complete both TWEAK and T-ACE screening questionnaires. Study enrollment began in December of 2006 and continued until November of 2008. Of 202 eligible participants, a total of 175 women (87%) were included in the study, upon providing informed consent (Appendix B). This cohort provided the opportunity to conduct research with minimal concerns for underreporting as it accessed women who willingly called to self-report exposures, out of a desire to define their risk of adverse outcomes and make well-informed decisions about their pregnancies. Since these women were quite motivated to offer full and accurate information, the study constituted an optimal opportunity to test the quality of widely used tools, such as the TWEAK and T-ACE.

This study was approved by the Hospital for Sick Children’s Research Ethics Board (Appendix E).

4.3.2 Study instruments and definitions

TWEAK is a five-item, provider administered scale developed originally to screen for risk drinking during pregnancy. It is an acronym for the following questions: T-Tolerance: “How many drinks can you hold?”; W-Worried: “Have close friends or relatives Worried or Complained about your drinking in the past year?”; E-Eye-openers:
“Do you sometimes take a drink in the morning when you first get up?”; A-Amnesia (blackouts) “Has a friend or family member ever told you about things you said or did while you were drinking that you could not remember?”; and K(C)-Cut down: “Do you sometimes feel the need to Cut down on your drinking?” On the tolerance question, two points were given if a woman reported that she required at least 3 or more drinks to feel the effect of alcohol. A positive response to the worry question yielded two points, and positive responses to the last 3 questions yielded 1 point each. On a 7-point scale, a woman who scored a total of 2+ or 3+ were considered at-risk drinkers (Table 9).

In contrast to the TWEAK tool, T-ACE (Tolerance, Annoyed, Cut down, Eye-Opener) is a 4-item screener that excludes both W-Worried and A-Amnesia questions, and instead, adds a question in reference to A-annoyance: “Have people ever annoyed you by criticizing you about your drinking?” Similar to the TWEAK, a response of “more than three drinks” on the tolerance question scored two points. A positive response to the subsequent 3 questions scored one point each. A total score of 2 or more out of 5 indicated risk of a drinking problem, and triggered a referral for further assessment (Table 8).

There are various measures of screening. The definitions and respective formulas of some of the performance characteristics that have been adapted for the present study are summarized below:

**Sensitivity** or true positive rate is a statistical measure of how well a binary classification test accurately identifies the proportion of truly exposed women as a result of their TWEAK or T-ACE score being greater than the CP threshold. A sensitivity of
100% means that the screening test identifies all women who may be at risk for problem drinking. However, this parameter alone does not tell us how well the test predicts non-problem drinkers.

\[
\text{TPR: } \frac{\text{True Positive (TP)}}{\text{True positive (TP) + False negative (FN)}}
\]

**Specificity**, also known as true negative rate, is a statistical measure of how effectively a binary classification test correctly identifies the negative cases, or in this study context, women who are not problem drinkers. That is, the specificity is the proportion of non-problem drinkers who test negative on the TWEAK or T-ACE tool, scoring below the threshold. A specificity of 100% means that the test recognizes all women who do not engage in risky drinking as non-problem drinkers.

\[
\text{TNR: } \frac{\text{True Negative (TN)}}{(1 - \text{FPR})} = \frac{\text{True Negative (TN)}}{\text{False positive (FP) + True negative (TN)}}
\]

**Positive predictive value** (PPV) or precision rate is the probability that a problem drinker will test positive on the screening test.

\[
\text{PPV: } \frac{\text{True Positive (TP)}}{\text{True positive (TP) + False positive (FP)}}
\]
Prenatal “problem” or “risk” drinking is commonly used to describe non-dependent drinking, which may not be sufficiently severe to meet the criteria for alcohol abuse disorder, but may still result in adverse consequences. As part of the standard intake form, pregnant women described their daily use of alcohol, recalling all episodes to the best of their abilities. In the context of this study, the standard criteria for risk or problem drinking during pregnancy was defined as an average consumption of more than one standard drink per day, or less if massed (binges of greater than 4 drinks per episode on any given day). Women were also asked “Would you consider yourself a problem drinker because you find it difficult to stop drinking alcohol?” A positive response to this denoted a problem drinker. This self-identification, further confirmed by reported levels of alcohol consumption, was used as the gold standard against which the TWEAK and T-ACE were compared.

Cut-Point (CP) refers to the score used to define a positive screen. For the first part of this study, “risk or problem drinking” was identified using the recommended CP of three and two for the TWEAK and T-ACE tools respectively.

4.3.3 Study Procedures

All study patients were recruited during the initial call to The Motherisk Alcohol and Substance Use Helpline. For the purpose of this study, only two specialized helpline counselors who routinely conduct interviews and document information using the standardized intake form (Appendix A) were used (in order to reduce variability of data collection). During the interview process, details pertaining to patients’ medical, psychiatric and pregnancy histories, including all exposures to alcohol and other
recreational substances in current pregnancy, were documented. At this time, the counselor also administered both screening questionnaires on the same patient as part of the initial intake process. Patients were clearly explained the directions for answering survey items as per published survey directions. In addition, the counselor utilized cognitive interviewing techniques to improve reporting by leading patients through each day of the recall period and by cueing personally memorable events to aid recall. All data were coded and scores were entered into an excel worksheet (Appendix C). The scores were then analyzed using the Statistical software – SPSS (version 12.0). Chi-square analysis was used to determine differences in categorical variables between women who were identified as problem drinkers using the TWEAK and T-ACE tools compared to those who were not (non-problem drinkers). Student t-tests and/or Mann-Whitney U tests was used to compare continuous data such as sensitivity and specificity rates between the TWEAK and T-ACE tools.
4.4 RESULTS

A total of 175 women were enrolled in the study, including 100 women who did not meet the criteria for problem drinking (non-problem drinkers) and 75 who were identified as problem-drinkers. A summary of maternal demographics, outlined in Table 13 for both groups indicate lack of statistically significant differences between the two groups in almost all maternal characteristics.

Table 13: Maternal Characteristics

<table>
<thead>
<tr>
<th>Maternal Demographics</th>
<th>Non-Problem drinkers (N=100)</th>
<th>Problem drinkers (N=75)</th>
<th>Overall P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal Ethnicity</td>
<td>N</td>
<td>%</td>
<td>N</td>
</tr>
<tr>
<td>Caucasian</td>
<td>57</td>
<td>57.0</td>
<td>42</td>
</tr>
<tr>
<td>Other</td>
<td>43</td>
<td>43.0</td>
<td>33</td>
</tr>
<tr>
<td>Maternal Education</td>
<td>N</td>
<td>%</td>
<td>N</td>
</tr>
<tr>
<td>Grade School</td>
<td>19</td>
<td>19.0</td>
<td>16</td>
</tr>
<tr>
<td>High school</td>
<td>47</td>
<td>47.0</td>
<td>38</td>
</tr>
<tr>
<td>College / University</td>
<td>34</td>
<td>34.0</td>
<td>21</td>
</tr>
<tr>
<td>Maternal Employment</td>
<td>N</td>
<td>%</td>
<td>N</td>
</tr>
<tr>
<td>Employed</td>
<td>73</td>
<td>73.0</td>
<td>51</td>
</tr>
<tr>
<td>Unemployed</td>
<td>27</td>
<td>27.0</td>
<td>24</td>
</tr>
<tr>
<td>Marital status</td>
<td>N</td>
<td>%</td>
<td>N</td>
</tr>
<tr>
<td>Married/ Common-law</td>
<td>43</td>
<td>43.0</td>
<td>26</td>
</tr>
<tr>
<td>Single/Divorced</td>
<td>57</td>
<td>57.0</td>
<td>49</td>
</tr>
<tr>
<td>Maternal age (yrs) (Mean ± SD)</td>
<td>29.1 ± 5.8</td>
<td></td>
<td>27.5 ± 6.3</td>
</tr>
</tbody>
</table>

SD: Standard Deviation
*Statistical significance (p-value <0.05)

While most women were from a Caucasian background in both groups, smaller clusters of women from Aboriginal, African-Canadians, Hispanic, South and East Asian origins were also part of this Motherisk cohort. In addressing highest education level completed
and employment status, problem drinkers were similarly educated (p= 0.084) and no less employed than non-problem drinkers (p= 0.141). However, there were a significantly higher number of women with problem drinking behavior, who identified themselves as single or divorced compared to non-problem drinkers (p= 0.044).

At various cut-points of TWEAK and T-ACE, individual scores were tabulated for each screening questionnaire and summarized in two by two contingency tables. As an example, Table 14A shows the proportion of problem drinkers and non-problem drinkers who screened positively on the TWEAK and T-ACE tool using a cut point score of two or more.

Table 14A  Identifying risk drinkers with TWEAK and T-ACE: CP of 2

<table>
<thead>
<tr>
<th>Cut Point Threshold 2+</th>
<th>TWEAK Positive</th>
<th>TWEAK Negative</th>
<th>T-ACE Positive</th>
<th>T-ACE Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-Problem Drinkers</td>
<td>64 FP</td>
<td>36 TN</td>
<td>81 FP</td>
<td>19 TN</td>
</tr>
<tr>
<td>Problem Drinkers</td>
<td>75 TP</td>
<td>0 FN</td>
<td>75 TP</td>
<td>0 FN</td>
</tr>
</tbody>
</table>

FP: False Positive  TN: True Negative  TP: True Positive  FN: False Negative

Problem drinking criteria: Greater than 1 drink daily and self-identification as a problem drinker
At a CP of two or more, TWEAK test was able to accurately identify all problem drinkers, as was T-ACE, resulting in 100% sensitivity (Table 15). However, both TWEAK and T-ACE had high false positive rates of 64% and 81% respectively. Specificity of both tests was poor, as represented by their low true negatives values (TWEAK=36 and T-ACE=19 women) (Table 14A). The TWEAK test had a positive predictive value (PPV) of 0.54 with a probability of positively identifying 54% of the risk drinkers. Similarly, the PPV of the T-ACE was 0.48. Statistical analysis indicated no significant differences (p=0.66) between the rates of sensitivity or specificity between the TWEAK and T-ACE tests at a cut point of two or more.

Table 14B. Identifying risk drinkers with TWEAK and T-ACE: CP of 3

<table>
<thead>
<tr>
<th>Cut Point Threshold = 3+</th>
<th>TWEAK Positive</th>
<th>TWEAK Negative</th>
<th>T-ACE Positive</th>
<th>T-ACE Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-Problem drinkers</td>
<td>63 FP</td>
<td>37 TN</td>
<td>66 FP</td>
<td>34 TN</td>
</tr>
<tr>
<td>Problem Drinkers</td>
<td>74 TP</td>
<td>1 FN</td>
<td>70 TP</td>
<td>5 FN</td>
</tr>
</tbody>
</table>

FP: False Positive  
TN: True Negative  
TP: True Positive  
FN: False Negative  

Problem drinking criteria: Greater than 1 drink daily and self-identification as a problem drinker

Table 14B shows the ability of TWEAK and T-ACE to effectively identify pregnant women at risk of continuing their alcohol use in pregnancy using a cut point of three or
more as a positive screen. At this slightly higher cut point, the TWEAK test is still able to capture almost all risk drinkers with almost perfect sensitivity of 99%, but with very little improvement in specificity. Similarly, T-ACE test was more effective at screening out an additional 15 non-problem drinkers, thereby improving its specificity rate (true negative = 34%). Unfortunately, this test was less sensitive at cut point of three and missed identifying five problem drinkers (sensitivity= 93%) (Table 15).

**Table 15. TWEAK and T-ACE: Summary of sensitivity, specificity and PPV**

<table>
<thead>
<tr>
<th>Cut Points</th>
<th>TWEAK</th>
<th></th>
<th>T-ACE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PPV</td>
<td>Sensitivity</td>
<td>Specificity</td>
</tr>
<tr>
<td>2 or more</td>
<td>0.54</td>
<td>100</td>
<td>36</td>
</tr>
<tr>
<td>3 or more</td>
<td>0.54</td>
<td>99</td>
<td>43</td>
</tr>
</tbody>
</table>

PPV: Positive Predictive Value

At this CP of three or more, the positive predictive value of TWEAK remained unchanged at 0.54, while the PPV for T-ACE test improved to 0.51. However, there was still no statistically significant difference in the sensitivity and specificity rate between the two tools at a cut point of three or more (p= 0.38).

An increasing trend for specificity rates was seen as the cut point used for a positive screen increased with both screening tests (Table 15). It appeared that the
sensitivity of both TWEAK and T-ACE started out at 100% at a cut point of two or more, perfectly capturing all women with a potential for risk drinking behaviour. However, as the threshold of the cut point score needed to denote a positive screen increased by one point, the sensitivity decreased.
4.5 DISCUSSION

The methodological strength of this study rested in the fact that in this cohort, women made the initial contact of their own volition and provided full accounts of their respective drug exposures. This completeness of data provision is unique in research involving high-risk pregnant women. In the past, women with problem drinking behavior were found to be predominantly college-educated, employed and of high socio-economic status\textsuperscript{46}. The demographics of our study cohort are representative of this population and further confirm previous research describing women most likely at risk for perinatal alcohol use.

Both the TWEAK and T-ACE have been used to screen for perinatal risky drinking in the general population, hospital outpatient, and inpatients\textsuperscript{232}. This is the first study comparing the effectiveness of TWEAK and T-ACE among women who voluntarily admitted to drinking alcohol at risk levels. As a result, any inherent concerns associated with under-reporting were minimal in our study. Moreover, to our knowledge, these two tests have not been previously compared in a population where women may be motivated enough to contact a health service, but still be at risk for continued alcohol use in pregnancy.

Although previous data indicates that TWEAK performed similar to T-ACE in detecting a range of drinking patterns in comparison to several other screening tests, it performed slightly better than T-ACE in predicting risk drinking using a threshold of two or more in one study\textsuperscript{246}. This was confirmed by our findings, with TWEAK having a trend toward a higher PPV compared to T-ACE, but remained statistically insignificant. Unfortunately, at a CP of two or more, with a large number of false
positives, a positive screen of both TWEAK and T-ACE is in itself was not very useful at identifying only risky drinkers. Both tools were, however, useful at identifying all drinkers.

In our study population, T-ACE performed better at a cut point of three or more (3+) (as opposed to cut point of 2+) and accurately identified up to 51% of risky drinkers, without significantly compromising on sensitivity.

The TWEAK appeared to perform adequately at cut points of both 2+ and 3+, identifying about 54% of perinatal risky drinkers accurately. However, upon examination of our sensitivity and specificity data, our results suggest that TWEAK test using a cut point of 3 or more performs better, without compromising sensitivity. To most effectively screen risky drinking, achieving both high sensitivity and specificity rates is ideal. However, in a clinical setting where time is limited and consequences of an omission may be high, a test capable of capturing all potential women at risk for consuming alcohol in pregnancy may be preferable to a more specific one, particularly as specificity can be improved with supplemental screening.

Upon comparing the TWEAK and T-ACE tools for their effectiveness in screening for problem drinking in pregnancy, the lack of statistical significance appears to suggest that the efficacy of both tests is not different. One possible explanation for this finding may be the small number of women in our study cohort. To address this limitation, results of this cohort were extrapolated four-fold, and subsequent analyses still failed to detect any statistical difference between the two groups.

Although the nature of our study cohort adds to the strength of this study, due to their voluntary self-report of alcohol use by the participants, it is important to recognize
that this forthcoming attitude may not be representative of all pregnant women, particularly at a first prenatal visit. To address this potential limitation, questions regarding alcohol and substance use could be incorporated into standard intake forms routinely used to document patient information during regular physician.

Pregnancy provides a unique opportunity to educate women and their partners about the adverse effects of alcohol and the benefits of stopping its use at any time during pregnancy or postpartum. The community childbirth educator, outreach worker, community health nurse, and other health care staff can reinforce these messages through discussions both prior to and during pregnancy. With successful efforts in preventing the deleterious effects associated with prenatal alcohol use, substantial cost savings, both social and financial, may be realized.
CHAPTER FOUR

PART II

IDENTIFYING THE MOST EFFECTIVE THRESHOLD FOR TWEAK AND T-ACE: MOTHERISK COHORT
4.6 INTRODUCTION

The first part of this study demonstrated that both TWEAK and T-ACE performed poorly using recommended traditional cut-points in our study cohort (high sensitivity but very poor specificity). These findings underscore the need to investigate other potential thresholds, to maximize the utility of these two screening instruments. The role of the screening questionnaire’s threshold in determining how well it may predict problem drinking is crucial. Varying cut-point thresholds has been shown to invariably alter the performance of these screening tests.\textsuperscript{229} A study investigating gender differences in performance of TWEAK at predicting risk drinking found it was necessary to assign different cut-points based on gender in order to achieve optimal results.\textsuperscript{232} In a second study examining 181 risky drinkers and 2536 non-drinkers, Russell et al demonstrated that increasing the CP of TWEAK from 1 to 2, decreased sensitivity by only 1%, but increased specificity by 10%. This translated to approximately 254 non-risk drinkers no longer screening positive on the test.\textsuperscript{212}

As such, in the second part of this study, the objective was to examine all available CP’s to determine the most effective threshold at which the TWEAK and T-ACE perform in this Motherisk cohort. Since this group of women was quite different from previous studies, combined with the knowledge that specificity is poor at traditional thresholds, our hypothesis in this second part was that using a higher CP than those recommended would better predict problem drinking in our study cohort.
4.7 METHODS

In the second part of the study, participants, settings and procedures are the same as outlined in section 4.3. However, in this study, the score used to define a positive screen was not limited to two or three. Instead, screening for risky drinking was investigated using all possible CP thresholds for both the TWEAK and T-ACE. Hence, for the TWEAK, CP’s of 2, 3, 4, 5, 6 and 7 were examined while in the case of T-ACE thresholds of 2, 3, 4 and 5 were considered. To do this, at various cut-points, individual scores were tabulated for each screening questionnaire and summarized in 2 by 2 tables. From this, a number of test performance characteristics were computed for each threshold.

Effectiveness of screener performance is based on how results of a screening test compare to a standard. As described in section 4.3.2, this reference standard was a given participant’s positive response combined with her reported level of alcohol use (i.e. if her usage met the problem drinking criteria), both of which were obtained from Motherisk intake questionnaire (Appendix A).

4.7.1 Operational Characteristics

To measure the performance of TWEAK and T-ACE in our participants’ risk for problem drinking, several operational characteristics were investigated. Using a test-based approach, all CP thresholds were examined in each screening test. Each of sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) were calculated according to formulas presented in Table 16 for each CP threshold of both tests.
Table 16. Set-up of 2 x 2 table to calculate test performance characteristics

<table>
<thead>
<tr>
<th>Screening test</th>
<th>Problem drinkers</th>
<th>Non-problem drinkers</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive screen Score ≥ CP</td>
<td>True Positive (TP) (a)</td>
<td>False Positive (FP) ((\text{Type I error})) (b)</td>
<td>(a + b)</td>
</tr>
<tr>
<td>Negative screen Score &lt; CP</td>
<td>False Negative (FN) ((\text{Type II error})) (c)</td>
<td>True Negative (TN) (d)</td>
<td>(c + d)</td>
</tr>
<tr>
<td>Total</td>
<td>(a + c)</td>
<td>(b + d)</td>
<td>(a + b + c + d)</td>
</tr>
</tbody>
</table>

Where problem drinkers and non-problem drinkers are determined by this study’s “reference standard” as stated in section 4.3.2.

The relationship amongst these variables is outlined below:

\[\text{Sensitivity} = \frac{a}{a + c}\]
\[\text{PPV} = \frac{a}{a + b}\]
\[\text{Specificity} = \frac{d}{b + d}\]
\[\text{NPV} = \frac{d}{d + c}\]

Please see section 4.3.2 for further discussion of these operational characteristics.

4.7.2 ROC Analysis

Further evaluation of the TWEAK and T-ACE performance was done using Receiver Operator Characteristic (ROC) curves, which were plotted for all CP thresholds for both screening tests (SPSS v. 12.0). The ROC curve provides an alternative to sensitivity and specificity methods and often used for cost/benefit analyses of a decision making process. The curve is constructed by plotting TPR (sensitivity) on the y-axis as a
function of FPR (1-specificity) for all possible cut-off points of each instrument. Subsequently, this test compares two operating characteristics (TPR & FPR) as the criterion changes. Using this statistical procedure, it is possible to determine the CP that produces maximum sensitivity (i.e., screening instrument correctly identifies women with problem drinking behaviour) and specificity (i.e., it correctly identifies those who are not at risk). The best possible prediction method (representing no false positives and no false negatives) would yield a point in the upper left corner, passing through (0,1) of the ROC space. In turn, a poor test will likely result in a ROC plot on the line y=x, producing as many false positive results as true positives. For both the TWEAK and T-ACE instruments, ROC curves were plotted using all possible CP and their respective true positives and true negative fractions. Two plots were constructed using 7 CP and 5 CP’s, reflecting the TWEAK and T-ACE tests, respectively. The higher the value of the area under the curve, the more accurate/effective the test was considered.
4.8 RESULTS

As previously reported, a total of 175 women were enrolled in the study, including 100 women who responded negatively to being a problem drinker and 75 who admitted to drinking at risky levels. The performance of both TWEAK and T-ACE as a test to screen for risky or problem drinking behaviour in the Motherisk cohort was evaluated by calculating different metrics of test performance as outlined in the previous section. Sensitivity, specificity and positive predictive values for all possible CP thresholds to identify at-risk women are presented in Table 17.

A trend for increasing sensitivity rates and decreasing specificity rates was observed with the lowering of CP scores used for a positive screen for both tests. At every CP, the five-item TWEAK was more sensitive than the four-item T-ACE. A significant decrease in the sensitivity of both tests was observed with shift in thresholds of 3+ to 4+. However, this decline in sensitivity for TWEAK performance appeared to be more gradual than that of T-ACE. For example, increasing the CP of both tests from 3 to 4, decreased the sensitivity of TWEAK by only 11%, but decreased that of T-ACE by 33%. In terms of non-problem drinkers who tested negative, the specificity of TWEAK increased by 20% (37% to 57%) with an even greater increase of 28% (34% to 62%) in the case of T-ACE. With 75 problem drinkers and 100 non-problem drinkers, every 4% increment in sensitivity meant that three more women with a risky drinking habit would test positive on the screening questionnaires; while, every 4% increase in specificity would translate to 4 more non-risk drinkers testing negative on the screeners.
Table 17. Summary of sensitivity, specificity and PPV for all CP

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>6 or more</td>
<td>28 [19-40]</td>
<td>85 [76-91]</td>
<td>58 [41-74]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7 or more</td>
<td>16 [9-27]</td>
<td>95 [88-98]</td>
<td>71 [44-89]</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Efficiency is an arbitrary parameter that maximizes the sum of sensitivity and specificity. Based on this measure, the best threshold values were those corresponding to the largest sum of sensitivity and specificity (bolded values in Table 17). In the case of TWEAK, a cut-off score of four or more appeared to distinguish non-problem drinkers from those at risk, represented by the highest sum \((0.88 + 0.57 = 1.45)\). In contrast, with T-ACE, the highest sum was obtained using a CP of three \((0.93 + 0.34 = 1.27)\) in our study cohort.

Predictive values are based on the prevalence of the true state (in this context being problem drinkers and non-problem drinkers) for both screening questionnaires. The PPV as described in section (4.3) is also noted in Table 17. The probability of accurately identifying a problem drinker ranged from 54 to 71 percent for the TWEAK and 48 to 71 percent for the T-ACE test. With minimal decrease in sensitivity of the tests, the use of a CP of 4 yielded a PPV of 61% for TWEAK. In the case of T-ACE, PPV was similar at two thresholds (CP 3+ =0.51 and CP 4+= 0.54), however, along with the slight increase in PPV came a significant drop in specificity (~33%) (by increasing CP from 3 to 4). Statistical analysis suggested that TWEAK was much more sensitive (88% vs. 60%, \(p=0.002\)), with a higher probability of positively screening problem drinking (61% vs. 51%, \(p=0.048\)) utilizing cut-off points of 4 or more, in comparison to the T-ACE test.

Further analyses to confirm and refine these results were done using the ROC curves as described in section 4.7.2. These analyses were done to determine the threshold at which each test performed most effectively. ROC curves for both T-ACE and TWEAK are plotted in Figure 7. In both cases, the general shape of the curve was reflective of a high rate of false positives. By inspection, the TWEAK at a CP of 4 was
closest to the upper left corner of the graph, indicating the optimal combination of sensitivity and specificity. The graphical representation for T-ACE, on the other hand, was not as evident. When focusing on the CP with the largest area under the curve (AUC), it appeared that a CP of 3 was most optimal for the T-ACE.

Figure 7: ROC Curve representation for TWEAK and T-ACE at various CP
4.9 DISCUSSION

To our knowledge, this was the first study to investigate the effectiveness of the TWEAK and T-ACE tools using all potential cut-points, in identifying risk drinking in obstetric patients. Our work highlights the influence of cut-points used to define positive scores on the screening questionnaires.

A few factors play a role in making the screen’s threshold so vital in how effectively the test performs. Firstly, the utility of both tests depends substantially on the question about tolerance to alcohol’s effects that assess alcohol intake indirectly. As tolerance to alcohol develops, increases occur in the minimum amount one must drink to feels the first effects or get high. This indirect approach avoids triggering denial or minimization of alcohol intake, especially when worded in the past. In our study, the tolerance question was found to be most sensitive. Varying the criteria for number of drinks required to screen positive may increase specificity, but will decrease the sensitivity of the test.

Generally, the highest sensitivity levels can be obtained by lowering the CP. But in a cohort of disadvantaged African-American pregnant women, Russell et al found there was little loss in sensitivity resulting from raising CP of one to two in screening tests\textsuperscript{230}. This was supported by our findings, but at a CP higher (i.e. sensitivity remained essentially the same at CP of two and three). The demographic characteristics of the present study cohort may be a possible explanation for this deviation, indicating a need to use slightly higher CP in women with more education and higher SES.
As specificity tends to be inversely related to sensitivity, especially when prevalence of the condition the test is screening for is not high, as in the case of problem drinking in pregnancy. This is evident from the clear inverse relationship that exists between sensitivity and specificity rates with each CP in both tests.

These results add to previous findings suggesting that TWEAK and T-ACE should be utilized strictly as preliminary screening tools and followed up with subsequent questioning to increase specificity. Given that both tests were very effective at capturing all potential at-risk women, but inclusive of many false positives, providers of prenatal care may need to suppress the cost of following up positive screens as much as possible to permit further screening. Alternatively, providers may have to contend with the fact that they may miss more risky drinkers by using more specific, less sensitive screening procedures.

The strengths of the second part of this study are as follows: First, the objective measure of alcohol intake that served as our ‘reference standard’ was optimal given the motivated nature of our study population. Second, to our knowledge, this was the first study to examine not only the effectiveness of both TWEAK and T-ACE at cut-points greater than the traditionally held thresholds, but it was also the first study to demonstrate an improvement in performance using higher CPs in a cohort with higher SES. Finally, a key finding of this research was that TWEAK compared favorably to T-ACE across a range of potential CP, combining high sensitivity levels with reasonable specificity levels.

The limitations of these findings remain the same as discussed in part 1 of this research (Section 4.5)
4.10 CONCLUSION

In summary, differences in the performance of both TWEAK and T-ACE occurred with changes to their respective CPs, illustrating the need to consider CP when selecting a screening method for a particular cohort. Both T-ACE and TWEAK tools performed poorly at identifying problem drinkers at recommended thresholds. However, the TWEAK appeared to be better suited for the Motherisk cohort than T-ACE, using a CP of 4+. This study illustrates the crucial need to be knowledgeable regarding the screening instruments used, particularly with respect to the populations on which their use is appropriate and the variability in cut point thresholds at which clinically significant disease may be detected.
CHAPTER 5

CHARACTERISTICS OF PREGNANT WOMEN USING METHAMPHETAMINE
5.1 ABSTRACT

**Background:** Methamphetamine (MA) is a CNS stimulant that has gained popularity due to its low cost, relative ease of access and high potential for abuse. Its use has markedly increased amongst teens and young adults over the past ten years. This study aims to characterize pregnant women who use MA, examine their pattern of perinatal use and to identify potential risk factors and demographics associated with this group.

**Methods:** This prospective, comparative study enrolled pregnant women from The Motherisk Alcohol and Substance Use Helpline. A total of 218 pregnant women who reported using MA were compared to 218 women not exposed to amphetamines. Maternal and pregnancy characteristics, patterns of alcohol and illicit drug exposures, psychiatric co-morbidities and details surrounding MA use were documented. Analysis was done using chi-square test and student’s two-tailed t-tests, as appropriate. Multivariate analysis was done using logistic regression. The MA exposed and non-exposed groups were matched for gestational age at initial time of call.

**Results:** The 218 pregnant women who used MA were significantly younger (mean 26.6 vs. 30.3 years, P<0.05), and were at higher risk for unplanned pregnancies when compared to pregnant nonusers (100% vs. 47.3%, RR=2.1, CI (1.8-2.4)). MA users were highly likely to be single (71.1% vs. 20.6%; RR=3.4, CI (2.6 - 4.5)), and later in recognizing their pregnancies (8.9 wks vs. 4.5 wks, P<0.05). While alcohol and cigarette use were the most popular concurrent drugs of choice among 168 MA users, THC (32.1%) and cocaine (25.7%) were the illicit drugs most often concurrently used with MA in this study. Other concomitantly used agents included: opioids, MDMA, psilocybin, ketamine and GHB.
Conclusions: Women with a history of untreated psychiatric disorders, STI or recreational drug use should be routinely asked about alcohol and/or illicit drug use. Given the significant association of heavy and binge drinking, smoking and poly-drug use, combined with a higher than expected rate of unplanned pregnancies in women carrying the above risk factors, our findings highlight the need to educate women not only about contraception but also the serious risk of deleterious pregnancy outcomes in the setting of perinatal illicit drug use. Finally, understanding the characteristics of this vulnerable group can help providers improve identification of women at risk so that timely preventative strategies may be developed and deployed.
5.2 INTRODUCTION

Methamphetamine (MA) is a potent central nervous system stimulant that has gained popularity as a recreational substance of abuse \textsuperscript{101,248}. Similar to other amphetamines, MA increases brain dopamine, enhancing central nervous system (CNS) stimulation \textsuperscript{79,80}. Commonly known as "speed", this street drug can be taken in pill form, can be injected, smoked or snorted. More recent studies suggest that crystal form ("crystal meth") of MA is gaining popularity as an injectible drug as it very rapidly achieves a high plasma drug concentration \textsuperscript{22,91,249}.

Use of MA is strongly associated with attending all-night raves and nightclubs \textsuperscript{250}. It continues to gain popularity since it is easy to produce, easy to use, and cheaper than cocaine. A recent report by the United Nations suggested that illicit use of MA has become epidemic worldwide, surpassing cocaine in several parts of the world \textsuperscript{74}. Moreover, with a terminal plasma half-life of approximately 10 hours, a MA "high" can last up to 12 hours following a single dose of 30 mg \textsuperscript{75}. This makes MA substantially different from other stimulants such as cocaine, where effects typically last only 20 to 30 minutes, adding to its dangerous appeal.

The prevalence of MA use has been shown to be higher in women \textsuperscript{17,251,252} compared to men, owing to its production of effects such as appetite suppression, weight loss and increased energy, traditionally attractive to young women of reproductive capability \textsuperscript{253,254}. Due to its widespread use in women of childbearing age, fetal exposure to MA during pregnancy is inevitable, making prevention strategies to minimize fetal adverse effects critical. Unfortunately, Canadian data on MA use among women of
reproductive age is currently quite sparse\textsuperscript{55, 96}. A longitudinal US study reported prevalence of MA use among pregnant women to be approximately 5.2\%\textsuperscript{31}. Other research found that among all pregnant women admitted to an addiction center, almost 40\% were dependent on MA. Based on data obtained from the Treatment Episode Data Set (TEDS), MA has become the primary illicit drug necessitating treatment in pregnant women\textsuperscript{30, 112}.

Relatively few studies have examined characteristics of women exposed to MA during pregnancy\textsuperscript{31, 124}. In the few studies available, findings appear to be based on self-reported data retrieved from retrospective chart reviews where issues such as poor documentation and lack of standardized data collection (generally inherent in retrospective research) were apparent. Moreover, much of the data available has been obtained from particularly affected pregnant women seeking treatment for a bona fide addiction to MA\textsuperscript{30}. It is important to recognize, however, that a significant portion of women exposed to or using MA may not be truly dependent on it; these women may be termed casual or low intensity users. This subgroup of pregnant users who may be less likely to be identified, owing to their less dramatic presentation, are equally essential to characterize in order to improve prevention strategies.

Finally, studies have consistently shown that MA users typically engage in high risk behaviours, such as poly-drug use\textsuperscript{94} and risky sexual practices\textsuperscript{102, 255} and are at high risk for HIV/Hepatitis C infection\textsuperscript{256, 257}. Moreover, children exposed in utero to MA are at increased risk for developmental concerns due to both the direct effects of perinatal MA exposure, as well as a lack of an adequate care-giving environment secondary to the effect of MA on their parent(s)\textsuperscript{125, 258}. These concerns, combined with increasing use in
pregnancy, makes it is essential to examine perinatal MA use in a pregnant population with a diverse pattern of use and determine the risk factors and demographic characteristics inherent to them. Elucidation of this information would greatly assist early identification so that timely intervention may follow.

The objectives of this study were to:

1) Characterize pregnant Canadian women who use MA
2) Examine the pattern and route of MA exposure
3) Identify potential risk factors associated with women who use MA.
5.3 METHODS

This prospective comparative cohort study included records of callers who contacted the Motherisk program of their own volition, and were pregnant during their initial call. The study group consisted of women reporting their use of MA, a minimum of two times, at some point during their pregnancy. The comparison group consisted of randomly selected pregnant women who called the program within the same week as those in an MA-exposed group and received counseling on exposures, including medications, alcohol or nicotine, but did not report any exposure to MA, or other amphetamines in their lifetime. The women who contact this national helpline across Canada are generally similar in nature hence both groups were recruited from the same program to ensure differences in endpoints would more likely be function of MA use.

Women who called the service for information regarding their exposures between September 2006 and December 2008 were included in the present study. At initial contact, following routine procedures, demographic data, obstetric history and any external exposures were provided willingly by women and documented on a standardized intake form by trained counselors. These included maternal age, marital status, education, current employment, pregnancy history, medical complications, psychiatric conditions, infectious diseases and details of their nicotine, alcohol and illicit drug use. For the MA-exposed group, additional data regarding details of method and pattern of MA use, including trimester and route of exposure, dose and frequency of use, concurrent drug exposures, and reports of maternal adverse effects after use were obtained. All participants were provided information and counseling over the telephone regarding their
specific exposures in pregnancy and subsequently referred to appropriate services, if needed. During this time, informed consent for data to be utilized in research (excluding all potential identifiers) was obtained from all women who agreed to participate in research.

5.3.1 Variable definitions

Consumption of alcohol and smoking were categorized as none, light, moderate and heavy. Light drinking was defined as consuming an average of less than two drinks/week; moderate use was greater than two drinks/week and less than an average of one drink/day; heavy drinking constituted consuming an average of two or more drinks/day and/or binge drinking at least once a week. Binge drinking was defined as consuming more than four drinks on one occasion. Smoking patterns were categorized as follows: Less than 10 cigarettes/day was considered light smoking; moderate smokers consumed 10–19 cigarettes/day; and heavy smokers were women who smoked 20 or more cigarettes/day. Exposure to MA was categorized by method of use (oral, smoking, intranasal or intravenous) and dosage (low to moderate use 20-40mg or heavy use greater than 40mg). For this study, pattern of MA use was stratified into types: (1) low intensity (to describe a user who is not psychologically addicted to the drug but uses MA on a casual basis by swallowing or snorting it); (2) high-intensity (users who are psychologically addicted and prefer to smoke or inject MA to achieve a faster and more intense high); and (3) binge use of MA (more than low-intensity use but less than high-intensity use). Poor prenatal care addressed both lack of prenatal vitamin intake and less than five prenatal visits during the course of the pregnancy.
5.3.2 Statistical Analyses

To determine the potential risk predictors associated with MA use, data were categorized and coded for both groups. Data were analyzed by SPSS software (SPSS for Windows, 2001. Chicago: SPSS Inc.). Univariate analysis was done on each variable in the data set, separately, when comparing both groups. To describe the data, frequency tables and their percentage estimates were derived using cross tabs. To determine significance of variables among MA users and non-users, continuous variables were compared using the two-tailed student unpaired t-test, while categorical variables (e.g. alcohol, smoking, MA pattern of use etc) were compared by chi-square tests. Relative risk (RR) ratios and 95% confidence intervals were reported to estimate the strength of an association between the risk factors and use of MA. In predicting which variables are possible risk factors for MA use in pregnancy, binary logistic regression was used to test the significance of the dichotomous variables in a multivariate model. Statistical significance was defined by a p-value of less than or equal to 0.05.
5.4 RESULTS

5.4.1 Characteristics of pregnant women

A total of 218 women were exposed to MA out of a total of 436 records included in the study. They were significantly younger (mean 26.6 vs. 30.3, \( P = 0.001 \)) and reported delayed recognition of their pregnancies (mean 8.9 vs. 4.5 weeks, \( P < 0.001 \)) compared to non-exposed controls (Table 18).

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>MA Users (N=218)</th>
<th>Non-MA Users (N=218)</th>
<th>RR (CI) P-value</th>
<th>Reproductive risks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single Status</td>
<td>71.1%</td>
<td>20.6%</td>
<td>3.4 (2.6-4.5) P &lt;0.001</td>
<td>Lack of support - ↑ risk linked to poverty, stress</td>
</tr>
<tr>
<td>Sexually transmitted infections</td>
<td>8.3%</td>
<td>0.9%</td>
<td>9.0 (2.1-38.3) P=0.003</td>
<td>Fetal infections and adverse effects due to HIV, HPV, Chlamydia infections in mother etc.</td>
</tr>
<tr>
<td>Psychiatric Condition Dx</td>
<td>51.8%</td>
<td>39.9%</td>
<td>1.3 (1.1-1.6) P=0.013</td>
<td>Poor Rx compliance; negative fetal effects due to concerns associated with untreated depression</td>
</tr>
<tr>
<td>Pregnancy recognition (wks)</td>
<td>8.9 ± 3.2</td>
<td>4.5 ± 1.9</td>
<td>P &lt;0.001</td>
<td>Indication of unstable lifestyle; continued use of potential teratogens</td>
</tr>
<tr>
<td>Lack prenatal vitamin intake</td>
<td>81.2%</td>
<td>20.2%</td>
<td>4.0 (3.1–5.3) P &lt;0.001</td>
<td>Spina bifida and other malformations</td>
</tr>
<tr>
<td>Unplanned Pregnancy</td>
<td>100%</td>
<td>47.3%</td>
<td>2.1 (1.8-2.4) P &lt;0.001</td>
<td>↑ Risky lifestyle e.g. continued use of other teratogen (e.g. alcohol) = ↑ risk for FASD</td>
</tr>
</tbody>
</table>

MA users were more than three times likely to be single [71.1% vs. 20.6%, RR=3.4, CI (2.6-4.5)] and unemployed, but did not differ from the comparison group in terms of the level of education attained. A sub-analysis examining pregnancy recognition...
in relation to education found that women with at least high school or higher level of education, recognized their pregnancy much earlier than those who failed to complete high school (p=0.002).

With respect to pregnancy history, MA users had significantly fewer pregnancies [46.9% vs. 62.1% RR=0.76, CI (0.64-0.91)] and a higher rate of therapeutic abortions [61.5% vs. 38.9%, RR=1.6, CI (1.3-1.9)]. However, no statistical difference was found in the rate of spontaneous abortions reported. As shown in Table 18, all MA users reported their pregnancy was unplanned [100% vs. 47.3%, RR=2.1, CI (1.8-2.4)], and moreover, failed to recognize their pregnancy more than a month after women who did not use MA.

Although physician visits during pregnancy were comparable between the two groups, only one out every five women using MA regularly took prenatal vitamins. This was significantly lower than their matched non-MA exposed comparators, the majority of whom reported daily prenatal vitamin intake [20.2% vs. 81.2%; RR=4.0, CI (3.1-5.3)]. Moreover, there was a nine-fold higher risk of a history of sexually transmitted infections (STIs) in MA users, compared to non-users [8.3% vs. 0.9%; RR=9.0, CI (2.1-38.3)]. Psychiatric disorders including attention deficit hyperactivity disorder (ADHD), depression, anxiety, bipolar and mood disorders were reported by both MA-exposed pregnant (51.8%) and their comparison group (39.9%). However, use of medications such as anxiolytics, antidepressants and mood stabilizers for therapy was significantly greater in the comparison group (62%), while MA users disclosed their poor compliance (38%) to these much-required drugs. The primary reasons for discontinuation of
medication therapy included concerns surrounding potential risk to fetus, negative side
effects of medications and/or lack of benefit from use (i.e. “medications were not
working for them”).

5.4.2 MA method and pattern of use

Table 19 provides a summary of how and when MA was used during pregnancy. Out of 218 women exposed to MA prior to knowledge of the pregnancy, half reportedly discontinued using it upon recognizing their respective pregnancies, with gestational age of last MA exposure averaging nine weeks (range 1–24 weeks). Over 90% of women were exposed during organogenesis, while up to 9% reported use throughout their entire pregnancies. In this self-reporting cohort, the most popular form of MA use was oral route in tablet/pill form (61.8%), followed by smoking (24.5%), intranasal use (8.9%), with only 10 women reporting injection MA use. Of those who ingested MA tablets (n=131), the average dose used per occasion was approximately 30 mg (range 10–120 mg), and 68.6% of the subjects used more than one tablet/pill per occasion. Most women chose to discontinue use soon after recognizing their pregnancy, with 56.7% having only three MA exposures during their pregnancy. While 59 women disclosed that their MA exposure was not limited to just one trimester, almost 9% used it intermittently throughout the pregnancy. In disclosing the primary reasons for using MA, the most common motivations included: enhancement of partying (57%), heightening of sexual experiences (21%), to stay up for work/school (13%) and for help with weight loss (9%). Finally, examining potential adverse effects experienced by pregnant women upon using MA, there were reports of accelerated heartbeat, anxiety, reduced appetite, elevated temperature and perspiration (possible hyperthermia). These symptoms were
documented as short term following exposure, and none of the women required hospitalization secondary to MA use while pregnant.

Table 19. Summary of Methamphetamine Use During Pregnancy

<table>
<thead>
<tr>
<th>Methamphetamine timing of exposure</th>
<th>N = 218</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total exposures in T1</td>
<td>196</td>
<td>89.9</td>
</tr>
<tr>
<td>Total exposures in T2</td>
<td>59</td>
<td>27.1</td>
</tr>
<tr>
<td>T1+ T2</td>
<td>61</td>
<td>27.9</td>
</tr>
<tr>
<td>T1+ T3</td>
<td>24</td>
<td>11.0</td>
</tr>
<tr>
<td>Throughout</td>
<td>19</td>
<td>8.7</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Route of exposure</th>
<th>N = 212</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral (tablet/pill)</td>
<td>131</td>
<td>61.8</td>
</tr>
<tr>
<td>Smoke</td>
<td>52</td>
<td>24.5</td>
</tr>
<tr>
<td>Intranasal (powder)</td>
<td>19</td>
<td>8.9</td>
</tr>
<tr>
<td>Injection</td>
<td>10</td>
<td>4.7</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Number of occasions used in pregnancy</th>
<th>N = 211</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Two – three times</td>
<td>104</td>
<td>49.3</td>
</tr>
<tr>
<td>Four – five times</td>
<td>81</td>
<td>38.4</td>
</tr>
<tr>
<td>&gt; Five times</td>
<td>26</td>
<td>12.3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Concurrent recreational drug use when taking MA</th>
<th>N = 218</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MA plus ≥ one concurrent drug</td>
<td>168</td>
<td>77.1</td>
</tr>
<tr>
<td>MA use only</td>
<td>50</td>
<td>22.9</td>
</tr>
</tbody>
</table>

5.4.3 Poly-drug Use

Concurrent use of other recreational drugs were reported by most pregnant women exposed to MA (77%) with only 50 women reporting use of MA alone. The most popular drugs included alcohol (53.7%), nicotine (51.4%), THC (32.1%), followed by cocaine (25.7%). Other concomitant recreational substances reported were: opiates, ketamine, LSD, GHB, psilocybin and PCP. A sub-analysis conducted to determine if
women exposed to MA alone (23%) differed demographically from poly-drug MA users, found no remarkable differences between the groups.

5.4.4 Alcohol and Cigarette Use

Alcohol-exposure patterns differed greatly between MA exposed and non-exposed groups. The MA users were almost three-fold more likely to consume alcohol in pregnancy [53.7% vs. 18.8%, RR=2.9, CI (2.1-3.9)], with almost a seven-fold increased risk of drinking heavily [RR=6.7, CI (2.4-18.6)] compared to non-MA users. As shown in Table 20, binge alcohol consumption, which is considered to be most harmful to the developing fetus, occurred nine-fold more often in pregnancies of MA-exposed women [38.9% vs. 4.3%; RR=9.2, CI (3.8-22.3)]. In both groups, alcohol use was not limited to weekend use alone as many women reported drinking low to moderate levels intermittently throughout their entire pregnancies.

Women who reported MA use were more likely to be smokers compared to the comparison group [51.4% vs. 21.5%; RR=2.4, CI (1.8-3.1)] (Table 20). There were two-fold more heavy smokers in the MA-exposed cohort than non-users. Rates of cutting down use of cigarettes or quitting in pregnancy did not differ significantly between the two groups.
Table 20. Comparison of common concurrent drugs use

<table>
<thead>
<tr>
<th>Types of Concurrent drugs</th>
<th>MA Users (N=218)</th>
<th>Non-users</th>
<th>RR</th>
<th>95% (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>%</td>
<td>%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol Binge</td>
<td>38.9</td>
<td>4.3</td>
<td>9.2</td>
<td>(3.8-22.3)</td>
</tr>
<tr>
<td>Nicotine (&gt; 9 cigs)</td>
<td>51.4</td>
<td>21.5</td>
<td>2.4</td>
<td>(1.8-3.1)</td>
</tr>
<tr>
<td>Cocaine</td>
<td>25.7</td>
<td>3.8</td>
<td>7.0</td>
<td>(3.4-14.33)</td>
</tr>
<tr>
<td>THC</td>
<td>32.1</td>
<td>20.1</td>
<td>1.6</td>
<td>(1.1-2.4)</td>
</tr>
<tr>
<td>Opioids</td>
<td>6.4</td>
<td>0.9</td>
<td>3.0</td>
<td>(1.6-30.4)</td>
</tr>
</tbody>
</table>

5.4.5 Illicit Drug Use

In comparing illicit substances, MA consumers had a greater tendency to use marijuana [RR=1.6, CI (1.3-1.9)] and cocaine [RR=7.0, CI (3.4-14.3)] as shown in Table 20. Club drugs such as ketamine [7.8% vs. 0.0%; RR=17.0, CI (2.3-126.6)], GHB [7.6% vs. 0.00%; RR=13.0, CI (0.74-229.4)], psilocybin “magic mushrooms” [4.5% vs. 0.00%, RR=17.0, CI (0.9-292.7)], LSD and phencyclidine were reported only by women using MA. It should be noted that number of exposures to LSD and phencyclidine were too small to conduct any statistical analysis.
5.5 DISCUSSION

To our knowledge, this is the first prospective study describing the characteristics risk factors inherent to pregnant women using MA. By collecting data prospectively in early pregnancy, and subsequently following participants through the length of their pregnancies, we sought to avoid concerns of reporting and recall bias. Reporting bias was further reduced as MA users contacted the Motherisk Program of their own will. The comparison group was comprised of women who also contacted the Motherisk Program but were not exposed to MA currently, or in the past.

From a clinical perspective, in order to identify users, it is important to understand the relationships that exist between various socio-demographic sub groups and their patterns of MA use. In characterizing women in our study groups, those who used MA prenatally were mostly Caucasian, younger, single and unemployed, confirming previous findings. However, it is conceivable that MA users being as educated as non-users very likely contributed to the significant number of discontinuations upon pregnancy recognition.

Route of MA exposure is also valuable in identification as it often determines the intensity of “MA high” experienced by the user. Consequently, level of dependency and potential physiological maternal effects may also be a function of how it is administered. MA users often initiate with intranasal or oral use and progress to smoking and injection use (which are generally associated with higher levels of dependency and chaotic use patterns). In the present study, most women reported oral use, which is indicative of low-intensity pattern of use, and potentially a less severely
dependent group, perhaps as a result of decreased bioavailability of the drug. This is in contrast to existing research from the US on pregnant women using MA at levels necessitating therapy at hospitals or treatment centers, where smoking and injection routes were significantly predominant. From an interventional standpoint, it is important to point out that almost all the women who discontinued were taking the drug orally, possibly because they were least addicted through this route. This suggests that our self-motivated patients represent a more mainstream group and in a way, represents the growing pervasiveness of MA use in society.

Many providers may first suspect use due to withdrawal-like symptoms in the patient. But with the exception of one case where there was clearly excessive use, most women in our cohort were free of withdrawal symptoms upon discontinuation to MA. These deviations from previous findings suggest our population may not share the appearance of MA addicts. Hence, screening becomes especially important in this group, as they are very likely to go through pregnancy unidentified by their providers.

The adverse effects following MA use in this group of women are commonly reported physiological effects among MA users. Unfortunately, when experienced during pregnancy, these can have negative implications for both mother and her developing fetus. Future outcome study will address the impact of MA-induced physiological changes in women following use.

The feelings of increased arousal and decreased inhibitions described by our cohort are also typical “highs” women want to achieve from using MA. In turn, these desired effects probably explain the unplanned nature of all pregnancies among exposed
women. Additionally, unplanned sexual intercourse “under the influence” has also been associated with an increased risk of unprotected sexual practices, as evident in the significantly higher rates of STI’s reported by exposed women. According to a US study, MA users were six times less likely to use condoms. Moreover, since pregnancy recognition among was delayed until end of the first trimester, women unknowing continued to expose their developing fetuses to periodic alcohol, illicit drugs and MA, with no prenatal care. This delay is unfortunate given that a significant portion of women did choose to discontinue use upon knowledge of their pregnancy.

Alcohol consumption, cigarette use, and experimentation with psychoactive substances have previous been shown to be inherent in MA using culture and our data suggest concurrent use of these drugs are just as prevalent among our pregnant women. As MA is known to cross the human placenta and accumulate in fetus, special attention needs to be brought to the significantly higher rates of heavy and binge drinking pattern disclosed by this group, and subsequently, the disastrous implications for the fetus. Findings from the present study demonstrates that low-intensity or occasional MA users are not at any decreased risk for fetal alcohol spectrum disorder (FASD), as their pattern of alcohol use is no different than MA dependent women, perhaps even more chaotic. In fact, providers need to be diligent of that fact that with MA discontinuation, alcohol use can increase. These findings signal the need to educate pregnant women about the adverse consequences of not just prenatal MA use, but alcohol consumption as well.
To our knowledge, our study is the first to examine co-usage of a wide range of other illicit drugs, specifically stimulants and hallucinogens, in pregnancy. From previous studies, it is well understood that in order to characterize women who use MA, it is essential to examine their use in a multiple drug-using context. In addition to fetal concerns stemming from higher rates of alcohol and nicotine intake, many MA users were also exposed to at least one other illicit drug during the pregnancy. Concurrent exposure to such substances of unknown reproductive risks, combined with additional concerns for additive or synergistic effects, highlights the critical need to address the role of multi-drug using behaviour even in this group of less severely dependent women. Impact of MA use adds another dimension of risk with respect to long-term implications for children. Concerns related to neuro-cognitive impairments in the domains of executive functioning, learning, motor skills, impulse control and sustained attention are possible concerns in children whose mothers are exposed to MA during pregnancy. Hence, future prospective observational studies on long-term fetal consequences are essential in light of the potential neuro-toxic effects associated with MA exposure. It would also be important to address the impact of such poly drug-using environment on children raised by women who continue to lead risky lifestyles, as a result of not being identified.

MA use has been linked with psychiatric disorders evidenced by the significant proportion of psychiatric co-morbidities including attention deficit hyperactivity disorder, depression, anxiety and social phobia in our findings. Moreover, numerous studies addressing the dilemma of dual disorders have demonstrated that untreated psychiatric disorders can often lead to self-medicating with recreational substances. In the present study, the high co-morbidity of ADHD (a condition MA was therapeutically indicated
for), combined with women’s failure to comply with conventional therapy may indicate that use of MA was an unconscious attempt to combat untreated symptoms. It is vital that health care providers not only be aware of concerns associated with dual disorders but also ensure that these women are appropriately diagnosed and treated. Our findings highlight the need for providers to routinely ask all women of childbearing age under their care about use of MA or other substances. Also, since these women appear to seek medical services, it provides an amazing opportunity to educate women regarding the adverse consequences of both recreational drug use and untreated psychiatric conditions in pregnancy.

While this is the first prospective study characterizing Canadian women who use MA in pregnancy, the generalizability of our results need to be addressed. Women who contacted the service were self-selected and motivated to seek help. It is conceivable, therefore, that women who did not contact us represent an even higher risk subgroup.
5.6 CONCLUSION

Pregnant MA users have a clustering of powerful reproductive risk factors that may result in adverse pregnancy outcomes. They tend to be younger, single, educated, with a history of therapeutic abortions and increased psychiatric co-morbidities. A relatively high rate of unplanned pregnancies, combined with heavy alcohol consumption, cigarette use, and concurrent illicit drug use increases the risk of fetal exposure to potentially harmful substances. Consideration of route and changing pattern of MA consumption is crucial as both can have an enormous impact on the rate of adverse fetal effects, especially FASD. The increasing trend worldwide, also implies an essential need for universal efforts to educate the public about the adverse health consequences associated with MA use, particularly in pregnancy. Presence of one or more of these risk identifiers should serve as an indication for further investigation during a routine prenatal visit. Our findings will help improve prevention strategies by providing clinicians a better understanding of risk predictors inherent in women who may moderately use MA. Effective screening will help improve identification, so that subsequent education and referral can follow.
CHAPTER 6

METHAMPHETAMINE USE: COMPARING MATERNAL SELF-REPORT DATA AND A BIOLOGICAL MARKER
6.1 ABSTRACT

**Background:** Over the past two decades, a dramatic increase in the use of methamphetamine (MA) worldwide has occurred. Poly-drug use is a common phenomenon among MA users, including pregnant women. Given that co-utilization of other illicit drugs is almost invariably part of the MA culture and given that perinatal poly-drug use can have serious negative implications for both mother and child, identification of this poorly studied population (pregnant MA users) is critical.

**Objective:** Our objective was to determine if the type and frequency of co-exposures to other illicit substances were comparable between women who self-reported their MA use and those who tested positive for MA through hair analysis.

**Methods:** This observational study examined two methods of identification utilized by the Motherisk program, Hospital for Sick Children. The study cohort consisted of two groups: 1) women calling to self-report their use of MA and 2) women who screened positive for MA use through hair analysis at the Motherisk laboratories. Univariate analysis were used to compare endpoints including the frequency and type of illicit drugs abused by both groups.

**Results:** Poly-drug use was self-reported by 74% for a total of 140 women who called, while 84% (of 142 women) were identified as positive for at least one other illicit drug by hair analysis. The most common co-exposures in both self-reported group and positive hair test group were cannabis (50% and 22%; p<0.001), cocaine (40% and 59%; p=0.002) and opiates (10% and 17%; p=0.158), respectively. Mann-Whitney U analysis revealed
the rate of frequency for using three (p=0.736), four (p=0.862) or five (p=0.246) other drugs concurrently, were similar in both groups.

**Conclusion:** Cocaine, cannabis and opiates appear to be the three most common drugs abused by both groups. Maternal self-reported frequency of using three, four or five other concurrent drugs was corroborated by positive hair test results. Healthcare providers can utilize both methods of screening for effective identification of potential MA users in order to avoid adverse long-term consequences
6.2 INTRODUCTION

The dramatic increase in MA use worldwide has caused great concern and highlights the need for research surrounding its use and its users, particularly in pregnancy, where there is a paucity of data. Several studies have determined prevalence of MA use among pregnant women to range between 1-5% \(^\text{31}\).

Various methods used to identify prenatal MA exposure may include interview, self-administered questionnaire, urine tests, and testing of maternal and infant hair or meconium. Although the simplest to obtain, maternal self-report is often considered unreliable due to inaccuracy of recall or concerns for under-reporting, as a result of societal stigma or legal ramifications of admitting to illicit drug use. Over the past decade, the use of biomarkers as a method of detecting illicit drugs has become increasingly popular \(^{110, 266}\). Hair analysis is presently a validated method used to screen for recreational drug use including amphetamines, opiates, cannabis, cocaine, alcohol and nicotine \(^{110, 267, 268}\). Analyzing a chronic use biological marker such as hair overcomes challenges presented by blood and urine test by providing evidence of chronic exposure to various drugs of abuse, given its significantly wider window of detection (months versus last 24 hours). MA use can be detected in hair, even after a year, if the section of the hair that grew during its use is still accessible \(^{269}\). Hence, use of hair analysis as a marker to enhance/assess reliability of self-reported claims of illicit substance use is inevitably a growing focus in this field of research \(^{270}\).
Studies have compared rates of illicit drug use detected by hair with rates obtained from self-reported data. While some have demonstrated discrepancy between self-report and biochemical test results, others have found good agreement between these two methods. In comparing hair, urine and self-report, Swartz and colleagues found 31% had a positive hair test for illicit drugs, but only 16.3% reported use and 12.4% had a positive urine sample. In contrast, Nayamathi et al. found homeless women’s self-reports of cocaine use to be fairly accurate when compared to data based on a radioimmunoassay of hair. A longitudinal study examining agreement between self reported illicit substance use (including MA) and hair analysis in a community sample found detection rates were not better than self-report in identifying the use of marijuana, opiates and MA. At present there are no data examining the degree of agreement between self-reported account of illicit substance use among pregnant women and exposure rates based on hair analysis. Given that failure to disclose MA use can have serious negative impact on both maternal and fetal health, it is important to explore potential discordance between self-report and objective evidence of MA exposure using a biological marker such as hair analysis.

This section of my thesis investigates the reliability of self-report as a method of data collection in pregnant women who use MA by comparing their account to exposure data obtained from hair analysis. This research is necessary due to the following reasons: 1) high prevalence of MA use in reproductive women 2) concerns of under-reporting inherent in self-reported data 3) previous work that documents hair analysis as a valid method of detecting MA exposures and 4) lack of research examining concordance of self-reported MA use with objective data (from hair analysis) in pregnant women.
6.3 SUBJECTS AND METHODS

A total of 361 exposures to MA were identified from the Motherisk Program databases and included in this comparative study. Of these, 282 women were sub-grouped with the knowledge that these individuals had been co-exposed to at least one other illicit drug of abuse. Our study consisted of two groups of women based on the method of identification used in confirming illicit drug exposure.

6.3.1 Subjects

6.3.1.1 Self-reported MA Group

Pregnant women routinely contact the Motherisk Alcohol and Substance use Helpline for evidence-based information about exposures to recreational drugs such as MA. Concern surrounding under-reporting in this Motherisk cohort is unlikely as study participants make the initial call of their own volition to self-report their exposure details to the service. In the present study, upon providing informed consent, women who contacted the Helpline due to concerns surrounding the use of MA (as their primary drug) at some point during their pregnancy (hereinafter referred to as “self-reported MA group”) were included.

6.3.1.2 MA-Positive Hair Test Group

The Motherisk Laboratory at the Hospital for Sick Children in Toronto, Canada conducts hair analysis for both adults and neonates from samples provided by child protection agencies and physicians upon clinical suspicion of illicit drug use. With the consent of subjects involved, hair samples are sent to the laboratory for hair analysis
using previously described methods. In this study, all subjects who had tested positive for MA in hair were included (hereinafter referred to as “MA hair-positive group”). Use of the clinical data was approved by our Research Ethics Board.

6.3.2 Study variables

Self-reported variables to compare with positive hair screens included the type, frequency, and pattern of illicit substances used in pregnancy. Aside from MA exposures, “club drugs” as defined by the National Institute on Drug Abuse were also of interest. Specifically, these “club drugs” were MA, 3,4-methylenedioxymethamphetamine (MDMA or Ecstasy), LSD (d-lysergic acid diethylamide), PCP (phenyl-cyclo-hexylpiperidine) and ketamine. For the purposes of the present study however, alcohol and nicotine use were not included, as they were not routinely examined in hair during the study period.

6.3.3 Self Report Procedures

At time of initial call, the self-report measures (for comparison with hair test results) were derived from questions on the standardized intake forms regarding maternal age, pregnancy history and exposure details of all recreational drugs used during pregnancy and the month prior. Pregnant women willingly provided the information that was subsequently documented on standardized intake forms collected by trained counselors (Appendix C). Callers were then counseled over the telephone regarding their specific exposures in pregnancy and subsequently referred to appropriate services, if needed. All such Motherisk records between December 2005 and June 2008 were
retrieved and data pertaining to MA and other illicit drugs were extracted. Exclusion criteria included any language barrier that prevented the mother from understanding the study and providing consent.

6.3.4 Hair Testing Procedures

Hair drug testing studies using the gas chromatography-mass spectrometry (GC-MS) technique have proven to be quite effective\textsuperscript{279-281}, particularly when standardized testing procedures are used\textsuperscript{282}. Hair drug testing is especially sensitive to qualitative (i.e., presence or absence) detection of substances; however, quantitative detection of some drugs and their metabolites (e.g., THC) is still considered difficult\textsuperscript{281}.

Analysis of hair samples was done following a standard process for hair drug testing analysis\textsuperscript{266}. To summarize, approximately 5-10 mg of hair was obtained primarily from the crown of the head (vertex posterior), finely cut into 1–2 cm sections (representative of 1-2 months) and incubated overnight at 52°C in 1 ml methanol. At the time of hair collection, information was collected on hair conditions that were known to affect hair testing, including woman’s use of hair treatments (i.e., permanent, dye, bleach), use of head rather than body hair, and length of hair sample. Additional precautions were taken to avoid contamination of hair samples including the interviewer wearing a head cap and using surgical gloves and sterilized scissors. The next day, methanol was pippeted and evaporated at 40°C under a nitrogen stream. The sample was re-suspended in 400 ml phosphate-buffered saline solution (pH 7.0). Individual drugs were analyzed by Enzyme-Linked Immunosorbent Assays (ELISA), and positive results confirmed by gas chromatography/mass spectrometry (GC/MS). For all drugs with the exception of THC, confirmation of drug exposure was coded positive if cut-off value was over 5ng/10
mg hair of drug was detected. While for THC, any positive conformation value was coded positive due to its low sensitivity in detection.

6.3.5 Statistical Analysis

To determine any differences between methods of screening, chi-square and Mann-Whitney tests were used for categorical data and continuous data (non-normal distribution) was analyzed using the two-tailed student unpaired t-test. For example, rates of exposure to concurrent illicit substances (e.g. cocaine, cannabis and opiates) among patients identified by the Motherisk clinical database (self-reported MR data) and Motherisk laboratory database (positive hair test results) was analyzed by chi-square tests. While frequency of illicit substance use (rank order) was conducted using a Mann-Whitney U test. Statistical significance was defined by a p-value of less than or equal to 0.05. Analysis was done using the Statistical software – SPSS (version 12.0).
6.4 RESULTS

6.4.1 Self-reporting MA Group

Over the period of December 2005 and June 2008, a total of 190 women who identified themselves as MA users were retrieved from the Motherisk Helpline database. The mean age for this group was 26.6 years (SD 6.9 yrs) (median 26.0 years). In this cohort, approximately 50 women (23.3%) reported using only MA as their drug of choice, while almost 74% co-used at least one other drug in pregnancy. Therefore, a total of 140 MA-exposed subjects also reported co-exposure to cannabis, cocaine and opiate as other most commonly used illicit substances, apart from MA (Table 21).

Table 21. Choice of concurrent drugs among MA-exposed women

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Cannabis</td>
<td>19</td>
<td>18</td>
<td>11</td>
<td>7</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>CANNABIS</td>
<td>23</td>
<td>25</td>
<td>11</td>
<td>4</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>Opiates</td>
<td>2</td>
<td>1</td>
<td>3</td>
<td>4</td>
<td>3</td>
<td>1</td>
</tr>
</tbody>
</table>

Cannabis was reported to be the most common substance used (50%), followed by cocaine (40%) and opiates (10%). With respect to rating these three substances, both cannabis (23, 25 women) and cocaine (19, 18 women) appeared to be popular first or second choices (respectively) among MA users (Table 21). On the other hand, opiates
tended to rate more as a 3rd, 4th or 5th drug of choice (3,4,3 women respectively) with only 14 reports of co-exposure.

Among the sub-group of women exposed to both opiates and MA, all 14 women reported use of multiple drugs consisting of at least three or more drugs. Of these, cannabis use was reported by all MA users who typically co-used opiates, while cocaine was the next common substance in this MA-positive opiate subgroup.

In this self-reported cohort, the most commonly observed drug combinations among women consuming MA were: MA + cannabis (50%), MA + cocaine (40%), MA + cannabis + cocaine (15%) and MA + cannabis + opiate (10%).

6.4.2 MA Positive Hair Test Group

Out of 171 MA hair positive subjects whose hair was also tested for other illicit drugs (including cocaine, cannabis and opiates), approximately 142 (83.5%) were identified to be positive for at least one other drug of abuse. This suggests that in only 19 individuals (16.5%), other drugs of interest were not detected. However, the number of women in this cohort exposed only to MA was not statistically different from women who self-reported their use (p=0.063).

The distribution of age for this cohort (n=171) was bimodal, ranging from 17.4 yrs to 46.7 yrs with a mean and median age of 29.3 years (SD = 8.7 yrs). Hence, women calling the helpline to report their use were significantly younger than this lab-identified group (p=0.041).

Cannabis, cocaine and opiates were also observed to be the most common co-exposures among women who tested positive for MA in hair. However, cocaine (58.8%) was found to be the most popular concurrent drug of choice among MA-exposed women,
while use of cannabis (22.5%) and opiates (16.6%) followed thereafter (Table 22). The most commonly observed poly-drug combinations in the MA lab positive were cocaine-MA (20%), cocaine-MA-cannabis (9.5%) and cocaine-MA-Opiate (7.6%).

6.4.3 Comparison of type and frequencies of co-exposures to other drugs

A summary of co-exposure to cocaine, cannabis and opiates by MA using patients identified either by self-reporting method (N= 140) or positive hair analysis (N=142) is provided in Table 22. Use of cannabis was more than double among women who self-reported their use (50%) in comparison to women identified by their positive hair test (22.2%, p <0.001).

Table 22. Common illicit substances in MA-exposed women

<table>
<thead>
<tr>
<th>Types of Concurrent drugs</th>
<th>Self – report N=140 (%)</th>
<th>Hair Test N=142 (%)</th>
<th>P-value</th>
<th>DF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cocaine</td>
<td>56</td>
<td>83</td>
<td>0.002</td>
<td>1</td>
</tr>
<tr>
<td>Cannabis</td>
<td>70</td>
<td>32</td>
<td>&lt;0.001</td>
<td>1</td>
</tr>
<tr>
<td>Opiates</td>
<td>14</td>
<td>23</td>
<td>0.158</td>
<td>1</td>
</tr>
</tbody>
</table>

Although cocaine was the most common co-exposure to MA-positive women (58.8%) identified from the lab database, this was not reflected by the responses of women who self reported use of MA and other concurrent drugs. With the latter group, cocaine was the second most popular drug of the three with 56 women (40%) disclosing their use. However, there was no significant difference between the two methods of identification when it came to their co-use to opiates (p=0.16). Both groups had a low
rate of co-exposure (10% and 17%) to this drug and found to be most prevalent in women who typically use at least three or more drugs.

In addition to the most common type of illicit drugs, we also wished to compare the number of concurrent drugs used between women who self reported versus those identified by positive hair test for MA. Table 23 outlines co-exposure frequencies of other drugs in both study groups, ranging from at least one other drug use to six or more drugs used by each individual.

Table 23. Frequency of illicit drugs use by MA-exposed women

<table>
<thead>
<tr>
<th># of Concurrent Drugs in MA Users</th>
<th>Self Report N=140 %</th>
<th>Pos. Hair test N=142 %</th>
<th>P-value (df=1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>47 33.6</td>
<td>14 10.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>2</td>
<td>38 27.4</td>
<td>50 35.1</td>
<td>0.009</td>
</tr>
<tr>
<td>3</td>
<td>43 30.7</td>
<td>46 32.7</td>
<td>0.136</td>
</tr>
<tr>
<td>4</td>
<td>18 12.9</td>
<td>17 11.7</td>
<td>0.862</td>
</tr>
<tr>
<td>5</td>
<td>7 5.0</td>
<td>11 7.6</td>
<td>0.246</td>
</tr>
<tr>
<td>6 or more drugs</td>
<td>12 8.7</td>
<td>3 2.3</td>
<td>0.042</td>
</tr>
</tbody>
</table>

The two study groups differ with respect to their co-exposure to one (p <0.001), two (p=0.009) and six or more drugs (p=0.042). Women who self-reported their MA use (33.6%) were three times more likely to report only one other drug compared to those identified by a positive test (10.5%). In contrast, upon examining co-exposure to two drugs, there was a 3.5-fold increase in the number of women identified by hair tests (35.1 vs. 10.5%), while fewer women self-reported using two other drugs compared to one
(24.4% vs. 33.6%). Finally, the use of 6 or more drugs was four times more common among women who reported use (8.7%) versus those identified by positive drug tests (2.3%) (p=0.042).
6.5 DISCUSSION

MA has become the stimulant of choice worldwide with its use being especially prevalent in an age group that encompasses women in their childbearing years. Because of its serious implications to maternal and child health, screening and identification of MA use in women is critical. Use of biological markers such as hair to identify MA exposure has become increasingly popular, especially in the context of pregnancy, where prolonged exposures are important to capture. Moreover, this is an objective, quantifiable, reproducible and validated.

An important consideration in research is the context in which the drug use occurs. Wu and colleagues demonstrated that among those using club drugs, 82% had used three or more types of drugs. Our findings reflect this tendency of poly drug use in both groups. It further confirms suggestions that MA is most frequently used in combination with other stimulants (e.g. cocaine) and/or depressants (e.g. alcohol) in order to aid with sleep, during the withdrawal process. Marijuana, often used to customize the amphetamine experience, may also be used during this time. Among women who self-reported their MA exposure, use of “speedballs” (amphetamines and cocaine or heroin) was a very common trademark. A possible explanation for this may be to offset some of the agitation inherent in using amphetamines alone.

Much of the research done on concurrent drug use in pregnant MA abusers has focused on alcohol, tobacco and THC use, but excludes use of other illicit substances. In this study, the focus was placed specifically on the latter due to the paucity of data in this understudied area of research. This adds to the originality of our research as the first to examine both pattern and frequency of concurrent illicit substances used by
pregnant MA users. Knowledge that cocaine, cannabis and opiates were most common to both study groups should prompt providers caring for a patient with a history of MA use to make further inquiries regarding other substances. Moreover, in the context of pregnancy, providers need to be aware of the prevalent culture of combination drug use in order to educate women about the fetal implications of multiple drug-using behaviors.

In comparing the frequency of co-exposures between the self-reporting and laboratory-confirmed cases, it is apparent that women who self-reported tended to mostly report only one other drug use, with fewer reports of using two concurrent drugs. One explanation can be under-reporting; however, this concern can be discounted given that there was no difference between the two groups when examining use of three, four, or five other drugs. In fact, four-fold more women who self-reported their use admitted to using six or more drugs in addition to MA. This was significantly higher than women who had been identified via a positive hair test result.

These differences can be looked upon as a limitation as they may reflect inherent differences in the nature of the two studied groups. The self-referred, self-reported women were younger, and were motivated to seek information on the reproductive effects of their drug abuse on the unborn fetus. In contrast, hair tested group was mostly tested at the demand of Children’s Aid, as a condition for child custody. While also being a high risk group, it can be expected that these women had different patterns of using drugs. Moreover, such a difference could also explain THC as the primary drug of choice among self-reporting women, and cocaine as the favorite choice in more high-risk group. Alternatively, the differences in the drug of choice between the two MA-exposed groups could simply be a function of the limitations inherent to each method. For
example, given the poor detection sensitivity of THC in hair analysis, the lower rate of THC exposure among women identified by a positive hair test result could simply be a function of equipment insensitivity, or inadequate hair sample.

In summary, limited research exists on effective strategies to screen and identify potential MA abusers. Consequently, practitioners are often unable to effectively care for patients who may be at risk without understanding the many variables affecting MA users. Our results on the self-reporting group of identification can definitely be valid, and further confirmed with hair test analysis, when possible. This is, of course, based on maternal motivation, and cannot be extrapolated to reports by women who are asked for their drug use in the context of general practice.
6.6 CONCLUSION

Our findings suggest that self-report can be considered a reliable method when used in a population that is motivated to seek prenatal care. Routine and subsequently reduce the frequency and adverse consequences among women of childbearing age. With high suspicion index, biomarker can be used to confirm suspect exposure. Providers need to be knowledgeable about the prevalent culture of combination drug use in order to educate women under their care about the potential reproductive risks.
CHAPTER 7

DISCUSSION, FUTURE DIRECTIONS AND CONCLUSIONS
7. DISCUSSION

Alcohol and substance use in pregnancy is a serious public health concern. In the absence of available screening guidelines, the decision on which method to use, especially in pregnancy is extremely challenging. To overcome this gap, this dissertation examined various methodological approaches to screening that are currently available to help providers in their task of identifying women at risk for using alcohol and illicit substance during pregnancy. These include instruments that screen for the presence of alcohol and substance misuse, those that obtain a descriptive account of frequency and quantity of use, and biological measures.

The decision-making process on the most effective choice of approach is largely dependent on a number of considerations. These include the nature of the population it is screening, the type and pattern of recreational drug use, and finally the context in which screening occurs (purpose, setting, techniques etc.) The five studies presented in this dissertation provide new insight regarding the performance of each screening method in identifying prenatal alcohol and illicit drug use, while taking the above factors into consideration.

In the first study, a systematic review revealed a range of available screening methods from basic practice based screening (comprising of single question) to more indirect approaches (structured questionnaires) and finally, objective methods utilizing biological markers. Of these, the most commonly practiced method in identifying prenatal alcohol and substance use relies heavily on maternal self-report account. Unfortunately, exposure accounts provided by mom herself is usually not considered the gold standard as its validity is limited by under-reporting concerns\textsuperscript{183}. However, Sobell
and colleagues demonstrated that in environments where pregnant women are self-motivated in seeking medical care and information, they are less likely to underreport their alcohol or drug use and be open to intervention\textsuperscript{151, 283}. This is representative of the Motherisk cohort, making it an optimal context in which performance of screening questionnaires can be assessed. One hypothesis of the second study examining the performance of TWEAK and T-ACE tools was that both questionnaires may be less effective at predicting problem drinking using recommended CP. Our results confirmed this hypothesis as both tests were highly sensitive, but also included a high rate of false positives. A probable explanation may be related to the prevalence of the condition (i.e. problem drinking). In general, when prevalence increases, so does the PPV\textsuperscript{167}. Since both TWEAK and T-ACE were developed in obstetric populations recruited from addiction services, it is conceivable that prevalence of alcohol misuse was much higher compared to the present cohort. This in turn would explain the low rates for PPV in a group with likely lower prevalence given that women are predominantly referred by their general practitioners and public health units. To our knowledge, this is the first study to demonstrate that a higher cut-off threshold is necessary to improve performance in women representative of problem drinkers. This, combined with decreased performance at recommended threshold highlights the need to limit use of these questionnaires only to populations it has been validated in.

The low specificity rates of our results also suggest that neither TWEAK nor T-ACE (at recommended cut points of 2 or 3, respectively) would be effective at predicting problem drinking on its own. For strictly screening purposes, sensitivity is usually given priority, while the less-than-ideal specificity (identifying the right ones) can be ruled out
with further questioning. From that perspective, a case can be made for using both questionnaires in situations where providers are uncomfortable initiating the alcohol topic with direct questions. However, subsequent follow-up would be essential with a positive screen, despite how time consuming it may be. For example, Sobell’s group demonstrated that time was a major limitation for a screening method such as TLFB in being implemented routinely.\textsuperscript{209, 283} But its ability to capture a detailed picture of a women’s alcohol history can be crucial in subsequent intervention and treatment process. Hence, this TLFB technique can be useful as a second step to screening upon a positive screen of TWEAK or T-ACE. However, in the interest of time and resources, combined with the knowledge that when prevalence of a condition is not high (as the case of problem drinking), a small decrease in specificity can greatly increase the FPR, screening test with both high sensitivity and specificity is desired. Situations where specificity is as important to achieve would be environments where a) funding is limited or b) opportunity for follow-up visit does not exist.

Effectiveness and accuracy associated with how well an approach works depends primarily on the population being screened, hence, knowledge of patient demographics and risk factors are also important for clinicians, especially when utilizing a practice-based approach. These demographics include ethnicity, socioeconomic status (SES), maternal age and age at first drink. With alcohol, a vast amount of work has been done in defining demographics of the group most likely to continue drinking prenatally. For example, CDC’s National Center for Health Statistics found that 25.4% of White, non-Hispanic women reported drinking during pregnancy compared with 12.2% of Black, non-Hispanic women and 10.6% of Hispanic women.\textsuperscript{284} This dispels the common belief
that prenatal alcohol use is predominantly a problem among aboriginals or other minority groups. Highest rates of drinking during pregnancy were found among those who were younger, more educated, employed, and unmarried. These characteristics inherent in problem drinkers were also common to women included in the present study. The lack of statistical differences between problem and non-problem drinkers not only highlights the need to screen all women of childbearing age, but also strengthens the validity of our results.

In contrast to the wealth of evidence pertaining to alcohol, the knowledge gap associated with the pregnant demographic at risk of illicit drugs use. The knowledge gap that currently exists pertaining to use of MA is concerning as prevalence of use is highest in reproductive women. Hence, the third study characterized pregnant MA users in an effort to gain knowledge of inherent reproductive risk predictors so that identification can be improved.

Our first hypothesis was confirmed by the fact that almost all risk factors common to severely addicted women were also characteristic of casual or low intensity users. A prime example of this is the multiple drug-using culture among pregnant MA users. Wu et al found 96% of women who use MA also engaged in poly-drug using behaviour of at least three or more drugs. This was reflected in our results, indicating that provider’s knowledge about a patient’s history of experimenting with illicit drug such as MA should prompt him/her to inquire about other drugs use as well. New insight into alcohol use among MA users was obtained from our findings and did not confirm our initial hypothesis that alcohol-using behaviour will not likely be problematic in a less risky group of MA users. To our knowledge, this is the first study to demonstrate that contrary
to previous beliefs, harmful use of alcohol is not limited to just MA-addicted women, but also a very common practice among casual or low intensity users. Binge drinking and heavy episodic drinking were reported by a significantly greater number of women who used MA than those who did not, regardless of their frequency of MA use. As shown in our study, co-use of MA and alcohol in pregnancy is a common phenomenon, making it difficult to separate effects of one drug from another. Moreover, combining drugs that individually have complex effects on mood, judgment and inhibition inevitably complicates things further, making these executive actions even less predictable and more subject to errors. Binge drinking is an important risk predictor of MA use in women because of its demonstrated association with not only unintended pregnancy but also higher peak blood alcohol levels that can result in increased risk for teratogenic effects for the fetus. One study reported that frequent binge drinkers were 7 to 20 times more likely to have unplanned and unprotected sexual activity \(^{285}\). Furthermore, combination of alcohol and MA use has also been associated with decreased contraceptive use among youth, putting a significant number of women at risk for unintended pregnancies \(^{196, 250, 286}\).

MA use has also been reported to enhance sexual pleasure in heterosexual women engaged in high-risk sexual behaviours such as unprotected and anonymous sex \(^{102, 287}\). This link is probably due to the fact that MA, like other psychomotor stimulants increases libido, alters judgment and decreases inhibition \(^{107}\). Though it can be argued that Motherisk cohort is more representative of intermittent and casual misusers, a number of studies have suggested that even intermittent use of recreational drugs can lead to risky sexual behaviours in young adults \(^{288}\). This is evident in the fact that most MA users in
our study had unplanned pregnancies and continued to drink and use illicit substances well into the first trimester prior to knowledge of their pregnancy. This has serious implications for pregnancy outcome as this is a particularly vulnerable time for the developing organ systems of the fetus. Hence, the fact that this group of women would be categorized as low-intensity or casual users makes it no less dire for providers to routinely ask about any use prior to knowledge of pregnancy, especially since patient may not be aware of the potential adverse implications of MA exposure during organogenesis. Maternal age is an important risk predictor of potential adverse fetal outcomes in MA users. Epidemiological studies found younger women are more likely to engage in binge drinking than are their older counterparts, which places them at risk for a host of negative consequences. Moreover, women ages 21 to 30 have the highest rates of intoxication, problem drinking and heavy episodic drinking. This age group made up 93% of the women classified as problem drinkers in our results. These reproductive risk factors emphasize the need to develop effective prevention strategies and address the diverse needs of all women of childbearing age, including those who are pregnant or trying to become pregnant. As a result, health professionals should be skilled in screening for illicit substance use with different SES backgrounds both during pregnancy and prior to conception.

Accuracy of self-report has been shown to decrease as a function of recent use, concurrent psychiatric problems and poor relationship with provider. Patients not assured of confidentiality or facing negative consequences can also affect self-report. However, in the absence of these factors, self-report can be considered reliable. Validation of biological markers to detect alcohol and illicit substances such as MA
is of great interest in pregnancy due to its ability to capture prolonged exposures in both mother and her neonate. In a study by Ling et al, pregnant women’s self-reports of their substance use were quite accurate when they were approached in a non-judgmental way and were provided useful information. In our fourth study examining the accuracy of self-reported MA use compared with positive hair test results, it was hypothesized that there would be agreement between the two approaches of identifying prenatal exposure. Our results confirmed this hypothesis as there were no statistical differences between the two screening methodologies. This suggests that maternal self-report can be considered a reliable method of screening as part of a practice-based approach, especially when provider engages the patient by incorporating motivational interviewing techniques, being supportive and assuring the patient of confidentiality.

Health care related to alcohol and substance use faces ethical issues such as weighing the rights of a pregnant woman and protecting the health of the fetus. Health practitioners are key players in advocating and delivering the best care to meet these needs. Several survey findings suggest pregnant women describe their health care providers as the best source of information and are willing to discuss issues of alcohol and drug use with their primary care providers when asked. A study involving high-risk, white, middle-class pregnant women in physicians’ offices found that assessment of alcohol consumption and simple advice to stop or cut down on drinking were effective in helping women reduce their drinking levels. This places providers in the unique position of influencing the health behaviors of pregnant women in their care.
Although evidence indicates need for all women of childbearing age to be screened for alcohol disorders, several barriers prevent implementation of routine screening. Many physicians are reluctant to take on a new responsibility in the context of time constraints and their discomfort in approaching the topic. Discomfort regarding the topic of alcohol or illicit drugs is best addressed by creating a non-judgmental, respectful environment in which alcohol screening questions are asked within a general health inquiry and by providing physicians with more information on available pregnancy outreach and treatment programs. Training has also been shown to increase clinician confidence and self-efficacy. Given the high prevalence of women of childbearing age encountered in virtually any medical practice, health care provider should receive specific training to increase their comfort, confidence, and competence. Joint training of professionals would allow for a broader perspective and lead to critically important collaboration between services. An example of a joint training approach is a program funded by Health Canada and piloted by Breaking the Cycle and the Canadian Centre on Substance Abuse, which trains prenatal and child services practitioners together, using a motivational, stages of change model for working with both pregnant women and affected children and families. Increasing access to confidential care, such as specialized over the phone information services (e.g. Motherisk Alcohol and Substance use Helpline) where women are not required to face anyone in person, may increase their willingness to disclose their substance use and get help.

Since all women have the potential of drinking some alcohol, health care providers are advised to routinely screen reproductive women for alcohol use in pregnancy. Many women with risky drinking habits who are seen by primary care
physicians often remain unrecognized and untreated, failing to present with the same stereotypical symptoms seen in alcoholic patients. Addiction experts estimate up to 90% of people who abuse drugs or alcohol are able to maintain their normal lifestyle\textsuperscript{301}. This is further complicated by the fact that casual users of club drugs such as MA often have the perception that intermittent use is safe\textsuperscript{287}. However, this idea is seriously misleading, as most of these compounds have the potential of causing adverse health consequences, especially if administered at high toxic doses and/or at the levels that cause drug overdoses. Denial is also characteristic of this population, as many users of these drugs believe that they are not dependent or addicted users\textsuperscript{302}. When they eventually realize that their level of drug use is inappropriate, it is too late to reverse the consequences.

Studies have linked substance use with alcohol drinking and tobacco use\textsuperscript{286}. One study of 226 pregnant women found that compared to addicts of other substances, MA users were much more uncertain about the effects of the drug on their fetus\textsuperscript{303}. While screening for alcohol use, providers should also ask about the types of alcoholic beverages most often consumed in addition to QF assessment as many women have misperceptions about the degree of risk associated with certain drinks. For example, many in our research considered wine to be safer than hard liquor. Hence, educating women on what constitutes a typical drink is an important step in the screening process.

The major strength of our research lies in the nature of our study cohort. Women not only initiate contact but also report all exposures willingly, leaving little to no room for under-reporting concerns. This is an optimal setting in which performance of a screening questionnaire can be examined. Further strengthening the clinical significance of our findings is that Motherisk cohort being a racially diverse, educated and largely
employed group of women who sought prenatal care, shares many characteristics with problem drinkers, the most prevalent group at risk of continuing their alcohol consumption at some level in pregnancy.

Unfortunately, the self-motivated and resourceful nature of these women can also serve as a limitation in generalizing the results related to the characteristics of women who use MA. But it is important to recognize that approximately 70% of these women were referred by their public health units, midwives and family doctors, as most women in the general population does upon recognizing their pregnancy. Furthermore, given that most previous studies defining risk factors associated with MA use involved severely dependent women, our data provided new insight into the lifestyle of a less risky population. A second limitation of the study was the use of two separate cohorts in comparing self-report account with positive hair test results. Although, both groups of women were part of the Motherisk cohort, variability in demographics between the two groups may have confounded the results. This is probably not likely because the likelihood of a less risky group to underreport illicit drug use would have resulted in decreased number of drugs used. Instead, twice the number of women reported using six or more drugs, than was tested positive through hair analysis.

Prevention should begin prior to pregnancy and continue till the post partum period. By incorporating one or more screening approach into clinical practice routinely, addressing alcohol and illicit drug use in pregnancy can be made easier. The significance of screening and its implications to society should be highlighted. By routinely screening all women, young women of childbearing age will expect to be asked about their recreational drug use, as they would any other lifestyle questions as part of their annual
check-up. When this is done prior to pregnancy, women are likely to report accurate levels of alcohol use, without the stigma of pregnancy attached. Since alcohol and illicit drug use prior to pregnancy is predictive of prenatal use, having a record of prior exposure will make it easier for physicians to choose the most appropriate method of screening those at risk of continuing their use during pregnancy. Finally, by ensuring that alcohol use is discussed as part of a practice based approach of screening, providers can have a significant impact on reducing the number of alcohol-exposed pregnancies.
7.1 FUTURE DIRECTIONS

The data derived from this dissertation will assist in directing the next wave of research. Identifying validated screening methods and examining their performance in a problem drinking population (who are less dependent, risky group) is only the first step. Future studies can focus exclusively on each of these approaches to better understand as well as improve on how well they are able to identify those women at risk. Given the significant gaps in knowledge surrounding this group of high-functioning risky drinkers, different types of research can follow from the knowledge gained from the present research. To start, given the lack of effectiveness of the only two tools (TWEAK and T-ACE) validated for use in pregnancy to identifying problem drinking, the need to develop a new tool in a population representative of problem drinkers is great. Most sensitive questions common to both tools should be isolated and combined with more appropriate questions specific to this cohort. Upon developing the tool, validation research based out of general practitioners’ offices should be carried out to determine both feasibility and effectiveness of the tool.

Secondly, frontline healthcare providers are in a key position to help with screening and getting an alcohol and substance use history. Since alcohol and MA use are both very widespread, it is important for all providers to be knowledgeable about drugs and their effects and be comfortable completing substance use histories in a non-judgmental approach. In order to identify the gaps in knowledge among healthcare providers, a survey study assessing both knowledge and risk perception in the field of alcohol and substance use in pregnancy should be done. The same questionnaire can be
administered on pregnant women themselves to determine differences in the knowledge gap between patients and practitioners.

Thirdly, evaluative research in training and professional development should be a priority: a) conduct research on the extent to which disseminating practice guidelines to health care providers and social workers will actually increase its routine implementation into the practice. B) conduct research on how well training provided to healthcare providers helps increase their comfort, confidence ultimately resulting in the adoption of those skills/tools. C) identify barriers in screening this specific group of high functioning women so they can be addressed.

Fourth, since the degree of under-reporting differs with the population studied, there is a need for further research into the ways in which differences in population characteristics (demographics, use patterns etc) contribute to under-reporting. Women are more likely to say they would lower their alcohol use during their pregnancy if encouraged by their spouse to do so. Hence, a study looking at partner’s influence on maternal alcohol and illicit drug use in pregnancy would be interesting to do.

Fifth, one of the main limitations in assessing the reliability of self-report in the last study of this dissertation can be attributed to the fact two different cohorts were used. To overcome this limitation, a future study should be done where both methods are employed on the same cohort to eliminate variability between groups.

Last but not least, given the immense popularity of MA among pregnant and reproductive women, combined with the 100% rate of unplanned pregnancies, fetal exposure to MA is inevitable. Pregnancy outcome study in a cohort such as Motherisk, where women report accurate levels of substance use is ideal to determine the potential
risks associated with this drug. Much of the data previous done were based on retrospective data, from a third party. This helpline provides the opportunity to conduct a prospective, comparative cohort study on pregnancy outcome as well as long term neurobehavioral and cognitive effects.
7.3 CONCLUSION

Alcohol use in pregnancy is known to cause FASD. This dissertation has demonstrated that no single effective approach exists to identify women at risk for alcohol and illicit substance use in pregnancy. Upon identifying three main approaches to screening, it then examined how each would perform in the problem drinking population. Results reveal that TWEAK and T-ACE tools, currently considered the most effective method of identifying alcohol use, were not effective in screening women who are representative of the problem drinking population. Moreover, they perform better using higher CP thresholds than traditionally recommended. As choice of instrument is normally based on target patient group, this dissertation highlighted the need to develop new tools validated in women who are problem drinkers. New insights were also gained into screening for drugs of abuse in pregnant and expectant women. Identifying risk predictors inherent in this population to improve provider’s ability to screen was also examined. Moreover, maternal self-report should not be discounted based on assumptions of under-reporting. All patients should be asked about their alcohol and illicit drugs use at minimum.

Recognizing that one size does not fit all, this dissertation demonstrated the need to use more than one screening method in order to optimize screening during pregnancy. Finally, use of these screening tools and motivational interviewing techniques in identifying women at risk for alcohol and substance use should not be viewed as sufficient in itself. Rather, they should serve as an indication for further follow-up and possible intervention, when needed.
CHAPTER EIGHT

REFERENCES


72. Prescribing information: Dexedrine. [Homepage on the Internet]. Mississauga, ON: GlaxoSmithKline. 2007 September 24 [cited June 29].

73. Adderall XR capsules [homepage on the Internet]. The US Food and Drug Administration.


95. Inoue. Methamphetamine-related sudden death with a concentration, which was of a 'toxic level'. Leg Med. 2006;8(3): 150.


131. Lester BM. Prenatal methamphetamine exposure and child development. National Institute on Drug Abuse, grant number 1-R01-DA14948-01.


168. Musshoff F and Madea BA. Analytical pitfalls in hair testing Anal Bioanal Chem. 2007; 388(7): 1475-94.


192. Introduction to FASD overview. [Homepage on the Internet]. Canadian Center on Substance Abuse (CCSA). 2009 [cited July 29, 2009].


237. Pragst F, Auwaerter V, Sporkert F, Spiegel K. Analysis of fatty acid ethyl esters in hair as possible markers of chronically elevated alcohol consumption by headspace solid-
phase microextraction (HS-SPME) and gas chromatography-mass spectrometry (GC-MS).

238. Rice JP. Statistical issues in the interpretation of tests. 1987:3-5.


CHAPTER NINE

APPENDICES
Appendix A: MOTHERISK: Alcohol Intake Form

Reason for call: __________________________ Date: ________________________
Have you called before?  No ○ Yes ○
Time started: ____________________________
Time finished: __________________________
Counsellor: ____________________________

1. PREGNANCY

Not pregnant: general info ○ planning ○ retrospective ○ breastfeeding ○
G_____ P_____ SA_____ TA_____ 

Current pregnancy was: Planned ○ Unplanned ○ Fertility Clinic ○

LMP (d/m/y) _____________ every ______ days  Certain? No ○ Yes ○
Gestation __________ wks mos  Weight________ lbs kg
EDC (d/m/y) _____________ by date ○ by ultrasound ○

Most recent ultrasound in current pregnancy: Not yet ○
At _______ weeks  Reason: __________________________ Results: __________________________

Maternal Serum Screening?  No ○ Yes ○ Amnio?  No ○ Yes ○ Advised ○

2. MEDICAL HISTORY

(a) Medical/Disease Complications

Heart?  No ○ Yes ○
Respiratory?  No ○ Yes ○
Diabetes?  No ○ Yes ○
Thyroid?  No ○ Yes ○
Allergies?  No ○ Yes ○
Other?  No ○ Yes ○

(b) Psychiatric

Anxiety?  No ○ Yes ○
Depression?  No ○ Yes ○
Social Phobia?  No ○ Yes ○
Mood Changes  No ○ Yes ○
Personality Changes?  No ○ Yes ○
Other(e.g. bipolar, OCD)  No ○ Yes ○

(c) Infectious Diseases

Chlamydia  No ○ Yes  Date of dx:
Gonorhea   No ○ Yes  Date of dx:
Genital Herpes  No ○ Yes  Date of dx:
Group B Strep  No ○ Yes  Date of dx:
Syphilis  No ○ Yes  Date of dx:
Other _________  No ○ Yes  Date of dx:

3. TREATMENT

☆ Have you ever received any treatment for alcohol or drug use?

No ○ Yes (where?) __________________________ Date: __________________________

☆ Are you currently receiving any type of treatment for alcohol or drug use?

No ○ Yes (where?) __________________________ Date: __________________________
Have you ever received any treatment for psychological or emotional problems?

No ☐  Yes ☐ (where?) __________________________ Date: __________________________

Are you currently receiving any type of treatment for psychological or emotional problems?

No ☐  Yes ☐ (where?) __________________________ Date: __________________________

4. ALCOHOL AND NICOTINE HISTORY:

(a) Tobacco/Nicotine  None ☐  Cigarettes ☐  Cigar ☐  Pipe ☐

Age of onset? __________________________  Quit/Cut Down?  No ☐  Yes ☐ (when) __________________________

How many? __________________________  Success?  No ☐  Yes ☐ (how long) __________________________

(b) Alcohol  None ☐  Date of Last Use: __________________________  Amount: __________________________

<table>
<thead>
<tr>
<th>T-ACE</th>
<th>Question</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tolerance</td>
<td>How many drinks does it take to make you feel the first effect?</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(3 or more = 2 points)</td>
<td></td>
</tr>
<tr>
<td>Annoyed</td>
<td>Have people ever annoyed you by criticizing you about your drinking?</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(yes = 1 point)</td>
<td></td>
</tr>
<tr>
<td>Cut Down</td>
<td>Do you sometimes feel the need to cut down on your drinking?</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(yes = 1 point)</td>
<td></td>
</tr>
<tr>
<td>Eye-Opener</td>
<td>Do you sometimes take a drink in the morning when you first get up?</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(yes = 1 point)</td>
<td></td>
</tr>
</tbody>
</table>

What is your typical pattern of drinking? __________________________________________

How many drinks have you had in the last seven days?

<table>
<thead>
<tr>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
<th>Day 4</th>
<th>Day 5</th>
<th>Day 6</th>
<th>Day 7</th>
<th>total/wk</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Comments: ______________________________________________________________________

Do you ever experience any of the following:

Blackouts?  No ☐  Yes __________________________  Falls/injuries?  No ☐  Yes __________________________

Insomnia?  No ☐  Yes __________________________  Diarrhea?  No ☐  Yes __________________________

Increased BP?  No ☐  Yes __________________________  Gastritis?  No ☐  Yes __________________________

<table>
<thead>
<tr>
<th>TWEAK</th>
<th>Question</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tolerance</td>
<td>How many drinks does it take to make you feel the first effect?</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(3 or more = 2 points)</td>
<td></td>
</tr>
<tr>
<td>Worry</td>
<td>Have close friends worried or complained about your drinking in the past year? (yes = 2 points)</td>
<td></td>
</tr>
<tr>
<td>Eye-Opener</td>
<td>Do you sometimes take a drink in the morning when you first get up?</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(yes = 1 point)</td>
<td></td>
</tr>
<tr>
<td>Amnesia</td>
<td>Has a friend or family member ever told you about things you said or did while you were drinking that you could not remember? (yes = 1 point)</td>
<td></td>
</tr>
<tr>
<td>Cut Down</td>
<td>Do you sometimes feel the need to cut down on your drinking?</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(yes = 1 point)</td>
<td></td>
</tr>
</tbody>
</table>

Total Score _____ Heavy /Problem Drinker (3 or more points)  No ☐  Yes ☐

Do you think you have a problem with alcohol?  No ☐  Yes ☐

Would you be able to stop drinking?  No ☐  Yes ☐
### 5. PSYCHOACTIVE DRUG HISTORY

(i) Drug: _______________ Date of Last Use: _______________ Amount?: _______________

Route: oral ○ nasal ○ iv ○ other: _______________  Typical Pattern of Use: _______________

▶ use on weekdays (i.e. Mon-Thurs)?

Adverse Effects? _______________  ▶ use on weekends (i.e. Fri-Sun)? _______________

Concurrent Drug Use? _______________  How long have you used this drug? _______________

Use in the last 7 days:

<table>
<thead>
<tr>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
<th>Day 4</th>
<th>Day 5</th>
<th>Day 6</th>
<th>Day 7</th>
<th>total/wk</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(ii) Drug: _______________ Date of Last Use: _______________ Amount?: _______________

Route: oral ○ nasal ○ iv ○ other: _______________  Typical Pattern of Use: _______________

▶ use on weekdays (i.e. Mon-Thurs)?

Adverse Effects? _______________  ▶ use on weekends (i.e. Fri-Sun)? _______________

Concurrent Drug Use? _______________  How long have you used this drug? _______________

Use in the last 7 days:

<table>
<thead>
<tr>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
<th>Day 4</th>
<th>Day 5</th>
<th>Day 6</th>
<th>Day 7</th>
<th>total/wk</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(iii) Drug: _______________ Date of Last Use: _______________ Amount?: _______________

Route: oral ○ nasal ○ iv ○ other: _______________  Typical Pattern of Use: _______________

▶ use on weekdays (i.e. Mon-Thurs)?

Adverse Effects? _______________  ▶ use on weekends (i.e. Fri-Sun)? _______________

Concurrent Drug Use? _______________  How long have you used this drug? _______________

Use in the last 7 days:

<table>
<thead>
<tr>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
<th>Day 4</th>
<th>Day 5</th>
<th>Day 6</th>
<th>Day 7</th>
<th>total/wk</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### 7. ACTION TAKEN

Baseline Risk explained ○ Risk no >1-3% ○ Level II U/S ○ Referral if required ○ Other: _______________________(CAMH, St. Joe’s)
APPENDIX B: Script for Verbal Consent

Like you, many young women who have been exposed to alcohol call our service for information and counseling. Unfortunately, many of them are at potential risk of continuing their use throughout pregnancy, despite their very honest intention not to. In order to effectively identify these women so that we can help them discontinue their use, we are currently conducting a study to determine which screening tool is most accurate and sensitive to screen for future alcohol use. In this study, some of your responses and scores pertaining to your alcohol consumption will be used to determine which tool is best. And just to be clear, your personal information will be kept completely CONFIDENTIAL. In our research studies, you will only be identified as a case number. Any identifiers e.g. your name, your phone number, etc. will NOT be used.

Are you comfortable providing verbal consent to participate in this study? Only if you give us permission, will we include your data in the study. By asking you some questions regarding your pregnancy, we will be able to assist them when they call us. The more knowledge we have the better.

If at any point you do not feel comfortable in answering a question, just let me know.
APPENDIX C: MOTHERISK Substance Use Questionnaire

Reason for call __________________________
Have you called before?  No ☐  Yes ☐

Date: __________________________
Time started: __________________________
Time finished: __________________________
Counsellor: __________________________

1. DEMOGRAPHICS

Province_______________________________
Date of Birth____________________________

Ethnic: White ☐  Black ☐  Asn ☐  Hisp ☐  Abrg ☐  E.ldn ☐  Othr ☐

Marital Status:married ☐  single ☐  common-law ☐  divorced ☐

Highest Education:
<high school ☒  gr:_____  high school ☐

college/university ☐  professional degree ☐

Current Employment:
employed ☐  Occupation: ________________________________

unemployed ☐  self-employed ☐  social assistance ☐  disability ☐

2. PREGNANCY

general info ☐  planning ☐  retrospective ☐  breastfeeding ☐

G_____P_____SA_____TA_____ SB _____  Ectopic _____  Molar _____

Defects in previous pregnancies?  No ☐  Yes __________________________

Current pregnancy was:  Planned ☐  Unplanned ☐  Untimely ☐  Fertility Clinic ☐

LMP (d/m/y)______________  every_____days Certain?  No ☐  Yes ☐  Weight ______ lbs  kg

EDC (d/m/y)______________  by date ☐  by ultrasound ☐  Gestation _________wks  mos

Conception (d/m/y) ______________ possible ☐  Pregnancy Recognition__________ date  wks

Most recent ultrasound in current pregnancy: Not yet ☐

At_______wks  Reason:___________  Results:_________

Vitamin Supplements?  No ☐  Yes ☐

At Maternal Serum Screening No ☐  Yes ☐

Amnio  N ☐  Y ☐  Advised ☐

When did you start? ________________  Ongoing ☐

Vitamin A:  amt advised __________________

3. Biological Father Exposure

Has he ever used needles?  Never ☐  Yes ☐

(i) Drug: ______________  Date of Last Use: ______________  Amount: ______________

Route:  oral ☐  nasal ☐

STD: No ☐  Yes-Dx ______________

Typical Pattern of Use: ______________

Adverse Effects  ______________  Concurrent Drugs  ______________

Route:  oral ☐  nasal ☐

iv ☐  other: ______________

How long has he used ______________

Adverse Effects? ______________  Concurrent Drugs  ______________

(ii) Drug: ______________  Date of Last Use: ______________  Amount: ______________

Route:  oral ☐  nasal ☐

iv ☐  other: ______________

How long has he used ______________

Adverse Effects? ______________  Concurrent Drugs  ______________
### 4. MEDICAL HISTORY

<table>
<thead>
<tr>
<th>(a) Medical/Disease Complications</th>
<th>(b) Psychiatric</th>
<th>Diagnosed</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart</td>
<td>Anxety</td>
<td>N</td>
<td>Y</td>
</tr>
<tr>
<td>Respiratory</td>
<td>Depression</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Diabetes</td>
<td>Social Phobia</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Thyroid</td>
<td>Mood Changes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Allergies</td>
<td>Personality Changes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Other</td>
<td>Other(e.g. bipolar, OCD)</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>(c) Infectious Diseases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chlamydia</td>
</tr>
<tr>
<td>Genital Herpes</td>
</tr>
<tr>
<td>Syphilis</td>
</tr>
<tr>
<td>Hep B</td>
</tr>
<tr>
<td>Hep C</td>
</tr>
<tr>
<td>HIV</td>
</tr>
</tbody>
</table>

### 5. TREATMENT

- **Have you ever/currently receiving any treatment for alcohol or drug use?**

<table>
<thead>
<tr>
<th>No</th>
<th>Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td>(where?)</td>
<td>Counseling</td>
</tr>
<tr>
<td>Start Date:</td>
<td>Length:</td>
</tr>
</tbody>
</table>

- **Have you ever/currently receiving any treatment for psychological or emotional problems?**

<table>
<thead>
<tr>
<th>No</th>
<th>Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td>(where?)</td>
<td>Counseling</td>
</tr>
<tr>
<td>Start Date:</td>
<td>Length:</td>
</tr>
</tbody>
</table>

### 6. ALCOHOL AND NICOTINE HISTORY:

<table>
<thead>
<tr>
<th>(a) Tobacco/Nicotine</th>
<th>Cigarettes</th>
<th>Cigar</th>
<th>Pipe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age of onset</td>
<td>Quit/Cut Down</td>
<td>Yes (when)</td>
<td>(amount)</td>
</tr>
<tr>
<td>How many</td>
<td>Previous attempts</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>(b) Alcohol</th>
<th>Date of Last Use:</th>
<th>Amount:</th>
</tr>
</thead>
</table>

- **What is your typical pattern of drinking?**

- **use on weekdays (i.e. Mon-Thurs)?**

- **use on weekends (i.e. Fri-Sun)?**

- **How many drinks have you had in the last seven days?**

<table>
<thead>
<tr>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
<th>Day 4</th>
<th>Day 5</th>
<th>Day 6</th>
<th>Day 7</th>
<th>total/wk</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- **# Binge episodes:_______ (# drinks:_______)**

- **Comments:**

- **Do you ever experience any of the following:**

  | Blackouts | Falls/injuries | Insomnia | Diarrhea | Increased BP | Gastritis | |
  |-----------|---------------|----------|----------|--------------|----------|
  | No        | Yes           | No       | Yes      | No           | Yes      |

7. PSYCHOACTIVE DRUG HISTORY

(i) Drug: _______________ Date of Last Use: _____________ Amount?: _______________________

Route: oral ☐  nasal ☐  iv ☐  other: ___________________  Typical Pattern of Use: _______________________.

(use on weekdays (i.e. Mon-Thurs)  ▶ use on weekends (i.e. Fri-Sun))

Adverse Effects ___________________  Concurrent Drug Use ___________________  How long have you used this drug? ___________________

Use from date of last use:

<table>
<thead>
<tr>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
<th>Day 4</th>
<th>Day 5</th>
<th>Day 6</th>
<th>Day 7</th>
<th>total/wk</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(ii) Drug: _______________ Date of Last Use: _____________ Amount: _______________________

Route: oral ☐  nasal ☐  iv ☐  other: ___________________  Typical Pattern of Use: _______________________.

(use on weekdays (i.e. Mon-Thurs)  ▶ use on weekends (i.e. Fri-Sun))

Adverse Effects ___________________  Concurrent Drug Use ___________________  How long have you used this drug? ___________________

Use from date of last use:

<table>
<thead>
<tr>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
<th>Day 4</th>
<th>Day 5</th>
<th>Day 6</th>
<th>Day 7</th>
<th>total/wk</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(iii) Drug: _______________ Date of Last Use: _____________ Amount?: _______________________

Route: oral ☐  nasal ☐  iv ☐  other: ___________________  Typical Pattern of Use: _______________________.

(use on weekdays (i.e. Mon-Thurs)  ▶ use on weekends (i.e. Fri-Sun))

Adverse Effects ___________________  Concurrent Drug Use ___________________  How long have you used this drug? ___________________

Use from date of last use:

<table>
<thead>
<tr>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
<th>Day 4</th>
<th>Day 5</th>
<th>Day 6</th>
<th>Day 7</th>
<th>total/wk</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Injection Drug Use

Have you ever used needles?  Never ☐  Yes ☐  (If yes, fill out details in psychoactive drug hex chart)

☆ Have you ever shared a needle, syringe, cooker/spoon, or cotton/filter with anyone at anytime in your life?
  Never ☐  Yes ☐  Date of last use: _______________  Drugs used: _______________________

☆ In the past 3 months, on how many days did you share?  Shared before 3 months ☐
  ___________ days  what was shared? _____________________________________________

☆ In the past 3 months, with how many different people have you shared?
  ___________ people
8. MEDICATION/EXPOSURE HISTORY

<table>
<thead>
<tr>
<th>Medication/Exposure</th>
<th>Start</th>
<th>Stop</th>
<th>Dose/Route</th>
<th>Indication</th>
<th>Do you take as prescribed?</th>
<th>MR Discussed</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

DO YOU MIND IF WE CALL YOU BACK AFTER THE BABY IS BORN? Call ☐  Don’t Call ☐
(Confirm phone number!)

9. ACTION TAKEN

- Baseline Risk explained ☐  Risk no >1-3% ☐  All or none period ☐
- Information given ☐  Level II U/S ☐  Followed-up ☐
- Treatment referral: BTC ☐  T-CUP ☐  Study FU complete________ __ ☐
- Other: __________________________________________________________