INVESTIGATION OF THE ALCOHOL, SMOKING AND SUBSTANCE INVOLVEMENT SCREENING TEST (THE *ASSIST*) IN PREGNANCY

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Abstract

Screening pregnant women for substance use appears unworthy of debate given the harmful impacts on the fetus, pregnancy outcomes, the woman herself and her offspring to adulthood. However while screening is routine for conditions such as impaired glucose control, obstetric care providers are often reluctant to intervene with substance use, citing knowledge deficits and a lack of effective screening tools. General negativity about the value of intervention and stereotypical views of substance users have also been identified. This study examined existing screening tools and investigated the World Health Organization's *ASSIST* (Alcohol, Smoking and Substance Involvement Screening Test) *Version 3.0*, focussed on tobacco, alcohol and cannabis, the substances most used in the targetted public hospital clinics. The *ASSIST Version 3.0's* performance in pregnancy was assessed using a two-pronged harm categorization: risk to the fetus and risk to the woman as an individual user. For the latter, levels of risk concordant with cut-offs for the general population were utilized. The *ASSIST Version 3.0* performed only moderately well *versus* established self-report tools: the *Revised Fagerstrom Tolerance Questionnaire* (RTQ) for tobacco, the *T-ACE* for alcohol, and the *Timeline FollowBack (TLFB)* for cannabis. Most participants used tobacco (98 of 104); predominance of tobacco use was likely linked to the recognized difficulty in stopping, despite cessation of other substances. *Kappa* analyses of Specific Substance Involvement Scores (SSIS) on *ASSIST Version 3.0* for tobacco did not support changing cut-offs for the woman as an individual user; however, ROC curves delineated an SSIS of 4 as indicative of fetal risk for both alcohol and cannabis. As all 98 tobacco users were 'high risk' users, a cut-off indicative of fetal risk for tobacco could not be determined but may be feasible by further research with first trimester women. Identifying tobacco use with an

established tobacco-specific tool should be the first screening for pregnant women. If tobacco use is identified, screening for other substance use can be initiated and there may be a place for the *ASSIST Version 3.0* in that context. Obstetric care providers need to then be willing and competent to address identified use, whilst avoiding unhelpful stereotyping.

Declaration

This work contains no material which has been accepted for the award of any other degree or diploma in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text.

I give consent to this copy of my thesis, when deposited in the University Library, being available for loan and photocopying.

Elizabeth Dorothy Hotham

Date

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Chapter 1

Substance Use in Pregnancy

1.1 Impact of Substance Use on Health

The World Health Organization (WHO) has identified the use of alcohol and other substances (AOD use) as one of the top 20 risk factors for ill-health in the global population (World Health Organization (WHO) 2002). Much of this burden is due to tobacco, which is responsible for 9% of the world's deaths and 4.1% of the global burden of disease as measured by disability adjusted life years (DALYs); alcohol is responsible for 3.2% of deaths and 4% of DALYs, and illicit substances (chiefly heroin and cocaine) for 0.4% of deaths and 0.8% of DALYs. Data for Australia indicate that tobacco is responsible for 7.8% of the total disease burden, alcohol 2.3% and all illicit drugs 2% (Begg, Vos et al. 2007).

1.2 Impacts of Substance Use in Pregnancy

The risks of substance use if the user is pregnant are compounded. Not only does substance use during pregnancy place the woman's own health at risk but also there is a risk of deleterious effects on the progression of her pregnancy and of adverse effects on the developing fetus and on the infant. Further, it is now known that antenatal substance use can result in continuing negative influences on development of the offspring, sometimes continuing into and during adulthood.

An issue attendant on antenatal substance use is what ethicists have identified as the clinical imperative of two patients - the woman and the fetus. The existence of two patients leads to the potential for conflict and controversy

(Fasouliotis and Schenker 2000), particularly if a clinician overrides a woman's autonomy in the interests of the health and well-being of the fetus. There have been attempts to frame the needs of woman and fetus as mutual rather than competing; further, to highlight the need for clinicians to structure care acknowledging the possibility of decisions that are discriminatory on ethnic or socioeconomic grounds (Harris 2000).

However, while today's societal and clinical approaches to antenatal substance use have been formulated against the background of expanding scientific understanding, the existence of such knowledge is a relatively recent phenomenon.

1.2.1 An Historical Perspective

Much of the focus in earlier centuries was on use of alcohol, as other substances known today were largely unknown then. Interestingly, the Greeks and Romans of earlier times focused on the time of conception and use of alcohol by the man, rather than by the woman [Abel (1999) cited in Sanders p.289](Sanders 2009). Further, there was an ancient custom prohibiting drinking on the wedding night by either of the newlyweds, in the belief that drunkedness at conception could lead to 'deformity' (Calhoun and Warren 2007). However, there was no injunction to abstain past the wedding night and moderate use of alcohol by the woman during pregnancy was even encouraged (Sanders 2009).

By contrast, an often-cited phenomenon with an emphasis on the dangers of antenatal alcohol use has been England's so-called 'gin epidemic'. In the first half of the 18th century, the availability of cheap gin led to widespread drinking and a number of reports on effects of antenatal drinking on the offspring: in 1726, the College of Physicians labelled gin as 'a cause of weak, feeble and distempered children' (Sanders 2009) and much attention has been paid to the

Gin Lane painting by William Hogarth in which the central figure, described by later writers as 'syphilitic', allows the breastfeeding infant in her arms to fall from a height to the ground (Rodin 1981; Abel 2001; Sanders 2009). Further, the infant's facial features have been suggestive to some of what later became identified as present in a child with fetal alcohol syndrome (FAS) (Abel 2001; Sanders 2009). However, there was no clear link recognized at that time between heavy alcohol consumption and a syndrome defined by clinical criteria. In fact, other commentators have focussed on the general poverty, deprivation and social chaos depicted in such scenes as *Gin Lane*, rather than on the alcohol use *per se* (Abel 2001).

The nineteenth century saw the rise of the temperance movement and interest in the effects of maternal alcohol consumption on human development (Sanders 2009). Sanders quotes a 19th century House of Commons report which noted that the children of 'alcoholic mothers' had a 'starved, shrivelled and imperfect look'. A 1899 study reported on a study of 600 children of alcoholic mothers versus controls that found higher rates of stillbirth and infant mortality in the alcohol-exposed group (Sullivan cited in Sanders 2009, p.e290). Early twentieth century experimental studies on animals showed delayed growth, dysmorphology, and increased mortality of offspring exposed to alcohol *in utero* (Warner and Rosett 1975). Findings such as these somewhat shifted the focus from use by the man at conception to the woman's use antenatally as the main determinant of infant harms (Sanders 2009), although the 'sins of the fathers visited on the sons' belief relating to damage from excessive paternal alcohol use, also retained currency (Warner and Rosett 1975).

In the early twentieth century, the impact of sociological factors such as poverty and abuse on infant wellbeing gained greater credibility and scientific

interest in the harms of antenatal alcohol use started to wane (Warner and Rosett 1975; Sanders 2009). However, 'antidrink' campaigners, sometimes aligned with those discomfited by the fledgling women's emancipation movement, continued to exhort women to abstain from alcohol consumption (Gutzke 1984).

The recognition of a fetal alcohol syndrome (FAS), and later of fetal alcohol effects (FAEs) and more recently fetal alcohol spectrum disorder (FASD), is described on 1.2.3. The latter part of the 20th century has seen dramatic shifts in the guidance given to pregnant women in relation to alcohol use. Women in the 1950s were advised by their medical carers that 'half a packet of cigarettes a day and a cocktail before dinner were harmless' (Oaks 2001); on the European side of the Atlantic, the advice was to 'take a glass of stout a day' (email Jeffrey Robinson 11th July 2009). However, from the 1980s, the 'pregnancy rules' have changed, resulting in prosecutions in the 1990s of over 200 pregnant women in the US for practices including use of alcohol (Oaks 2001)(Paltrow 1999). In this century, the global movement is towards abstinence from alcohol use in pregnancy; this shift in approach will be discussed in 4.3.2.1. Interestingly, on a therapeutic note, oral and/or intravenous ethanol was used to prevent uterine contractions in threatened preterm labour as recently as the 1970s (Chapman and Williams 1951; Halmesmaki and Ylikorkala 1988; Briggs, Freeman et al. 2008).

Shifting attitudes to tobacco use have also been observed since the 'half a packet of cigarettes a day' advice cited earlier. From the 1920s, tobacco smoking, largely reserved for men, had become a fashionable activity for women, linked with the 'flappers' and the 'Roaring 20s' (Fitzgerald 1989; Amos and Haglund 2000). In 1929, an editorial in the Journal of the American Medical Association declared that smoking during pregnancy did not cause

harm despite recent reports to the contrary in successive bulletins of the Methodist Episcopal Church (JAMA Editorial 1929). The Church's publications were labelled by the JAMA editor as being associated with 'cult' activity, with the editor declaring that '*smoking by women is not a medical concern any more than … whether … they should go bareheaded into church*.'

However, the acceptance of smoking by pregnant women lasted for only a few decades. The 1957 report by Simpson based on data from 7,499 patients found the incidence of premature births was twice as great for smoking mothers as for non-smoking mothers, with the rate increasing as the number of cigarettes smoked increased. These data were collated from women in 'private hospitals' and allowed much clearer conclusions than with data from women attending 'public hospitals' where factors such as poor nutrition, 'high incidence of unwed mothers', and low attendance at antenatal care, were confounding factors (Simpson 1957).

The seminal 1964 report on *Smoking and Health* by the US Surgeon General's Advisory Committee advised pregnant women that smoking would reduce the average weight of their offspring (United States Surgeon General's Advisory Committee on Smoking and Health 1964); however, the mechanism behind this reduction could only be speculative, and it was unclear whether reduced birth weight had any influence on the 'biological fitness of the newborn' (United States Surgeon General's Advisory Committee on Smoking and Health 1964). This message could be viewed as relatively insignificant in a 386 page report. By 1977 however, the Surgeon General's report was much more fulsome, with higher rates of perinatal mortality, associated with, and probably caused by, antenatal smoking highlighted, these effects having been reported in a British study (Butler, Goldstein et al. 1972). In addition, preterm delivery and other labour complications, and impairment of physical and mental

development in the infant were included as harms linked with antenatal smoking (US Surgeon General 1978).

In the US, the public health message of 'no smoking in pregnancy' that built on this accumulated research became particularly strident (Oaks 2001). From the 1980s, smoking has been used in child custody cases as evidence of unfit parenting (Oaks 2001). Commentators have identified that, in the promulgation of public health messages of the harms associated with smoking in pregnancy, health authorities have, intentionally or not, encouraged open criticism of pregnant smokers (BBC News 2009). In addition, authorities have subliminally promoted societal policing of this behaviour (Oaks 2001). Such campaigns however, rarely, if ever, place maternal tobacco smoking in the context of the social and economic environments in which the pregnant women live their lives. A similar conclusion could be reached with regard to the antenatal use of other substances including alcohol.

The approach in the US to substance use by women, including pregnant women, across the 19th and 20th centuries, has been explored by Kandall, prompted by his professional testimony in support of a disadvantaged black American prosecuted for 'delivering a controlled substance to a minor', her unborn baby (Kandall 2005). Although substance use by pregnant women – and the attendant victimization – is likely to be regarded as a late 20th century phenomenon continuing into the 21st, women's use of mind-altering substances can be traced back to tonics, powders, and other patent medicines widely promoted in the 19th century, most of which contained opioids and/or alcohol (Kandall 1996).

1.2.2 Tobacco

It has been stated, and often reiterated, that 'cigarette smoking during pregnancy is the single largest modifiable risk for pregnancy-related morbidity

and mortality' (Dempsey and Benowitz 2001). Effects of maternal tobacco use have been well documented (Rogers 2009; British Medical Association and Board of Science and Education and the Tobacco Control Centre 2004). The woman's pregnancy is at a heightened risk of: ectopic pregnancy, miscarriage, placental complications, and premature rupture of amniotic membranes. Growth restriction of the fetus and low birthweight may be accompanied by prematurity and an increased risk of perinatal death. A 1992 analysis of over 13,000 births of women who smoked found that, by controlling for other factors including the number of cigarettes smoked, 85% of this increased risk of perinatal mortality was attributable to low birthweight *per se* (English and Eskenazi 1992).

Although research has directly linked maternal smoking with long-term effects on the blood pressure of the offspring, effects discernible even in childhood (Morley, Leeson et al. 1995), the link between low birth weight and diseases of adulthood, such as cardiovascular disease, diabetes and the metabolic syndrome, is increasingly understood (Barker 1990; Barker 2008). Further, research is also being directed towards the influence of the intrauterine nutritional environment on postnatal health, with recognition that high as well as low fetal nutrition can have an impact, and that effects vary between male and female offspring, indicative of interaction with the 'hormonal milieu' (McMillen and Robinson 2005).

The child whose mother smoked during pregnancy is more likely to have compromised lung function and hence respiratory disease in childhood (Moshammer, Hoek et al. 2006; Rogers 2009; British Medical Association and Board of Science and Education and the Tobacco Control Centre 2004). Further, damage has been postulated to cross generations with the offspring of tobacco users more likely to suffer from asthma even if the mother does

cease use prior to pregnancy (Babbington 2007). The increased risk of contracting otitis media in childhood due to fetal exposure to smoking (British Medical Association and Board of Science and Education and the Tobacco Control Centre 2004) is further amplified if the child then lives in a household where he/she is exposed to environmental tobacco smoke (Jacoby, Coates et al. 2008).

Increasingly, research is highlighting further effects of fetal exposure to tobacco. Evidence through animal studies shows that such outcomes are attributable to the direct effects of nicotine as a developmental neurotoxicant, through its impact on synaptic development (Paz, Barsness et al. 2007; Slotkin 2008). These changes in synaptic activity have been shown to be permanent, making the infant more susceptible to hypoxic insults, but also resulting in cognitive and learning deficits in childhood (Slotkin 2008).

Human studies have supported the association of adverse behavioural outcomes with maternal smoking in pregnancy (Cornelius 2000; Faden and Graubard 2000; Cornelius, Goldschmidt et al. 2007; Pickett, Wood et al. 2008; Yolton, Khoury et al. 2008), although other factors in the lifestyle of the pregnant women may also be implicated (Linnet, Dalsgaard et al. 2003). A follow-up, at three years of age, of over 8,000 live births registered with the US National Center for Health Statistics, concluded that, at that age, the effects of maternal substance use (tobacco, alcohol and cannabis) were more evident in behavioural dysfunction, rather than in developmental indices (Faden and Graubard 2000). An exception was the tardiness in language development which was clearly related to maternal smoking during pregnancy (Faden and Graubard 2000). A Danish study of 3 044 singleton births concluded that maternal cigarette smoking (recorded in the third trimester)

showed a negative association with the intelligence of the adult offspring (measured at 18.7 years) (Mortensen, Michaelsen et al. 2005).

In a Canadian study of 420 neonates, a dose-response relationship was found between the cigarette smoking and alcohol consumption of mothers and concentration of lead in cord blood, a relationship which held for women using either or both of these substances (Rhainds and Levallois 1997). This is of concern given the dangers of intrauterine lead exposure, ranging from the possibility of neurobehavioural effects at levels of at least 10mcg/dL to congenital abnormalities at concentrations above 30mcg/dL to (Thomson MICROMEDEX (R) 2008).

Smoking has been associated with congenital septal and right-sided obstructive defects of the heart (Cornelius 2000; Malik, Cleves et al. 2008) and it is thought to be implicated in orofacial clefts (Lorente, Cordier et al. 2000), although some studies have been ambiguous. However, it has now been shown that there is clearly a heightened risk of orofacial clefts for fetuses lacking glutathione S-transferase enzymes, essential in the detoxification of chemicals derived from tobacco (Lammer, Shaw et al. 2005).

Although the mechanism is unclear, the pregnancy-associated plasma protein A (PAPP-A), the strongest of the serum markers for Down syndrome, is reduced in smokers by as much as twenty percent (Neimimaa, Heinonen et al. 2003), affecting the accuracy of risk evaluation in the pregnant smoker.

1.2.2.1 Mechanisms of Fetal Harm

The impact of nicotine *per se* as a teratogen through its actions on nicotinic cholinergic receptors has been noted in 1.2.2. (Paz, Barsness et al. 2007; Slotkin 2008) and is increasingly understood. However, the impact of nicotine on growth is also of interest. A recently published longnitudinal study using animal models showed growth deficits in infancy; however, through young

adulthood and into later adulthood, the male rats showed significant elevations in body weight whereas females continued to show slight deficits (Slotkin, Hyde et al. 2010). The results are concordant with the work of Barker and his colleagues (Barker 1990; Barker 2008), with the use of animal models allowing comprehensive follow-up through the lifespan. These effects on growth at birth and through life were also attributed to nicotine's impact on nicotinic cholinergic receptors (Slotkin, Hyde et al. 2010).

The method of delivery of nicotine to the fetus, viz by maternal tobacco smoking, itself introduces a major mechanism for fetal harm through hypoxia (Wakefeld and Wilson 1988). Elevated levels of erythropoietin isolated from the umbilical cord post-delivery are a measure of tissue hypoxia in the fetus (Jazayeri, Tsibris, et al. 1998), are correlated with maternal tobacco smoking, and are associated with growth restriction. With the stronger affinity of carbon monoxide for fetal haemoglobin than for adult haemoglobin, the delivery of oxygen to the fetus is more compromised than to the pregnant woman (Lambers and Clark 1996). Hypoxia is also related to vasoconstriction in the maternal-fetal circulation to maintain mean arterial pressure and support the circulation to key fetal organs (Dyer, McMillen et al. 2009). Growth restriction is also part of this adaptive process.

The negative impacts on the fetus of the other chemicals in tobacco smoke (nearly 4,000) remain largely undetermined (Lambers and Clark 1996). Beratis and his colleagues measured alpha-fetoprotein, the principal serum protein in early ontogenic development, and determined that elevated levels were linked with the intensity of maternal smoking and associated with growth restriction (Beratis, Varvarigou et al. 1999). They concluded that growth restriction was the direct or indirect result of one or more components of tobacco smoke and linked to compromised blood flow.

Later work by this team of researchers has focussed on leptin, a protein secreted from adipocytes, whose circulating levels signal the status of energy stores in the brain (Mantzoros, Varvarigou et al. 1997). This study demonstrated that leptin concentrations were significantly lower in all offspring of smokers, regardless of gestational age at birth, with concentrations in the premature infants almost half those of full-term infants (Mantzoros, Varvarigou et al. 1997). Lower leptin levels could be expected on the basis of growth restriction in the offspring; however, when the researchers adjusted for maternal body mass, the findings held, leading them to conclude that leptin itself could be one of the mediators of endocrine dysfunction in the offspring. The mechanism of this effect could be related to the raised catecholamines in the blood of smokers which increase lipolysis, as animal studies have shown that raised catecholamines are linked to lower leptin levels through a cyclic AMP pathway (Slieker, Sloop et al. 1996). Recent work has shown that the negative impact on growth is correlated with the number of cigarettes smoked, with male offspring more adversely affected (Varvarigou, Asimakopoulou et al. 2009).

1.2.3 Alcohol

Despite historical concerns of maternal alcohol use being related to poor pregnancy outcomes, the existence of a 'fetal alcohol syndrome' (FAS) was formally credited to the study of 8 infants by Jones and Smith published in the *Lancet* in 1973. Syndrome characteristics included evidence of growth restriction and central nervous system anatomical and neurodevelopmental abnormalities, and a pattern of facial anomalies such as flattened philtrum (Jones and Smith 1973) and it is now understood that this constellation of abnormalities resulting from the teratogenicity of alcohol is due to 'heavy' alcohol use.

However, the characteristics of the syndrome had already been reported in 1968 in a French study of 127 cases by Lemoine and colleagues, a publication translated into English many years later (Lemoine, Harousseau et al. 2003). Follow-up work on 105 of the cases as adults revealed persistent deficits (Lemoine 2003). Other early work (Ulleland 1972) had also identified that intrauterine growth 'retardation' was significantly higher in the offspring of 'alcoholic women', after adjusting for confounding factors such as tobacco use and undernutrition, and that these infants subsequently failed to thrive.

However, some infants compromised by maternal alcohol use will not display the full range of abnormalities, due at least in part to lower maternal alcohol use; such infants may be described as exhibiting 'fetal alcohol effects' (FAEs) (Burd 2004). More recently, the term 'fetal alcohol spectrum disorder' has gained acceptance (Sokol, Delaney-Black et al. 2003). Neuro-psychological and neuro-behavioural sequelae have been found to be correlated with the level of maternal alcohol consumption and to be independent of tobacco or other drug use and socio-demographic status (Streissguth 2007). Further investigation not only of dose, but also of timing, is warranted (Testa, Quigley et al. 2003).

Epidemiology data on FAS collected over a four year period from January 2001 to December 2004 by the Australian Paediatric Surveillance Unit (Elliott, Payne et al. 2008) are the only such prospective national data available globally. Through monthly reports submitted by 1150 paediatricians, the unit researchers established that 92 children fulfilled their criteria for FAS. For all but two of the children, high intrauterine exposure to alcohol could be confirmed, with almost 80% of the children being also exposed to one or more other substances, principally tobacco and cannabis. Given the severe impact of the syndrome on the prognosis of the affected children, it was disturbing that

only six of the 92 children were diagnosed with FAS at birth (Elliott, Payne et al. 2008).

In a longitudinal study over 25 years (Streissguth 2007), deficits in early childhood and adolescence such as difficulty with problem solving and dealing with received information were shown to be followed by substance use problems and mental illness in young adulthood. A review of the fetal effects reported for a large range of substances (Chiriboga 2003) concluded that there is generally a 'catch-up' phase exhibited in growth and neurobehavioural abnormalities; however, with alcohol, if there is damage such as mental retardation and microcephaly, there will be no 'catch-up', a conclusion supported by others (Sampson, Bookstein et al. 1994). A similar determination was made for the behavioural effects related to nicotine use (Chiriboga 2003).

It has been recognized however that it is difficult to separate the growth restriction caused by alcohol use from the adverse effects of other substance use and of other environmental factors of risk (Mathias 1998; Yang, Chung et al. 2001). This difficulty in separating deficits caused by use of one substance from other confounding factors is a universal one (Hawley, Halle et al. 1995; Reichman and Pagnini 1997; Bergin, Cameron et al. 2001). The potential for the moderation of deficits present at birth, both intellectual (Jacobson, Jacobson et al. 2004) and others that are more subtle (LaGasse, Seifer et al. 1999), will not be realized if adverse environmental factors exist.

In another longitudinal study, children's academic achievement at the age of ten years - on the brink of adolescence - was found to be correlated with maternal exposure to both alcohol and cannabis (Goldschmidt, Richardson et al. 2004). First trimester cannabis exposure of one or more 'joints' per day showed a marked association with the children's mental ill-health at ten years of age while a similar exposure in the second trimester was linked to lower

academic scores (Goldschmidt, Richardson et al. 2004). Exposure to alcohol in the first or second trimester was also linked with lower academic achievement, an association which still held with second trimester maternal consumption of as little as one drink of alcohol daily. The study did not show that adverse effects were compounded if women consumed both alcohol and cannabis (Goldschmidt, Richardson et al. 2004).

Although it has not been shown that infrequent, low levels of alcohol use are harmful in pregnancy (Royal College of Obstetricians and Gynaecologists (RCOG) 2006), it has been suggested that certain mother-infant 'dyads' may be at particular risk of moderate alcohol consumption (Mukherjee, Hollins et al. 2005). However, the identification of specific dyads at risk is not currently possible.

The dose-related effects of maternal alcohol use on the newborn's immune system was assessed in a US-based study of over 11,000 births which showed that alcohol exposure increased the risk of neonatal infection (Gauthier, Drews-Botsch et al. 2005). The association was strongest (6.83 times higher) for women consuming at least seven drinks per week in the second trimester but held throughout pregnancy. This risk was also significantly higher in the neonates of women who smoked, both pre-conceptionally and across pregnancy. Iron deficiency anaemia at 12 months of age has also been associated with heavy maternal alcohol use (defined as four or more alcohol drinks daily)(Carter, Jacobson et al. 2007). Further, a dose-related effect of alcohol use in the peri-conceptional period (two months before and after conception) has been shown to be associated with an increased risk of both conotruncal heart defects and cleft lip defects (Grewal, Carmichael et al. 2008).

Binge drinking behaviours of pregnant women have also received attention. In recent work, binge drinking (at least five drinks in a session) both in the three months preconception and in the second and third trimesters has been found to be significantly associated with increased risk of newborn infection (Gauthier, Drews-Botsch et al. 2005). Earlier work (Tolo and Little 1993; Kesmodel 2001) reported that parameters such as birthweight and intrauterine growth were not affected by occasional binge drinking episodes against a background of otherwise moderate alcohol consumption in pregnancy, although it has since been suggested that methodological limitations may have impeded meaningful findings (Kesmodel 2001).

A study of fifty-one children whose mothers reported at least one binge alcohol episode in early gestation, generally before awareness of their pregnancy, showed that the children did not exhibit cognitive deficits; however, they did exhibit a greater incidence of disinhibited behaviour compared to controls, with such behaviour recognized as likely to predispose the children to later psychological disorders (Nulman, Rovet et al. 2004).

The understanding that 'heavy' alcohol use could lead to an increased risk of first and second trimester vaginal bleeding and an increase in placental abruption was documented nearly 25 years ago (Sokol and Miller 1980). In addition, moderate alcohol consumption (defined as greater than two alcoholic drinks per week up to and including two drinks per day) has been found to be associated with an increased risk of spontaneous abortion, although a decreased risk of stillbirth (Makarechian, Agro et al. 1998). A prospective study in the US of 2714 singleton births showed an increased risk of growth restriction with consumption of more than twenty-eight grams of alcohol daily in early pregnancy, and increased risk of preterm birth with even light consumption of alcohol later in pregnancy (Lundsberg, Bracken et al. 1997).

Recent epidemiological data suggests an increase in pre-term birth with as few as four drinks per week (Albertsen, Andersen et al. 2004).

1.2.3.1 Mechanisms of Fetal Harm

The mechanisms of alcohol teratogenesis continue to be investigated (Goodlett, Horn et al. 2005), with recent work focussing on the pleiotropic influence of alcohol, given its damaging effects not only on the fetus but also as a neurotoxin in adult users with demonstrated negative effects on most organ systems (Miranda, Pietrzykowski et al. 2010). In this recently published review, the authors evaluated evidence that alcohol impacts on micro RNAs as 'master switches' in regulation, leading to disruption of neural stem cell proliferation and differentiation in the fetus, as well as other pathological processes in later life (Miranda, Pietrzykowski et al. 2010).

However, a number of other mechanisms are believed to play a role, including oxidative stress (Goodlett, Horn et al. 2005). The normal physiological response of the body's cells to the production of reactive oxygen species by toxins including alcohol is the mobilization of anti-oxidants and free-radical scavengers to neutralize the reactive oxygen species; the inability of the fetus to mount that response is believed to contribute to congenital anomalies (Ornoy A 2007).

Other studies have focussed on the damage alcohol can cause *in utero* to the neurons that synthesize serotonin (Goodlett, Horn et al. 2005), as animal studies have indicated that reduction in serotonin innervation compromises development of the forebrain (Zhou, Sari et al. 2002). Attention has also been given to the deleterious role of acute withdrawal from alcohol (Thomas and Riley 1998). These researchers focussed on the N-methyl-D-aspartate (NDMA) receptor, the receptor for the neurotransmitter glutamate. Its activation is complex and results in a balance of neuronal growth-promoting and excitotoxic

effects. Acute withdrawal could disrupt this balance and interfere with neuronal development, an impact that may occur even with a single heavy exposure (Thomas and Riley 1998).

Increasing interest is now focussed on epigenetic involvement in fetal alcohol spectrum disorders (Haycock 2009). A body of evidence reviewed by this author supports the view that these disorders may not only arise from *in utero* exposure to alcohol, but also from preconceptional exposure. The possibility of damage to the germ line preconception has major public health ramifications. Whether the impacts are likely to manifest across a range of maternal alcohol use behaviours, to include paternal alcohol use, and to affect several generations, warrant further investigation (Haycock 2009).

1.2.4 Cannabis

Maternal use of cannabis exposes the fetus to many of the same risks as tobacco if it is smoked, and clearly, many users of cannabis are concurrent users of tobacco. An analysis of US data on over 43,000 adults from the 2001-2002 *National Epidemiologic Survey on Alcohol and Related Conditions* found the use of cannabis to be highly associated with tobacco use (Agrawal, Knopik et al. 2008). Concurrent use was more likely by smokers of tobacco than by those using tobacco by the smokeless route (Agrawal, Knopik et al. 2008), the latter practice being popular in several parts of the world including the United States.

In a 1992 review, Fried concluded that from approximately three years of age of the offspring, it is evident that maternal use of cannabis while pregnant has a negative impact on the development of executive function. This complex cognitive process is chiefly mediated in the pre-frontal cortex (Fried 2002). A cohort of children whose mothers had reported any use of cannabis in pregnancy (concurrently with alcohol or tobacco use) in a 1978 longitudinal

study of nearly 700 women in the Ottawa Prenatal Prospective Study, were contacted and 157 participants ranging from thirteen to sixteen years were interviewed (Fried, Watkinson et al. 2003). Earlier interviews had been conducted at younger ages (Fried, O'Connell et al. 1992; Fried 1995; Fried, Watkinson et al. 1998). The results in this cohort showed maternal cannabis use to be negatively associated with an ability to focus attention and with poor results in tasks requiring visual memory, analysis and integration, findings consistent with those from the earlier interviews (Fried, Watkinson et al. 2003).

Further, by adjusting statistically for confounding factors, including use of substances by the adolescents themselves and other maternal substance use *in utero*, the researchers were able to show that the derived IQ (as measured by a shortened version of the Wechsler Intelligence Scale for Children) was linearly and negatively associated with maternal use of tobacco and not of cannabis (Fried, Watkinson et al. 2003). The results in the thirteen to sixteen year old cohort also showed that negative impacts on intelligence indices from maternal tobacco use *in utero* had extended into adolescence. Memory tests based on verbal functioning were particularly affected, further demonstrating the higher vulnerability of the auditory-verbal domain of cognitive processing (Fried, Watkinson et al. 2003).

A longitudinal study in Britain of 12,000 pregnant women (ALSPAC Study Team, Fergusson et al. 2002) concluded that cannabis users were more likely to be at risk of adverse outcomes of pregnancy even if no specific effect of cannabis use could be proven, because of the concurrence of other pregnancy risk factors such as young age, lower parity and use of other substances. However, when confounding factors were adjusted for by multiple regressions, cannabis use still showed a statistically significant association with reduced

birthweight and birth length, although not with perinatal mortality and morbidity (ALSPAC Study Team, Fergusson et al. 2002). When women used cannabis less than once per week however, there was little difference in birthweight outcomes compared to non-smokers. Regular use appears to cause dose–related effects and the authors concluded that a larger study (only five percent of their sample reported cannabis use) would be needed to firmly establish the dose threshold for effect.

1.2.4.1 Mechanisms of Fetal Harm

A number of researchers have in recent years focused on the adverse effects on reproduction of cannabis (specifically its psychoactive ingredient delta-9-tetrahydrocannabinol, known as THC) through studies of cannabinoid receptors (CB1 and CB2), and of the metabolic pathway of endogenous cannabinoids such as anandamide (Maccarrone, Valensise et al. 2000; Piomelli 2004; Sun and Dey 2008). Using knockout mouse models, Dey and colleagues have demonstrated that endogenous cannabinoids have a critical role in female fertility: on transport of the ovum, to embryonic development pre-implantation, and finally, to the implantation of the embryo. Any disturbance in the signaling of endogenous cannabinoids through CB1 receptors was shown to impair implantation (Sun and Dey 2008).

Park and colleagues, utilizing techniques of immunohistochemistry to study the human placenta, have been able to show the presence of CB1 receptors in all layers of the placenta (Park, Gibbons et al. 2003). The presence of the enzyme, fatty acid amide hydrolase (FAAH), has also been demonstrated, with higher levels in layers in which CB1 receptors were low and lower levels where CB1 expression was high. A strong correlation has also been established between decreased FAAH activity and its expression in human peripheral blood mononuclear cells (PMBCs) and subsequent abortion (Maccarrone, Valensise et

al. 2000); low FAAH levels result in higher endogenous cannabinoid activity, which is detrimental to implantation. It is possible that the exogenous cannabinoid THC is implicated in the higher rate of miscarriage among users of cannabis, by its interference in the signalling pathway of endogenous cannabinoids.

In vivo studies have found that both endogenous and exogenous cannabinoids, by action on the CB1 receptor, exert a potent relaxant effect on the human uterus (Dennedy, Friel et al. 2004). However it is unclear currently whether this is a factor in human parturition. These findings do not support an association with pre-term delivery and cannabis use, but conversely, suggest that labour could be inappropriately delayed, with possibly negative outcomes, in the regular cannabis user (Dennedy, Friel et al. 2004).

1.2.5 Other Substances

Opioids, cocaine and amphetamine-type stimulants (ATS) are also known to be used by pregnant women. In an Australian study of babies born during a 27 month period in the major Perth maternity hospital, maternal use of either opioid drugs (91 women) or ATS (50 women) in pregnancy was shown to be associated with growth restriction in the infant (Ludlow, Evans et al. 2004). This association in ATS-exposed infants was also found in a study in Thailand of 128 women (Phupong and Darojn 2007).

Babies of all the mothers in the Australian study were more likely to be born before 37 weeks' gestation and to require admission to the special care nursery. Babies born to users of ATS were likely to have had low APGAR[1] scores (Beischer and Mackay 1986); those born to users of opioids were more likely to require resuscitation and to exhibit neonatal withdrawal (Ludlow,

[1] APGAR score: a number indicating physical condition of the neonate at birth, as calculated from five different areas.

Evans et al. 2004). Although neonatal abstinence syndrome (NAS) can generally be well managed with morphine administration to the affected infant, management is complicated if the infant is exhibiting a 'mixed' withdrawal, that is, concurrent withdrawal from a number of substances (McPhee 2004). However, the study was limited by not being able to control for factors such as smoking, maternal age and nutritional status. Further, the researchers noted that it was difficult to separate the effects of individual drugs given the possible lack of accuracy in the documentation of drug consumption (Ludlow, Evans et al. 2004).

Despite the need for NAS management in the infants, pregnant women are advised not to undergo an acute withdrawal from opioids during pregnancy, since such withdrawal has been associated with intrauterine death (Chappel 1972; Rementeria and Nunag 1973). Oral methadone can be substituted for opioids such as heroin, leading to enhanced pregnancy outcomes (Burns, Mattick et al. 2006). Even a tapered withdrawal is not advised (Luty, Nikolaou et al. 2003). By contrast, women using ATS during pregnancy are encouraged to cease use and the babies are managed supportively after birth (Women's Drug and Alcohol Service 2005).

Women who used ATS during pregnancy also have an increased risk of adverse outcomes such as pre-term delivery (Ludlow, Evans et al. 2004; Phupong and Darojn 2007). Premature separation of the placenta leading to both abortion and premature delivery has been specifically linked with abuse of methamphetamine (Stewart and Meeker 1997); other work has shown growth restriction (birthweight, length and head circumference) in the offspring of methamphetamine-using women due to localized ischaemia and possibly infarcts (Phupong and Darojn 2007) (Ludlow, Evans et al. 2004). Given the

lower incidence of antenatal care for ATS-using women in their study, Phupong and Darojn speculated that the high incidence of anaemia in the women probably resulted from a combination of inadequate nutrition and lack of required iron supplements (Phupong and Darojn 2007). The researchers did not report adjusting for any other substance use in their analyses.

In the Infant Development Environment and Lifestyle (IDEAL) study in the US, 13,808 subjects were screened, with 166 enrolled in a longitudinal follow up for 36 months, of whom 74 were methamphetamine users (Smith, La Gasse et al 2008). More methamphetamine users were users of tobacco, alcohol and marijuana than were the controls and the results of the effects of methamphetamine use on the offspring were adjusted for these confounders, as well as others such as socioeconomic status and birthweight. The methamphetamine-exposed newborns were more difficult to arouse but, once aroused, exhibited an increase in physiologic stress (Smith, La Gasse et al. 2008). The effects were related to trimester of exposure, with increased stress signs related to first trimester use and poorer quality of movement associated with use in the third trimester. Despite limitations in analyses of trimester-related effects and correlating metabolite concentrations in meconium with time and quantity of drug use, the results were concordant with previous findings in cocaine-exposed newborns (Eyler, Behnke et al. 1998).

Another longnitudinal study in the US, the Maternal Lifestyle Study (MLS) examined the neurobehavioural outcomes for the offspring born to women who were users of opioids and/or cocaine (Lester, Tronick et al. 2002). Of the 1388 infants in the study, 600 had been exposed to cocaine and 115 to opioids, with 658 exposed infants in total. The mothers of these infants were significantly more likely to use either tobacco or alcohol than the women who had not used opioids or cocaine. With adjustment for confounding factors,

infants exposed to cocaine *in utero* showed lower arousal, lower regulation, and higher excitability than infants who were not exposed to cocaine; no differences could be found between infants exposed to opioids and those not exposed, after adjusting for confounding factors (Lester, Tronick et al. 2002). The researchers noted, however, that these neurobehavioural deficits from maternal cocaine use were subtle, and reflective of vulnerability to a later sub-optimal home environment, rather than indicative of an established disorder *per se*.

A number of follow-up studies on selected cohorts of the original participants have been conducted, exploring aspects of childhood development and behaviour. Data collected during follow-up of a sub-sample of 162 of the original 208 offspring in the Providence Rhode Island cohort showed more sleep problems at 18 months and at 9 years in those children exposed to opioids and/or cocaine antenatally than in those not exposed (Stone, High et al. 2009). In this follow-up study, participants were divided into: those whose mothers had used cocaine with or without other substances, those whose mothers had used substances but not cocaine, and those with no history of antenatal substance use. The addition of cocaine to the list of substances used antenatally was not shown to increase sleep problems (Stone, High et al 2009). The researchers commented that other factors such as the environment also play a major role in sleeping patterns.

Another follow-up study investigated 360 cocaine-exposed and 480 non-cocaine exposed infants with complete behavioural outcome data at 7 years; the opioid-exposed infants (n=115) were not included in this structural equation modelling analysis (SEM) as their demographic characteristics were too different from the rest of the sample, and numbers were relatively small - <10% of the sample (Lester, Bagner et al. 2009). Results suggested both

direct and indirect effects of prenatal exposure to cocaine and other substances on behavioural problems in childhood. The researchers concluded that neurobehavioural dysregulation, evident at 1 month and still manifest at 7 years, were direct effects of antenatal cocaine use and could be regarded as "true teratogenesis" (Lester, Bagner et al. 2009 p. 1359). Socioeconomic status (SES) was found in the model to influence childhood behavioural problems; however the authors commented that low SES is a surrogate for a number of factors in the home environment, including maternal health and parenting difficulties, none of which independently had a statistically significant impact on neurobehavioural dysregulation (Lester, Bagner et al. 2009).

Findings related to 3,4 - methylenedioxymethamphetamine (MDMA)- 'Ecstasy'- are emerging which may have serious implications for the fetus of a pregnant user of this amphetamine derivative. In a recreational use setting, MDMA users were found to have plasma concentrations consistent with those resulting in deficits of brain serotonin in previous studies conducted with non-human primates (Irvine, Keane et al. 2005). A 1999 research letter in The Lancet documenting 136 offspring of MDMA users reported that, given the limited number of subjects, findings on the risk of specific birth defects were inconclusive (McElhatton, Bateman et al. 1999). However, studies with rats have shown a number of developmental and adverse behavioural sequelae arising from exposure *in utero* to MDMA, including learning and memory deficits (Skelton, Williams et al. 2008).

1.3 Prevalence of Substance Use in Pregnancy

1.3.1 Australian Data

There are currently limited data on the prevalence of substance use by pregnant women in Australia, although national and state-based surveys attempt to elucidate the situation.

Some state health authorities record smoking prevalence for pregnant women. The most recent estimate for South Australia was 16% (2007), down from 25% in 1998 (Chan, Scott et al. 2008). These reports are completed by midwives at the time of delivery as part of a broader collection of perinatal statistics that begins with first antenatal visits.

Some national data are also available from the Australian Institute of Health and Welfare through household-based surveys conducted via self-completion booklets every three years. In the 2001 National Drug Strategy Household Survey (NDSHS), data collected on a cohort of approximately 400 women - those who were pregnant or breastfeeding in the total household sample (men and women) of 25,000 - indicated that 53% used alcohol, 23% tobacco, 7% cannabis, and 4% an illicit drug other than cannabis (Australian Institute Health and Welfare 2002). These contrast with data from the general (non-pregnant, non-breastfeeding) population where the prevalence of use of all drug types canvassed was higher, particularly alcohol (alcohol: 83%, tobacco: 24%, cannabis: 13%, and an illicit other than cannabis: 9%).

Analysis of responses from 976 pregnant and/or breastfeeding participants in the 2004 NDSHS indicated that women who used substances (including alcohol, cannabis and other illicit drugs), while pregnant or breastfeeding were more likely to be older and better educated, of higher income, and to live outside a capital city (Wallace, Burns et al. 2007). These women were significantly less likely to use alcohol than females generally (47% versus 85%

in the 2004 NDSHS). However, the difference in smoking rates (20% versus 25% in the 2004 NDSHS) was not significant.

An Australian retrospective study linked data from New South Wales (NSW) health administration databases over the five years from 1998 to 2002: admissions data from the Inpatient Statistics Collection and data in the NSW Midwives Data Collection related to provision of care and pregnancy outcomes (Burns, Mattick et al. 2008). The admissions included women in the so-termed 'drug group' (3,352) who had been flagged as positive to drug use (alcohol, cannabis, opioids or stimulants) with a confirmed diagnosis under the *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Australian Modification* (ICD-10-AM). The tobacco use patterns of these women and those with no recorded drug diagnosis (412,731 women) were also analysed. Women in the 'drug group' were more likely to be smokers and to smoke 'heavily' (Burns, Mattick et al. 2008). Fifty-six percent smoked more than 10 cigarettes per day (compared with only 8% in the 'non-drug' group) and 26% of this group smoked 1 to 10 cigarettes per day (with again only 8% in the 'non drug' group). This link between tobacco use and use of other substances has also been found in other studies (Archie, Anderson et al. 1997; Svikis, Henningfield et al. 1997; Coleman, Reardon et al. 2005; Hjerkinn, Lindbaek et al. 2007).

A separate further analysis was conducted on the separate cohort in the 'drug group' with an alcohol-related ICD-10-AM diagnosis (Burns, Mattick et al. 2006). The 342 women in this sub-group were also more likely to smoke tobacco (57%) than those in the 'non-drug' group (8%).

Data collected on women in 2000 as part of the Australian Longitudinal Study on Women's Health (Turner, Russell et al. 2003) showed that, with the youngest cohort of 9512 women (aged 22 to 27 years), 58% had used an illicit

drug at some time, with 57% reporting cannabis use. ATS were used by 16% of the cohort, 'Ecstasy type' drugs by 15% and lysergic acid diethylamide (LSD) by 14%. These data of use by women of child-bearing age give some elucidation of potential use by women when pregnant. It has been recognized that any pre-pregnancy use of alcohol or cigarettes, but particularly use during the month before pregnancy, is predictive of drug or alcohol use while pregnant (Chasnoff, Neuman et al. 2001).

1.3.2 United States Data

In the United States, a population with many common cultural influences to Australia, extensive data has been collected, not only at the national level but also in state-based and smaller local studies. A broad insight into alcohol and other drug use in pregnancy can be gained from the *National Survey on Drug Use and Health* (formerly the National Household Survey of Drug Abuse). The 2007 data were collected via personal interviews with 67,870 people in households selected to be reflective of the population generally (Office of Applied Studies Substance Abuse and Mental Health Services Administration (SAMHSA) 2008). Respondents were specifically asked about episodes of 'binge drinking' (defined as 5 or more standard drinks on at least 1 day in the past 30) and 'heavy drinking' (defined as the above behaviour on 5 or more days in the past 30). Both patterns are of concern, in particular for the fetus. Among pregnant women aged between 15 and 44 years of age, an estimated 11.6% reported current alcohol use (versus 53% in non-pregnant participants), 3.7% reporting binge drinking (versus 24.1%), and 0.7% reporting heavy drinking (versus 5.5%) (Office of Applied Studies Substance Abuse and Mental Health Services Administration (SAMHSA) 2008). A sub-analysis of the 2004 'pregnancy' data based on age showed that overall, fewer than 1% of all respondents reported 'heavy' drinking, with 'binge' drinking

reported by 4.5% of women in the 15-25 year old age group, by 3% in the 15-44 age group and by 0.5% in the 26-44 age group (Office of Applied Studies Substance Abuse and Mental Health Services Administration (SAMHSA) 2008).

Data on use of tobacco and other substances by pregnant women are also available through this same data collection. Combined data for 2006 and 2007 indicated that the rate of tobacco use in the past month was 16.4%, significantly lower than those who were not pregnant (28.4%). This pattern held for women aged 18 to 25 (23.3% compared with 33.9% by women not pregnant) and for women aged 26 to 44 (11.6% versus 28.3% in the non-pregnant female population). Contrary to this pattern, tobacco use by women aged 15 to 17 was higher for pregnant participants (24.3%) than for those who were not pregnant (16%) (Office of Applied Studies Substance Abuse and Mental Health Services Administration (SAMHSA) 2008).

In another SAMHSA publication (Office of Applied Studies Substance Abuse and Mental Health Services Administration (SAMHSA) 2001), the age-related data for the use of illicit substances indicated that use of illicit substances was lower at any age for pregnant compared with non-pregnant women: for women aged 15 to 25 (7% *versus* 14%) and for women aged 26 to 44 (2% - *versus* 6%).

Other US studies have also investigated the overall use of substances; yet others have focused on use of specific substances. In a large Californian study in which urine samples were collected from nearly 30,000 women giving birth at 202 hospitals, toxicological testing was used to determine the prevalence of recent substance use (Vega, Kolody et al. 1993). Results indicated the use of one or more illicit substances by over 5% of women and of alcohol by nearly 7%. Nearly 9% of women self-reported smoking (Vega, Kolody et al. 1993). In further analysis of these data, use of both illicit drugs and tobacco was

found to be correlated with ethnicity. The prevalence of substance use in the African-American women cohort was higher for all substances (Noble, Vega et al. 1997). However, given the higher numbers of Hispanic and white non-Hispanic women in the Californian population, concerns still existed with the prevalence of antenatal substance use in these populations: half the women using alcohol were of Hispanic origin and half of all substance users were white and non-Hispanic (Noble, Vega et al. 1997).

A similar analysis was done on the basis of socioeconomic status. The antenatal care of 47% of the study population was funded under public assistance programs and just over 46% were privately insured or 'self-pay', this latter categorization being regarded as a surrogate for economic wellbeing. The remaining 7% fell into an 'other' category indicating payment for antenatal care by any other means. Substance use was markedly higher in the publicly funded cohort compared with the privately insured or self-pay cohort: 51% of those positive for alcohol (compared with 42%); 67% of those positive for illicit substances (compared with 24%); and 64% of those using tobacco (compared with 30%) (Noble, Vega et al. 1997). The finding that tobacco use was strongly associated with use of other substances (smokers were 10 times more likely than non-smokers to use marijuana, 22 times more likely to use cocaine, and 21 times more likely to use ATS) supports other similar findings cited earlier.

The primary aim of the IDEAL study (cited earlier in 1.2.5) was to investigate antenatal exposure to methamphetamine (Arria, Derauf et al. 2006). The researchers focused recruitment in four city-based clinic sites in the US known to have many clients with issues related to methamphetamine use. In its analysis of data from 1,632 women based on both testing of meconium and self-report, the investigators determined that 5.2% used methamphetamine,

while 25% used tobacco, 6% used cannabis, 1.3% used barbiturates and fewer than 1% used other illicit substances (Arria, Derauf et al. 2006). Use of alcohol was measured only by self-report (22.8% of participants), given the lack of an appropriate toxicological screen (Arria, Derauf et al. 2006).

In a study in Utah (Buchi, Zone et al. 2003), 1,202 meconium samples from nearly twenty nurseries (including those for well babies and intensive care facilities) were assayed for antenatal exposure to methamphetamine, cannabis, and cocaine. Tests were positive for methamphetamine in 0.4%, for cannabis in 1.8% and for cocaine in 0.3%. The prevalence of positive meconium assays was higher in those in the intensive care nurseries than in those for well babies. Although these rates had declined in the 10 years since the researchers had conducted a prevalence study in Utah using urine samples given by women delivering at ten urban and suburban hospitals, the changes did not reach significance levels (Buchi, Zone et al. 2003).

In another US study conducted in Alabama public health clinics, the point prevalence of use of specified illicit substances by 6,195 women was determined by analysis of urine samples (Pegues, Engelgau et al. 1994). Findings indicated that just over 10% of participants were using one at least of the substances tested: cannabis (7.3%), cocaine (1.3%), opioids (1%), barbiturates (0.9%) and amphetamines (0.3%) (Pegues, Engelgau et al. 1994).

1.3.3 Alcohol Prevalence

Studies have often focused specifically on alcohol use due to its higher prevalence in the general population of many countries in the world. In addition, it is recognized that even if women do not have an established alcohol dependence diagnosis, women generally are drinking more problematically (Roche and Deehan 2002) (de Crespigny, Vincent et al. 2000).

With younger women, such patterns are likely to reflect use around the time of conception (Jonas, Dobson et al. 2000; Roche and Deehan 2002).

A national survey in which 6,000 Australian women were randomly selected from electoral rolls to complete the *AUDIT* questionnaire (a screening instrument to detect problematic alcohol use) attracted a 66% response rate (Fleming 1996). Of those currently drinking alcohol (just over 80% of respondents), 34% were classified according to *AUDIT* definitions as hazardous drinkers, 4% as harmful drinkers and 1% as alcohol dependent. Although the sample was from the general population, it further indicates problematic drinking by Australian women.

Western Australian researchers analysed self-report data from 4839 women twelve weeks after delivery (Colvin, Payne et al. 2007). The participants were a 10% randomly selected sample of all non-indigenous women giving birth in the state from 1995 to 1997. Women were asked questions about their alcohol use in the three months before pregnancy and in each of the trimesters of pregnancy. As is the usual pattern, nearly half of the women had not planned their pregnancy; almost 80% had consumed alcohol in the last three months before pregnancy; and over fifty percent had used alcohol in at least one of the trimesters (Colvin, Payne et al. 2007). The amount consumed outside the existing NHMRC guidelines for pregnancy (fewer than seven standard drinks per week and no more than two standard drinks on any one day)(National Health and Medical Research Council [NHMRC] 2001) did decline from the first trimester (when 14.8% of women used outside this guideline) to ten percent in both the second and third trimesters (Colvin, Payne et al. 2007).

In addition to the *National Survey on Drug Use and Health* in the US (highlighted earlier), other surveys sponsored by the Centers for Disease Control (CDC) give valuable information on alcohol use patterns in the US

(Floyd and Sidhu 2004). The Behavioural Risk Factor Surveillance System (BRFSS) collects state-based data on risk behaviours including alcohol use by pregnant women and those of child-bearing age. Analysis of data from 1991 to 1999, collected from women who were pregnant at interview, indicated that there was no significant change in alcohol use by these women over the ten year period (12.5% in 2001 compared with 12.4% in 1991), nor with binge drinking (11.2% compared with 12.3%) or with frequent drinking behaviour (1.6% compared with 0.8%)(Floyd and Sidhu 2004) (Morbidity and Mortality Weekly Report (MMWR) 2002).

The Pregnancy Risk Assessment and Monitoring System (PRAMS), another CDC program, conducts surveillance on maternal health-related behaviours (including alcohol use) through a mail-out sent postpartum (Floyd and Sidhu 2004; Phares, Morrow et al. 2004). The questionnaire enables enquiry of alcohol use before pregnancy and during the third trimester. Analysis of data from eight states in the US determined a prevalence of alcohol use during pregnancy ranging from 3.4% to 9.9% (Phares, Morrow et al. 2004). Predictors of alcohol use in seven of these states were: being older than 35, not of Hispanic ethnicity, having a high school education, and being in a higher income bracket. This contrasts with a Californian study cited earlier in which half those using alcohol were of Hispaqnic ethnicity (Noble, Vega et al. 1997).

International studies have also highlighted alcohol use by pregnant women and the potential for harm to the fetus. In a study by May and associates, data from three samples of women, two from the US and the third from South Africa, were analyzed (May, Gossage et al. 2004). The US samples were drawn from a large epidemiological and FAS prevention study being conducted with women of Indian ethnicity from the Northern Plains: the first sample was drawn from women attending Indian Health Service Clinics, the second from

those referred with their children to specialized developmental clinics, with a possible FAS diagnosis for the child based on antenatal alcohol consumption (May, Gossage et al. 2004). The third sample was of South African women whose children had a definite FAS diagnosis at birth.

Unsurprisingly, this prevalence of alcohol use in the latter sample (94.3%) was much higher than either of the US samples: 16.2% in the standard health clinics and 47% in those attending the developmental clinics. Binge drinking, at the five drinks per session level, was reported by 40.6% of the women attending the standard clinics, 53% of those attending the developmental clinics and 68.7% of women whose children had a confirmed FAS diagnosis. However, data on total drinks consumed over 30 days were less predictable. The number of drinks reported as having been consumed over 30 days was lower (47) for the Plains women attending the developmental clinics than for women attending the standard clinics (105 drinks) or the South African women (83 drinks). The researchers concluded that the variation in social conditions and belief systems between the three samples had a major impact on the women's drinking behaviours (May, Gossage et al. 2004).

A large Chilean study also focused on the identification of women whose alcohol consumption was at harmful levels (Aros, Mills et al. 2006). Over a period of five years (between August 1995 and July 2000), interviews were conducted with 9,628 women receiving antenatal care at a clinic in a lower middle-class area of Santiago. Those women who reported levels of alcohol use of 12 grams or more of absolute alcohol per month were subsequently interviewed if one of the other designated criteria was also fulfilled: reports of drinking at least 48 grams of alcohol on any occasion either during or before pregnancy, drinking every weekend or on more than three days per week, appearing nervous when alcohol consumption was raised, or having a past

history of substance abuse (Aros, Mills et al. 2006). Partners' reported drinking habits were also considered when selecting interviewees.

Interviews of the 987 women identified at risk and a cohort of non-drinkers women (n= 298) who served as a control group were all conducted in the interviewees' homes. Of the women at risk, 101 women were identified as consuming, on average, 48 grams of alcohol per day: 48 of the women admitted that level of use, while the other 53 were identified using a selection of criteria including social distress and previously reported alcohol use patterns. Hence, one percent of the total clinic sample was drinking at levels known to be toxic to the fetus. In addition, 72.3% of the cohort of 101 women was smoking an average of 9.8 cigarettes daily, further adding to potential fetal harm (Aros, Mills et al. 2006).

A smaller Californian study examined the prevalence of alcohol use by 826 pregnant women attending a Special Supplemental Nutrition Program for women and their children in the south of the state. Twenty-four percent of the women were consuming alcohol. White non-Hispanics, African-American, and English-speaking Hispanics, were twice as likely (30% for each of these ethnic groups) to be using alcohol compared to non-English-speaking Hispanics (O'Connor and Whaley 2003). The association between integration with the broader US society, so-termed 'acculturation', (principally measured by the preferred use of English and the place of birth being in the US) has also been documented with tobacco use (Detjen, Nieto et al. 2007). This latter study with 1,231 Hispanic women found a smoking prevalence of 21%; Hispanic women with higher acculturation were three times as likely to smoke as those leading more conservative and traditional lives (Detjen, Nieto et al. 2007).

1.4 Reduction in Use Associated with Pregnancy

In the 2001 National Drug Strategy Household Survey (NDSHS) in Australia, women who were either pregnant or breastfeeding were asked whether their consumption of alcohol had changed when pregnant – most drank less alcohol than usual (59%), four percent drank more, while 36% did not consume alcohol at all (Australian Institute Health and Welfare 2002). The 2007 NDSHS results showed that being pregnant and/or breastfeeding (*sic*) was more likely to be nominated as the reason for reduction of alcohol use by those who reported currently drinking at 'low risk' levels (10.5% of women interviewed) compared with the 5.5% of women who reported currently drinking at 'high risk' levels (Australian Institute of Health and Welfare 2008). The levels of risk were defined by the NHMRC guidelines at that time (National Health and Medical Research Council [NHMRC] 2001). In addition, the survey found that 11.3% of current smokers regarded being pregnant or 'wanting to start a family' as a motivator to change smoking behaviour (Australian Institute of Health and Welfare 2008).

US National Survey data (collected between 1996 and 1998) (Ebrahim and Gfroerer 2003) indicated that women decreased their use of illicit substances over the duration of pregnancy, with 28% of the users (2.8% of the sample of pregnant women) stopping use in the first trimester and 93% of the users being abstinent from illicit drug use by the third trimester. However when measured postpartum, the net reduction attributable to pregnancy was only 24%. In these data, use of illicit substances by women who were not pregnant but were of childbearing age was reported as 6.4%, with cannabis accounting for three-quarters of the illicit drug use. Ebrahim and colleagues in an analysis of alcohol data from an earlier survey (1991-1995) found that pregnant women were one-fifth as likely as non-pregnant women to binge drink. This

reduction was smallest among African-Americans and largest in those under thirty and those who had quit smoking (Ebrahim, Diekman et al. 1999). Generally, this analysis found that the factors significantly associated with binge drinking were being unmarried, being employed and being a current smoker.

In a study of an obstetric population in Ireland, the researchers examined two cohorts - 504 antenatal patients and 515 postnatal patients - with the use of toxicological screening via enzyme-linked immunoassay techniques (Bosio, Keenan et al. 1997). The rate of alcohol or illicit drug use was higher in the postnatal sample (7%) than in the antenatal population (3.6%), with cannabis being the most prevalent illicit substance (2.7% postnatally and 1% antenatally). Although not a measure of reduction in use for a specified cohort, the study's findings do indicate lower use patterns in women while pregnant.

A Philadelphian study followed 77 substance-using women throughout pregnancy who were given enhanced antenatal care with access to addiction counselling and extra family support: the Angels Program (Corse and Smith 1998). Discriminant analysis techniques were used to determine participant characteristics that were associated with likelihood of change in substance use while pregnant. Coming late to antenatal care, frequently using cannabis or cocaine, and having a range of psychosocial problems, were all indicative of difficulty in changing substance use habits.

1.5 Screening for Substance Use by Obstetric Care Providers

Given the high levels of risk associated with substance use in pregnancy, there is a clear need for effective screening by obstetric care providers, chiefly medical practitioners and midwives. Screening is generally understood as a preliminary procedure used to gather information about the likelihood that an

individual has a particular disease or condition, or is at risk. A screening tool sits within a public health approach of early intervention for a disease state or a problematic behaviour (Bowling 1997). Self-report and biological markers are the traditional tools used.

The need for effective screening tools within the pregnant population is evident, given the two patients (mother and fetus) being cared for, and the potentially higher levels of risk to the fetus than to the woman with any antenatal substance use.

However, it is well-documented, particularly in the tobacco literature, that health care providers do not always screen pregnant women for substance use (Moran, Thorndike et al. 2003) (Langer, Nigenda et al. 1998; Zapka, Pbert et al. 2000; Hotham, Atkinson et al. 2002). This inaction is happening despite the recognition for many years, specifically in relation to alcohol use, that pregnant women will at least reduce their use if counselled (Halmesmaki 1988; Rodgers and Lee 1988; Corse and Smith 1998).

Care providers may lack confidence in the substance use area and may even conclude, mistakenly, that their pregnant patients are not using substances (Weir, Stark et al. 1998; Chasnoff, Neuman et al. 2001). Certainly with the general population, it has been recognized that care providers not only fear losing rapport with patients if they discuss sensitive issues such as alcohol consumption but also hold negative views about those with drinking problems (Lock 2004). Pregnant patients often fear experiencing judgmental attitudes by care providers, and this has been recognized as one of the major barriers to substance-using women seeking antenatal care (Tobin 2005).

When screening does occur in clinical practice, it may not occur uniformly. Screening may be influenced by patient characteristics such as age, marital status and ethnicity (Weir, Stark et al. 1998; Kerker, Horwitz et al. 2004).

Care providers in public clinics have been recognized as more likely to give information on the importance of not using drugs during pregnancy than those practicing privately, with white educated women least likely to be questioned (Weir, Stark et al. 1998).

Research with tobacco has highlighted that the level of use is generally higher in older women (Cornelius, Goldschmidt et al. 2007), as is the level of alcohol use (Australian Bureau of Statistics 2006). A pregnant woman may have a further pregnancy; hence, by intervening in one pregnancy, enhanced outcomes in later pregnancies may result. Without assessment, with its potential for intervention, poorer pregnancy outcomes are likely to result (Quinlivan, Petersen et al. 1999).

In a Western Australian study with pregnant adolescents, many in the control group having usual care had no psychosocial or substance use history taken. However, those in the treatment group, who did undergo such assessments, were found to have higher substance use than in the general adolescent population in Western Australia, findings that provided a trigger for intervention (Quinlivan, Petersen et al. 1999).

1.5.1 Interventions Post-Screening: Brief

If performed at all, interventions are likely to be 'brief', given the time constraints in clinical settings. However, brief interventions are established as often leading to positive outcomes.

A Wisconsin study, in which women were given a brief intervention (two 15 minute counselling sessions) and followed up 48 months later, showed a significant effect in the treatment group compared to the controls in reduction of alcohol used in any 7 day period and in the number of binge drinking episodes. Those in the treatment group who became pregnant during the 48 month period showed the greatest reduction in use. The researchers concluded

that the sustained reduction in risky drinking in women of child-bearing age subsequent to this brief intervention had significant potential public health implications (Manwell, Fleming et al. 2000).

Another group of US researchers trialled a brief intervention with 45 pregnant women who completed a questionnaire and were briefly interviewed at the 1st, 2nd and 6th antenatal visit (Svikis and Jones 2005). Those women with a family history of alcoholism and a diagnosis of lifetime dependence on caffeine were less likely to cut down caffeine use while pregnant. This behavior was significantly linked with lifetime use of other substances ($p<0.05$), although not with pre-pregnancy alcohol use ($p<0.058$). The researchers suggested that their brief intervention could have application for the range of substances used antenatally (Svikis and Jones 2005).

1.5.2 Interventions Post-Screening: Higher Intensity

A number of researchers have conducted studies in which the level of intervention was more intense. In a large Californian study, following screening of nearly 50,000 pregnant women via an antenatal substance abuse screening questionnaire at first antenatal appointment, just over 2000 substance-using pregnant women were enrolled in the *Early Start* program, (Goler, Armstrong et al. 2008). Clinician referral, self-referral or positive urine toxicology results were the criteria for entry. The ongoing *Early Start* program integrates the services of a substance abuse expert and extra family support with standard antenatal care. There were significantly lower rates of neonatal assisted ventilation, preterm delivery and low birth weight if women participated in these additional interventions (Goler, Armstrong et al. 2008).

1.5.2.1 Motivational Interviewing

Other studies have focussed on the use of motivational interviewing to enhance patient outcomes. This patient-centred approach aims to increase the

likelihood of changing a behaviour by resolving any ambivalence (Miller and Rollnick 1991). In one multi-site US study, women of child-bearing age with risky drinking behaviours were enrolled in a program of four motivational interviewing sessions focused on alcohol use and one visit to a family planning service (Sobell, Sobell et al. 2003). There was both a reduction in alcohol use and an adoption of effective contraceptive methods by women in the study. These behaviours were greater in those with lower alcohol use at enrolment (as measured by the *AUDIT* score). Reduced alcohol consumption and adoption of effective contraception are both valuable contributors to minimizing the risk of an alcohol-exposed pregnancy (Sobell, Sobell et al. 2003).

Motivational interviewing had earlier been implemented in a small New Mexico study with 42 pregnant women who reported drinking at least one drink in the past month (Handmaker, Miller et al. 1999). All participants completed a structured interview and a detailed calendar record of their alcohol use over the past 2 months and were randomised to either treatment (one hour motivational interview) or control (informed about the risks of ante natal alcohol use and advised to consult local medical practitioner). Of the 34 women available for follow-up, there were small differences in number of drinks consumed; however, there were significant differences in the estimated blood alcohol concentration - a measure of potential fetal harm - in those exposed to the motivational interview (Handmaker, Miller et al 1999).

1.5.3 Reasons for Lack of Intervention

One of the obvious reasons for lack of intervention is unfamiliarity with screening methods and hence a compromised capacity for identification. Further, care providers have attributed failure to intervene, or intervene adequately, on lack of knowledge both of thresholds for adverse outcomes and

of referral resources, specifically with regard to alcohol use (Diekman, Floyd et al. 2000; Holl and Lussky 2003).

A small Melbourne study trialling a six month educational initiative for midwives and doctors showed that participants were subsequently significantly more likely to ask directly about psychosocial issues (such as substance use) and less likely to report being 'overwhelmed' by the prospect of intervention (Gunn, Hegarty et al. 2006). In a large Canadian study targeting midwives and physicians (n= 1088), just over 30% of physicians and 63.5% of midwives completed the survey on their use of standard screening tools for detecting antenatal substance use. Use of such a tool was significantly more likely by a recent graduate less than 40 years of age; further, those using tools were also more likely to discuss other psychosocial issues such as depression and past sexual abuse (Tough, Clarke et al. 2003).

1.5.2 Current Screening in Antenatal Care

It is evident that care providers do not always intervene with pregnant substance users. However, following a positive result to screening, they are clearly well positioned to do so. Currently, with the antenatal population in the Australian setting, 'routine' screening does occur for a number of conditions of potential risk. In 1999-2000, Australian hospitals providing maternity services were surveyed to ascertain the nature of screening that they conducted, with responses obtained from 119 hospitals of the 225 approached (Hunt and Lumley 2002). It was evident that the selection of conditions for routine screening may not be based on evidence of efficacy or identifiable guidelines (Hunt and Lumley 2002) (Dodd, Crowther et al. 2002). For example, national guidelines in Australia suggest that screening for Hepatitis C and HIV be reserved for higher risk individuals, yet there is a developing trend towards universal screening, as was indicated by close to 50% of respondents (Hunt

and Lumley 2002). At the time of Hunt and Lumley's survey, 90% of hospitals screened for diabetes, using variable protocols, despite a lack of evidence of effectiveness. However, the later findings of the Australian Carbohydrate Intolerance Study in Pregnant Women (ACHOIS) supported screening all pregnant women for gestational diabetes based on the potential to reduce adverse perinatal outcomes and improve maternal quality of life (McIntyre, Cheung et al. 2005).

A similar case can certainly be made for universal antenatal interventions in relation to tobacco use (Dodd, Crowther et al. 2002; Lumley, Oliver et al. 2004). However, despite good evidence of the efficacy of interventions, only 2 of the 119 respondents (1.6%) had written protocols, while another 30 (25%) included only an item on a checklist in their antenatal protocols (Hunt and Lumley 2002).

Hunt and Lumley's survey (2002) did not investigate the use of antenatal screening in relation to use of substances other than tobacco and there has been limited research into Australian practice in the area (Quinlivan, Petersen et al. 1999) or indeed into antenatal care practices more generally (Dodd, Crowther et al. 2002). More recently, a West Australian study showed that only 45% of health care providers regularly ask about alcohol consumption during pregnancy, with even fewer (25%) giving information on consequences of use (Payne, Elliott et al. 2005). The updated *Pregnancy Record* in South Australian public hospitals (SA Health 2008) now queries the number of 'drinks' (sic) of alcohol per week, and the number of daily cigarettes, instead of the previous *yes/no* in a simple check list. However, (other) 'recreational drug use' is queried without quantification (SA Health 2008). This assessment of substance use falls within a 'social history' section of the *Pregnancy Record*, with the injunction: '*all items should be reviewed as pregnancy progresses*'

(SA H ealth 2 008). C urrently, the l ikelihood o f s uch re view c an o nly b e speculative.

Although screening can only be regarded as the first step in intervening with a pregnant woman in relation to her substance use, it is an essential first step, and one currently not generally effectively performed. A possible explanation is the lack of an appropriate and effective screening tool. This need has been highlighted in Australia and elsewhere (IGCD Cost Shared Funding Project 2005), (McPherson and Hersch 2000; Jones and Johnson 2001). However, the emergence of a tool fulfilling all desired criteria has not yet occurred.

The investigation of screening tools appropriate for use with pregnant women is detailed in Chapter 3.

Chapter 2

Phase I Study: Substance Use in the Study Population

Prior to the investigation of screening tools for substance use in pregnancy, a Phase I study was conducted to determine the patterns of substance use in the selected pregnant population in which screening tools would be investigated. In addition, it was recognized that such data could augment current Australia data related to pregnancy, which do not demonstrate pregnancy-related changes or distinguish between pregnant and lactating women (Australian Institute Health and Welfare 2002).

2.1 Methods

2.1.1 Questionnaire

A questionnaire was developed to investigate the patterns of substance use by antenatal patients at two South Australian public hospitals- the Women's and Children's Hospital and the Lyell McEwin Health Service. Together, these two hospitals account for 35% of births in South Australia (Chan, Scott et al. 2008) (Chan, Scott et al. 2005). The study was approved by the Human Research Ethics Committee at the Child, Youth and Women's Health Service (CYWHS) [Approval Number 1713 5/2008] of which the Women's and Children's Hospital is part. A copy of this approval is in *Appendix One* to this thesis. Due to cross-institutional arrangements, this conferred approval for research at the Lyell McEwin Health Service and fulfils the ethics approval requirements of the University of Adelaide.

The questionnaire entitled *Use of Drugs in Pregnancy Prevalence Study (*see *Appendix One)* was designed to determine use of the full spectrum of

psychoactive substances, both *'in a typical month when you were not pregnant, not trying to become pregnant, and not breastfeeding'* and '*in the last month'*. In addition, women were asked to nominate, for each of those time frames, the '*number of days of use in a typical month*' and the '*maximum amount used in any one day or session'*. The content of the questionnaire not only enabled collection of data on substance use in pregnancy and prior to pregnancy, but, due to the inclusion of a short section of socio-demographic data, was able to link these data with age of the participant and trimester of pregnancy, reproductive history, and medical and pregnancy complications in both this and earlier pregnancies.

2.1.2 Sample Size

Based on data from the 2001 National Drug Strategy Household Survey (Australian Institute Health and Welfare 2002), data confirmed in the most recent of these surveys (Australian Institute of Health and Welfare 2008), it was anticipated that the illicit substance of highest prevalence would be cannabis. The number of participants to be interviewed was based on this prevalence estimate which found that 7% of pregnant and/or breastfeeding women used cannabis (Australian Institute Health and Welfare 2002). For the purposes of this study, a 95% confidence level with absolute bounds on the accuracy of the estimate of prevalence at +/- 2% resulted in the minimum required sample size estimate of 626. Power calculations were performed using *nQuery Advisor 5.0 (*Statistical Solutions, Saugus, Massachusetts).

Given the relative proportion of births at the two hospitals (24.7% at the Women's and Children's Hospital and 11.2% at the Lyell McEwin Hospital) (Chan, Scott et al. 2005; Chan, Scott et al. 2008), it was planned that approximately 400 participants would be from the Women's and Children's Hospital and approximately 200 from the Lyell McEwin Service. However,

towards the end of 2005, a large multi-site international study began at the Lyell McEwin Health Service and it was recognized that continued research at this site would be difficult, with the competition between studies for participants. Hence, the focus of this research shifted to the Women's and Children's Hospital earlier than originally anticipated.

2.1.3 Study Duration

Prior to the commencement of the study, informal consultative meetings were held with antenatal clinic staff at both hospitals to inform them of the study's purpose. During the period from July 2005 to April 2006, clinic staff at the two hospitals agreed to hand the questionnaire for self-completion to all first visit antenatal women, with an envelope to seal for return to any staff member in the clinic. This ensured the participants' anonymity. Insistence on first visit women was based both on the wish to contact every antenatal patient and the need to avoid any woman being surveyed on more than one occasion. The researcher visited both sites on a weekly or bi-weekly basis: between July and September 2005 at the Lyell McEwin Health Service and between October 2005 and April 2006 at the Women's and Children's Hospital. These visits served the purpose of collection of completed questionnaires, of ensuring sufficient 'blank questionnaires were held for future use, and of continuing liaison with the clinic staff to encourage ongoing cooperation.

2.1.4 Analysis of Data

Log-binomial models were used to compare the prevalence of substance use across the different subgroups. McNemar's test was used to compare substance use between pregnancy and pre-pregnancy states. All these calculations were performed using SAS Version 9.1 (SAS Institute Inc., Cary, NC, USA). Where there was a significant difference across the defined

categories (trimester of pregnancy, age and pregnancy history), post-hoc comparisons were performed.

2.2 Results

A total of 748 out of 2173 first visit antenatal patients (34.4%) returned questionnaires, 100 from 398 eligible women (25%) at the LMHS and 648 from 1,775 eligible women (36.5%) at the WCH. There were no reports from staff of women refusing to answer the questionnaire. A total of 418 respondents were in their 1st trimester, 272 in their 2nd trimester, and 32 in their 3rd trimester. Twenty-six participants did not give the date of their last menstrual period; hence, the trimester at interview could not be determined.

Overall, the most prevalent substance '*used in [the] last month*' was tobacco (18.5 %). Alcohol was used by 11.9% of respondents and cannabis, the most common illicit substance, by 4.5%. Reported substance use while pregnant and in a typical month prior to pregnancy are both shown in Table 1. There were highly significant differences for all substances ($p < .0001$) between use in a typical month and use while pregnant. Prevalence of use in a typical month before pregnancy was tobacco (29.9%), alcohol (89.2%) and cannabis (8.2%).

There were low numbers of women reporting use, either before or during pregnancy, (B) and (D) respectively, of illicit substances other than cannabis: amphetamines (B20, D 2); hallucinogens (B 4, D 0); 'non-medical' use of benzodiazepines (B 10, D 0); and 'non-medical' use of opioids (B 4,D3). No respondents reported use of cocaine, either prior to or during pregnancy. Of the 748 respondents, 26 women did not respond to one or other of the questions pertaining to these substances.

Women were asked the maximum amount consumed in a day and the number of days that use occurred. Tobacco was usually used daily; other substances were used less regularly. This pattern is demonstrated in data presented in Tables 2 through to 7 which show the reported use of tobacco, alcohol and cannabis during pregnancy, categorized by trimester. Data are only shown for those participants who answered both questions: 'number of days of use' (in the last month) and 'maximum amount used in any one day or session': 138 tobacco users, 89 alcohol users and 61cannabis users. Several participants did not answer either or both of these questions: 26 women for tobacco, 32 for alcohol and 27 for cannabis.

Table 1

Substance use before and during pregnancy

n = 748

	Tobacco	**Alcohol**	**Cannabis**
Typical month *	**224 (29.9%)**	**667 (89.2%)**	**61 (8.2%)**
While pregnant	**138 (18.5%)**	**89 (11.9%)**	**34 (4.5%)**
Ceased use when Pregnant	**86 (38.4% of those using typical month)**	**578 (86.7% of those using typical month)**	**27 (44.3% of those using typical month)**
***P*-value**	**< 0.001**	**< 0.001**	**< 0.001**

'not pregnant, not trying to become pregnant, and not breastfeeding'

Table 2

Number of Days of Tobacco Use per Month during Pregnancy

in Relation to Trimester

n = 722*

Days of Tobacco Use /Month		**0**	**1-5**	**6-10**	**11-20**	**21-29**	**30**
1st Trimester	418	349	8	5	5	1	50
2nd Trimester	272	222	4	5	6	1	34
3rd Trimester	32	26	2	0	0	0	4
Total	**722**	597	14	10	11	2	88

*Question specifying trimester not answered by 26 women in study (of whom 13 reported tobacco use)

Table 3

Maximum Number of Cigarettes per Day

during Pregnancy in Relation to Trimester

n = 125*

Maximum Number Cigarettes/Day		**1-5**	**6-10**	**11-15**	**16-20**	**21-25**	**26 +**
1st Trimester	69	26	25	10	6	1	1
2nd Trimester	50	24	11	6	5	3	1
3rd Trimester	6	3	1	0	1	1	0
Total	**125**	53	37	16	12	5	2

*Question specifying trimester not answered by 13 women who reported tobacco use

Table 4

Number of Days of Alcohol Use per Month during Pregnancy

in Relation to Trimester

n = 722*

Days of Alcohol Use /Month		**0**	**1-5**	**6-10**	**11-20**	**21-29**	**30**
1st Trimester	418	370	42	4	0	0	2
2nd Trimester	272	238	27	5	1	0	1
3rd Trimester	32	26	6	0	0	0	0
Total	**722**	634	75	8	1	0	3

*Question specifying trimester not answered by 26 women in study (of whom 2 reported alcohol use)

Table 5

Maximum Amount of Alcohol Consumed (standard drinks)

per Day during Pregnancy in Relation to Trimester

n= 87*

Maximum Amount Alcohol (in standard drinks) /Day		**1**	**2**	**3-5**	**6-10**	**11+**
1st Trimester	48	35	7	3	2	1
2nd Trimester	34	23	10	0	1	0
3rd Trimester	5	4	1	0	0	0
Total	**87**	62	18	3	3	1

*Question specifying trimester not answered by 2 women who reported alcohol use

Table 6

Number of Days of Cannabis Use per Month during Pregnancy

in Relation to Trimester

n = 722*

Days of Cannabis Use /Month		**0**	**1-5**	**6-10**	**11-20**	**21-29**	**30**
1st Trimester	418	402	11	2	0	0	3
2nd Trimester	272	262	4	0	2	0	4
3rd Trimester	32	29	0	0	1	0	2
Total	**722**	693	15	2	3	0	9

*Question specifying trimester not answered by 26 women in study (of whom 4 reported cannabis use)

Table 7

Maximum Amount of Cannabis Consumed (cones or joints)

per Day during Pregnancy in Relation to Trimester

n = 30*

Maximum Amount Cannabis (in cones or joints) /Day		**1**	**2**	**3-5**	**6-10**	**11+**
1st Trimester	17	12	2	3	0	0
2nd Trimester	10	3	1	5	0	1
3rd Trimester	3	0	1	1	0	1
Total	**30**	15	4	9	0	2

*Question specifying trimester not answered by 4 women who reported cannabis use

For all data pertaining to the current pregnancy, women were classified according to the following parameters self-declared at interview: (1) trimester of pregnancy, (2) pregnancy history, (3) age, as well as the hospital at which antenatal care was being given. The data relating to these parameters at interview are shown in Table 8.

2.2.1 Trimester of Pregnancy

Prevalence of use was analyzed in relation to trimester of pregnancy at first visit. There was no significant difference between the three trimesters in the prevalence of tobacco use (p=0.797), alcohol use (p=0.749), or cannabis use (p=0.313).

2.2.2 Pregnancy History

The pregnancy history of the participants was classified according to whether they had previous pregnancies and whether these had resulted in 'live births'; substance use was analysed in relation to this documented history (Table 8). Women in their first pregnancy and those with no pregnancy losses had significantly lower tobacco use than women with previous pregnancy losses, p= 0.012 and p= 0.005 respectively.

Women in their first pregnancy also had significantly lower alcohol consumption than women with previous pregnancy losses (p= 0.008). There were no significant differences in the prevalence of cannabis use between the three pregnancy history groups.

2.2.3 Age

Participants were divided into three age categories, a modified version of categories used in the National Survey on Drug Use and Health in the US (US Department of Health and Human Services 2004), and substance use analysed on this basis. Tobacco use by women aged 15-24 years was significantly greater than use by either women aged 25-29 years ($p < .0001$) or women

aged 30-44 years (p< .0001). However, there was no significant difference in prevalence between women in the two older age groups (25-29 years and 30-44 years).

In addition, there was significantly greater cannabis use by women aged 15-24 years than by women aged 25-29 years (p = 0.0113) or by women aged 30-44 years (p= 0.038). However, there was no significant difference in prevalence of use of cannabis between women in the two older age groups. There were no significant differences between women in the three age categories in relation to alcohol use.

Table 8

Substance Use during Pregnancy

	Tobacco	Alcohol	Cannabis
Trimester			
Trimester 1 (*n* = 418)	69 (16.5%)	48 (11.5%)	16 (3.8%)
Trimester 2 (*n* = 272)	50 (18.4%)	34 (12.5%)	11 (4.0%)
Trimester 3 (*n* = 32)	6 (18.8%)	5 (15.6%)	3 (9.4%)
Unknown (*n* = 26)	13 (50.0%)	2 (7.7%)	4 (15.4%)
P-value	0.797	0.749	0.313
Pregnancy history			
First pregnancy (*n* = 258)	41 (15.9%)	20 (7.8%)	13 (5.0%)
Previous pregnancies but no losses (*n* = 258)	38 (14.7%)	33 (12.8%)	5 (1.9%)
Previous pregnancy losses (*n* = 231)	58 (25.1%)	36 (15.6%)	15 (6.5%)
Unknown (*n* = 1)	1 (100.0%)	0 (0.0%)	1 (100.0%)
P-value	0.005	0.030	0.059

Age group			
15–24 years (*n* = 196)	**62 (31.6%)**	**18 (9.2%)**	**16 (8.2%)**
25–29 years (*n* = 219)	**28 (12.8%)**	**23 (10.5%)**	**5 (2.3%)**
30–44 years (*n* = 320)	**44 (13.85)**	**47 (14.7%)**	**12 (3.8%)**
Unknown (*n* = 13)	**4 (30.8%)**	**1 (7.7%)**	**1 (7.7%)**
***P*-value**	**< 0.001**	**0.131**	**0.016**

2.2.4 Hospital Attended

Prevalence of substance use while pregnant was also analysed according to which of the two surveyed hospitals the women were attending. There was a significant difference in the prevalence of use of tobacco between women at the LMHS and the WCH (p <.0001), with 30 women (of 100) -30% - at the LMHS recording tobacco use and 97 women (of 648) -14.9% - at the WCH recording tobacco use. There was no significant difference in the prevalence of use of either alcohol or cannabis between the two institutions.

2.3 Parameters Associated with Cessation of Use of Specified Substance

The data were analysed to determine if any of the parameters at interview (first antenatal visit): trimester, pregnancy history, or age, were associated with the change in use of the substance in question from user to non-user (ceased use). These analyses are shown in Table 9.

Neither 'trimester when questioned' (p=0.610), 'pregnancy history' (p=0.166) nor 'age' (p=0.207) were independently associated with the likelihood of

having ceased tobacco. In relation to alcohol, neither 'trimester when questioned' (p= 0 .795) n or 'age' (p=0.185) were i ndependently as sociated with the likelihood of ceasing use. However, the likelihood of ceasing alcohol use was f ound to d iffer ac cording to ''pregnancy history (p = 0.014), with women i n the ir f irst pre gnancy s ignificantly more l ikely t o c ease a lcohol u se than women who had experienced previous pregnancy losses (p = 0.005).

The limited number of women using cannabis prior to pregnancy did not allow analysis of whether any of the nominated factors were independently associated with the likelihood of ceasing use.

Table 9
Cessation since Pregnant (Linked to Interview Parameters)

	Tobacco	Alcohol	Cannabis
Trimester	(*n* = 224)	(*n* = 667)	(*n* = 61)
Trimester 1	51 of 120 (42.5%)	324 of 371 (87.3%)	19 of 34 (55.9%)
Trimester 2	31 of 81 (38.3%)	215 of 247 (87.0%)	10 of 20 (50.0%)
Trimester 3	2 of 8 (25.0%)	23 of 28 (82.1%)	1 of 4 (25.0%)
Unknown	2 of 15 (13.3%)	19 of 21 (90.5%)	0 of 3 (0.0%)
P-value	0.610	0.795	-
Pregnancy History			
First pregnancy	36 of 77 (46.8%)	209 of 228 (91.7%)	14 of 27 (51.9%)
Previous pregnancies but without losses	18 of 56 (32.1%)	203 of 234 (86.8%)	5 of 9 (55.6%)
Previous pregnancy losses	32 of 90 (35.6%)	169 of 205 (82.4%)	11 of 24 (45.8%)
Unknown	0 of 1 (0.0%)	-	0 of 1 (0.0%)
P- value	0.166	0.0114	-

Age group			
15–24 years	**30 of 92 (32.6%)**	**146 of 163 (89.6%)**	**10 of 24 (41.7%)**
25–29 years	**25 of 53 (47.2%)**	**175 of 197 (88.8%)**	**9 of 14 (64.3%)**
30–44 years	**30 of 74 (40.5%)**	**252 of 299 (84.3%)**	**11 of 22 (50.0%)**
Unknown	**1 of 5 (20.0%)**	**8 of 8 (100.0%)**	**0 of 1 (0.0%)**
***P*-value**	**0.207**	**0.185**	**-**

2.4 Medical or Pregnancy-related Complications

Pregnancy-related or medical complications in the current pregnancy and/or in previous pregnancies were also queried.

Sixty-five women noted 'complications' in the current pregnancy and 151 in a previous pregnancy or in a number of previous pregnancies. Those reporting complications in the current pregnancy that are known to be associated with substance use (n=7) are shown in Table 10 with reported substance use both *in the last month* and *in a typical month when not pregnant, not trying to become pregnant, and not breastfeeding.*

Table 10

Reported Pregnancy Complications in Current Pregnancy: Substance Use Last Month and Typical Month Prior to Pregnancy (n=7)

Participant Number	**Report of complication (in current pregnancy) known to be associated with substance use**	**Substance use *in the last month***	**Substance use *in a typical month when you were not pregnant, not trying to become pregnant, and not breastfeeding***
136	Gastroschisis (baby)	Daily tobacco 6/day	Daily tobacco 6/day
142	Loss of one twin	Nil	Nil
196	Heart defect (baby)	Nil	Nil
206	Asthma	Daily tobacco 15/day	Daily tobacco 15/day
214	Loss of one twin	Occasional heavy* alcohol	Occasional heavy alcohol Occasional cannabis
326	Breathing difficulties	Nil	Nil
661	Asthma	Nil	Nil

***** ≥4 standard drinks in a session

Most participants did not report pregnancy-related or medical complications that are known to be associated with substance use. For those that did report such complications in the current pregnancy, only three of the seven reported use of substances *in the last month*: a tobacco user whose baby had been diagnosed *in utero* with gastroschisis, a tobacco user reporting asthma, and a woman with occasional heavy alcohol use (≥4 standard drinks in a session) who had already lost one of the twins she was carrying. None of these three women had changed their use from the pre-pregnancy situation.

Of the 151 women who reported medical or pregnancy-related complications in one or more earlier pregnancies, 35 reported complications known to be associated with substance use. Table 11 shows these data and the substance use of these women *in the last month.* Use prior to the current pregnancy for

these women (that is, use '*in a typical month when not pregnant, not trying to become pregnant, and not breastfeeding*') is also shown in this table.

Table 11

Reported Complications in Any Previous Pregnancy: Substance Use Last Month and Typical Month Prior (n=35)

Participant Number	**Report of earlier pregnancy with complication known to be associated with substance use**	**Substance use *in the last month***	**Substance use *in a typical month when not pregnant, not trying to become pregnant, and not breastfeeding***
7	Postpartum haemorrhage	Nil	Nil
53	Asthma	Nil	Nil
57	Premature rupture of membranes	Daily tobacco 10/day	Daily tobacco 15/day
91	IUGR, oligohydramnios	Occasional tobacco Occasional alcohol	Occasional tobacco
109	Asthma	*No response*	Daily tobacco/number cigs per day not disclosed
137	Placenta praevia	Nil	Daily tobacco 1/day
140	Placenta praevia (Grade 3)	Nil	Occasional alcohol
168	Miscarriage	Nil	Occasional alcohol
188	Placenta praevia	Nil	Nil
189	Post-partum haemorrhage	Nil	Nil
195	Miscarriage	Nil	Nil
201	Miscarriages	Nil	Occasional heavy* alcohol
218	Miscarriage	Nil	Nil
238	Stillbirth	Nil	Nil

240	Preterm labour	Nil	Daily tobacco / number cigs per day not disclosed
255	Miscarriages	Nil	Occasional alcohol
267	Loss of one twin	Daily tobacco 15/day	Daily tobacco 15/day
297	Miscarriage	Nil	Occasional alcohol
301	Miscarriages	Nil	Nil
319	Miscarriage	Nil	Daily alcohol 3 standard drinks/day
323	Labour complications-emergency caesarean section	*No response*	Daily tobacco 20/day
331	Miscarriage	Nil	Nil
360	Preterm labour. Placental abruption.	Nil	Nil
368	Preterm premature rupture of membranes	Tobacco 5/day 20 days/month	Daily tobacco 5/day
381	Preterm labour	Occasional alcohol	Occasional heavy alcohol
460	Miscarriage	Nil	Occasional heavy alcohol
475	Preterm labour	Nil	Occasional alcohol
486	Severe asthma attack	Daily tobacco10/day Daily heavy cannabis 4 cones/day	Daily tobacco15/day Daily heavy cannabis** 6 cones/day
535	Miscarriage	Nil	Occasional smoker Occasional heavy alcohol
557	Miscarriage	Nil	Occasional alcohol
568	Preterm labour	*No response*	*No response*
668	Miscarriage	Occasional alcohol	Occasional heavy alcohol
705	Miscarriage	Daily tobacco 3/day	Daily tobacco 12/day Occasional heavy alcohol
707	Miscarriage	Occasional heavy cannabis	Occasional heavy cannabis
720	Miscarriage	Nil	Occasional heavy alcohol

***** ≥4 standard drinks in a session ** ≥3 cones/ joints/day

Of participants who reported pregnancy-related or medical complications associated with substance use in a previous pregnancy or pregnancies, three were using *in the last month* at pre-pregnancy levels, although six reported some reduction in use. Thirteen of the 35 women had used previously, but were currently abstinent, while ten of the 35 women were non-users of substances both *in the last month* and prior to pregnancy.

2.5 Discussion of Results

This Phase I study showed that tobacco, alcohol and cannabis were the substances of highest use in pregnancy in the study population. Tobacco prevalence was concordant with other data sources (Chan, Scott et al. 2005; Chan, Scott et al. 2008), while cannabis prevalence was somewhat lower than predicted from previous data (Australian Institute Health and Welfare 2005). However, alcohol prevalence while pregnant was significantly lower than expected, 47% of pregnant or breastfeeding women having reported alcohol use in the 2004 NDSHS (Australian Institute Health and Welfare 2005).

These alcohol data may reflect the impact of an ongoing state government-supported campaign in South Australia, which commenced in late 2004, and has heavily promoted the need for an 'alcohol-free' pregnancy (Children Youth and Women's Health Service 2004). It is uncertain whether the campaign affected the accuracy of respondents self-reports, given that it has been identified that many women experience guilt if using any substances while pregnant (Poole and Dell 2005). Certainly, a higher proportion of nulliparous women stopped using alcohol, with a significantly higher likelihood than for women who recorded previous pregnancy losses. This could be interpreted as first-time 'mothers-to-be' keen to adhere to the 'no alcohol' message; on the other hand, it could be expected that women who had had pregnancy losses

would be more conservative about alcohol use. However, the majority of multiparous women are likely to be older than those in their first pregnancy. It is recognized that while the overall proportion of females in Australia using alcohol at 'risky' or 'high risk' levels has increased over recent years, the behaviour is known to steadily increase in women from their mid 20s to mid 60s, with only those in their late teens and early 20s using more problematically (Australian Bureau of Statistics 2006).

There were no significant differences in prevalence of use of any of the substances between women in the three trimesters. Earlier studies have indicated decreasing use of alcohol throughout pregnancy (Condon and Hilton 1988; Colvin, Payne et al. 2007) and of cannabis (Chen and Kandel 1998), although this has not been observed in heavier users (Fried, Barnes et al. 1985). In this study, prevalence of use for cannabis was higher for women presenting in their third trimester, (9.4%, compared with 4.1% in the second trimester, and 4.1% in the first trimester); inability to detect a statistically significant difference from use in earlier trimesters may be reflective of the lower power with the small sample of third trimester women. The relatively small number of third trimester women is not unexpected given that women were interviewed at first visit and the majority of women book earlier than the third trimester. The higher reported rates of cannabis use by these late-booking women could relate to the characteristics of women who book into antenatal care late in pregnancy, such as use of tobacco (Kupek, Petrou et al. 2002) and fear of detection of drug use (Reis, Mills-Thomas et al. 1992).

The group of women with previous pregnancy losses was more likely to be users of both alcohol and tobacco, an unsurprising association given the established harms of these substances; however, it does indicate extra caution was not being exercised in this subsequent pregnancy. Interestingly, recently

published data indicate that, even if postnatal women were given advice regarding avoidance of unfavourable lifestyle influences such as use of tobacco and alcohol, better pregnancy outcomes, specifically increased birth-weight, did not occur in future pregnancies. This is possibly reflective of failure to heed such advice or perceived inability to effect such lifestyle changes (Lumley and Donohue 2006).

Although there was no difference in prevalence of alcohol use between women across the three delineated age groups, younger women (15-24 years) were more likely to use both tobacco and cannabis. No comparable Australian data are available for age-related prevalence of substance use during pregnancy. US data reports higher rates of 'binge' drinking in the 15-25 year age group, although that survey does not report age-related overall prevalence of alcohol use (US Department of Health and Human Services 2004). US data also indicates higher rates of smoking prevalence for women under 26 (US Department of Health and Human Services 2004); however, no age-related data are available for pregnancy-related prevalence of cannabis use specifically, as data collection focused on illicit substance use in general (US Department of Health and Human Services 2004).

In this study, there was a significant difference in the reported use of tobacco between the two institutions. This was not unexpected as women attending the LMHS are, in general, of lower socio-economic status and hence more likely to smoke (Turrell, Stanley et al. 2006). Possibly due to the low number of participants from the LMHS, there was insufficient statistical power to detect a difference between the two institutional groups with respect to prevalence of alcohol and cannabis use, with similar reported alcohol use by the LMHS participants, and a trend towards higher cannabis use.

Overall analysis to determine whether any of the recorded factors present at start of pregnancy (trimester at interview, age, or pregnancy history) were useful predictors of the likelihood of then ceasing the major substances under consideration was of limited value. Nulliparous women were more likely to cease alcohol use but none of the factors was independently associated with changes to tobacco use. The limited number of women reporting use of cannabis did not enable such analysis for this substance.

These data relating to these women with complications known to be associated with substance use reflect the overall findings for this Phase I study, namely that women reduce use of all substances when pregnant. However, clearly not all women do, and this is especially of concern when women have already had a significant health problem diagnosed in this pregnancy or a tragic event such as an intrauterine fetal death in this, or a previous, pregnancy.

2.5.1 Limitations to this Study

The fact that only 34.4% of those eligible entered the study weakens the value of the data in augmenting the existing Australian picture of substance use by pregnant women. Reasons for this low entry rate are not evident as there were no reports from clinic staff of women refusing to respond. It is possible that some non-respondents may have used substances while pregnant, but did not wish to disclose such use even in an anonymous, self-administered questionnaire which was sealed before return. Further, it is possible, but can only be speculative, that partners or others accompanying the women to their first antenatal visit negatively influenced their willingness to respond.

In addition, not all participants answered all the questions. This was most apparent with questions relating to use of substances while pregnant and with report of trimester of pregnancy. Reluctance to disclose this information could

be related either to innate concerns about the anonymity of the survey or simply disinterest in answering all questions in the three page questionnaire.

Further, the study relied heavily on the participation of antenatal clinic staff (to hand questionnaires to all first visit patients) and this participation may have been jeopardized by busy work-loads. The negligible reporting of other illicit substances compared with existing data (Australian Institute Health and Welfare 2005) may be reflective of the low return rate. The possible experience of guilt has already been noted. If this was the situation in the population surveyed here, identified rates of use would be an under-estimate, noted earlier as possible in relation to reporting of alcohol use. Intuitively, this is more likely than the possibility that the prevalence of use in the sample is an over-estimate.

However, the concordance of study data relating to tobacco with the prevalence rate reported for tobacco use for all pregnant women in South Australia at first antenatal visits (19.4%) (Chan, Scott et al. 2005) does add support to the validity of the findings.

It would have been useful to elicit further information from the participants, such as socioeconomic characteristics and marital status. However, with a self-administered questionnaire, the researchers had to balance a desire for more comprehensive data with the likelihood that women would not respond at all to a questionnaire that was 'too' lengthy. Hence, apart from age and pregnancy history, no other demographic data were collected. Age and pregnancy history are not independent variables; however, their relationship is a complex one and it could not be controlled for in statistical analysis of the data.

Another limitation is that, owing to the study utilizing a self-administered questionnaire, it was impossible to reliably quantify the amount of substance a woman was using on any one day or occasion. Even tailor-made cigarettes are

subject to variation from the labelled nicotine content due to possible compensatory smoking (Strassera, Lermana et al. 2004). Further, it is recognized that the concept of a standard drink is not generally well understood in the community (DrinkWise.com.au 2009). This potential for inaccurate estimation of alcohol use is also a feature of the SA Health's *Pregnancy Record* with its query of 'number of drinks' (SA Health 2008).

Chapter 3

Screening Tools for Substance Use in Pregnancy

'Self-report' questionnaires and biological markers are the tools traditionally used to screen for substance use. Their use allows risk assessment and early intervention if appropriate.

This next section examines available tools for detection of substance use during pregnancy, their features, a perspective on their origin and development, and current usage.

As the Phase I study had confirmed tobacco, alcohol and cannabis as the substances of highest prevalence in pregnancy in the populations under study, this review of screening tools (those involving both 'self-report' and biological markers) primarily focuses on those used for these three substances.

3.1 Screening Tools: Self-Report

Reviews of self-report tools have largely focussed on screening tools for alcohol (Russell, Martier et al. 1996; Svikis, McCaul et al. 1996; Bradley, Boyd-Wickizer et al. 1998; McPherson and Hersch 2000; Karoll 2002; Savage, Wray et al. 2003; Tough, Clarke et al. 2003)(Russell 1994), although tools developed to detect a broader range of drugs have also been reviewed (Alexander 2003;NSW Department of Health 2006;Center for Substance Abuse Prevention 1993; McPherson and Hersch 2000).

However sometimes, 'alcohol use' or 'substance use' questions have been embedded in general health questionnaires (Burd, Martsolf et al. 2003), in questionnaires investigating wellbeing more broadly (Lindenberg, Strickland et

al. 1999), and in questionnaires examining the likelihood of pregnant women engaging with health services (Tobin 2005).

Because historically the emphasis on pregnant women's substance use has been on alcohol use, a number of tools have been developed, including the *T-ACE* (Chang, Wilkins-Haug et al. 1998; Chang 2001) (Sokol, Martier et al. 1989), the *TWEAK* (Russell 1994a), and the *4Ps* (Chasnoff, McGourty et al. 2005). Tobacco screening has not attracted as much attention, despite the continuing use of tobacco in pregnancy and its recognized negative impacts. However, the tool, *Four Maternal Smoking Questions*, has been used (Kharrazi, Epstein et al. 1999), as has the *Fagerstrom Tolerance Questionnaire* and revisions of that questionnaire (Fagerstrom 1978; Heatherton, Kozlowski et al. 1991; Tate and Schmitz 1993).

Cannabis and other illicit substances have more recently received greater emphasis. Modification of the *CAGE* (C= cut down, A= annoyed, G= guilt, and E=eye-opener) has been employed for detection of illicit substance use by pregnant women (Midanik, Zahnd et al. 1998), although tools for detection of cannabis use specifically are limited. The *Timeline FollowBack*, a tool developed for detection of problem alcohol use, has been used to detect cannabis use in the general population (Sobell, Brown et al. 1996) and for adolescents specifically (Duhig, Cavallo et al. 2005); however, it has only been used with pregnant women for detection of alcohol use (Chang, Wilkins-Haug et al. 1998; Chang 2001).

The databases, *Academic Search Premier*, *BioMed Central*, *PsychInfo* and *PubMed* were searched from 1966 to December 2006 using the terms 'screen' AND 'drug' AND 'pregnan*', and the *Cochrane Library* was searched using the terms 'screen' OR 'drug' AND 'pregnan*', thus enabling a review of published screening tools for substance use in pregnancy.

Investigation of the development of screening tools for pregnant women revealed that most have not undergone any validation or statistical exploration and that use has been implemented on a somewhat *ad hoc* basis, with subsequent use leading to acceptance and then further use. The more entrenched has become the use of a tool, the more the use has been legitimized. Published Australian research on the development and trial of self-report questionnaires with pregnant women is extremely limited with the literature on screening tools heavily weighted to research in the United States. The only Australian screening tool reported was developed for smoking cessation (Project Team Mercy Hospital for Women Southern Health and Women's and Children's Health 2001) and is discussed in 3.1.2.

3.1.1 Alcohol

A brief questionnaire - the *T-ACE* - was developed almost twenty years ago as arguably the first pregnancy-specific tool to enable care providers to detect risky drinking (Sokol, Martier et al. 1989) although standard quantity-frequency questionnaires have also been popular, both in pregnancy (Waterson and Murray-Lyon 1989; Clark, Dawson et al. 1999) and for pre-pregnancy assessment (Kaskutas and Graves 2001).

In the development of *T-ACE*, Sokol *et al* interviewed 971 women at their first antenatal visit who admitted to use of alcohol at 'some time' and administered two questionnaires: the 25 question Michigan Alcoholism Screening Test (*MAST*) to detect alcohol-related psychosocial problems, and the four question *CAGE* (Sokol, Martier et al. 1989). Both have been well-regarded and well-used screening tools for problematic drinking behaviours. In addition, a 'tolerance' to alcohol question was added: '*how many drinks does it take to make you feel high*?', as it was recognized that women may answer this question honestly, since it may not be perceived as enquiring about their level

of alcohol consumption *per se*. Of the 971 interviewed, only 42 were found to be drinking at risky levels for pregnancy - this being defined as the equivalent of ≥ 1 ounce (approximately 28 grams) of pure alcohol in a day, and drinking at that level four to five days per week. This drinking history was elicited by querying a one-week recall around the time of conception and a recent two-week drinking history (Sokol, Martier et al. 1989).

The *MAST* scores for all the risky drinkers (but none of the non-drinkers or low-risk drinkers) were ≥ 5 , a score indicative of someone with alcohol use at an 'early' or a 'middle' stage of developing problems (with a score ≥ 6 being indicative of an alcohol user with established problems). The *CAGE* scores were up to four times higher for those identified as drinking alcohol at risky levels. Discriminant analysis revealed that three of the *CAGE* items (C, A and E) were significantly related to whether or not absolute alcohol intake was risky; however, the 'guilt' question (G) did not add to the prediction of risky drinking. In addition, responses to the 'tolerance' question were found to be heavily predictive of risky drinking and to have more weight than any of the other three questions (C, A and E) (Sokol, Martier et al. 1989).

On the basis of this analysis, the researchers proposed a new pregnancy-specific tool which they named the *T-ACE,* with the 'tolerance' question replacing the 'guilt' question of *CAGE*, and having a score of 2 assigned to it if it took more than two drinks to '*make* [the woman] *feel high*'; otherwise this question scored zero. The other three items had scores of 1 or zero. An overall score of > 2 was determined as indicative of problematic drinking while pregnant and hence demanding care provider intervention. Further analysis of the study data indicated that *T-ACE* had superior sensitivity and specificity to both *MAST* and *CAGE* (Sokol, Martier et al. 1989). However, it was recognized that these findings may not be generalizable as all the participants in the study

were black Americans attending an inner-city antenatal clinic (Sokol, Martier et al. 1989). In addition, the researchers acknowledged that setting the level for risky drinking at≥ 1 ounce (28grams) of pure alcohol in a day could be controversial and that others may see risk as associated with a lower level of consumption (Sokol, Martier et al. 1989).

Further studies utilizing the *T-ACE* have been conducted by a group of researchers in Boston with pregnant women drawn from socioeconomically and ethnically diverse backgrounds (Chang, Wilkins-Haug et al. 1998; Chang, Goetz et al. 1999). In a study which commenced in 1994, 350 women (of 886 approached) at an inner metropolitan hospital clinic were enrolled, having completed a preliminary screening questionnaire at their first antenatal visit (Chang, Wilkins-Haug et al. 1998). This questionnaire added the *T-ACE* to a 'health and habits' survey, which asked about health behaviours such as diet and smoking. Of the 350 women enrolled, 250 had scored positive on the *T-ACE* and 100 had scored negative. The characteristics of those who refused to participate were similar to those who agreed - 75% of participants were privately insured, 71% Caucasian, and most reported a high level of social functioning. All participants were administered a series of screening tools to determine alcohol use and/or the consequences of such use: the alcohol and drug abuse modules of the Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised (*DSM-III-R*), the *AUDIT*, the *S-MAST* (a shortened version of the *MAST*), the *Timeline FollowBack (TLFB)* and an Alcohol Craving Score (Chang, Wilkins-Haug et al. 1998; Flannery, Volpicelli et al. 1999).

Receiver operating characteristic (ROC) graphs were used to compare the ability of the tools to predict DSM-III-R diagnoses of: lifetime alcohol use, current drinking and risky drinking. The ***T***olerance scoring (of 2) was modified

to reflect two or more drinks, and not more than two drinks as in earlier studies (Sokol, Martier et al. 1989); hence, an overall score of ≥2 was now classified as indicative of 'at risk' drinking. The sensitivity of *T-ACE* (with this revised scoring) increased from 60% to 88% for detecting lifetime alcohol diagnoses, from 74% to 92% for detecting risk drinking, and from 60% to 89% for detection of current drinking. However, specificity dropped from percentages in the high 60s to approximately 37% for each criterion (Chang, Wilkins-Haug et al. 1998). The researchers noted, however, that false positives were less of a concern than false negatives, since a positive result for 'at risk' alcohol use (even if later determined to be false) could trigger a useful dialogue between practitioner and pregnant patient (Chang, Wilkins-Haug et al. 1998). Although 96% of the participants reported being questioned about their alcohol use by their obstetric care providers, only 33 women (9% of the participants) were identified as having used alcohol at any time.

In further analyses of these 1998 data, a series of statistical models was created, using either (1) each of the instruments (including the *T-ACE*) alone, (2) just clinical parameters (including alcohol craving in the last week and being over 30 years old) or (3) the instrument plus the clinical parameters (Chang, Goetz et al. 1999). Current alcohol consumption (the use of alcohol at any time in the pregnancy up to study enrolment) was the variable of interest. Of the instruments used, the *T-ACE* and the *AUDIT* were best at identification of the 120 current drinkers (65% and 70% respectively); the ability of clinical parameters to identify antenatal alcohol consumption was 0.688 (with a standard error of 0.030). Adding clinical parameters to either of these two instruments enhanced the predictive ability of the instrument; however, only the *T-ACE* was enhanced significantly (Chang, Goetz et al. 1999). The researchers concluded that, even when consideration of clinical parameters

was factored in, the *T-ACE*, with its ease of administration, could be seen as potentially the most effective diagnostic screen for alcohol use in busy antenatal clinical settings.

In later work, Chang examined the use of both the *T-ACE* and another alcohol screening tool, the *TWEAK.* This tool - a five item questionnaire - used questions from the *MAST*, the *CAGE*, and the *T-ACE* and queries: **T**olerance, whether close friends or relatives **W**orried or complained about your drinking, the **E**ye opener question, an **A**mnesia question (*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 the cut-down question (cut spelt with a **K**). Chang confirmed earlier work (Russell, Martier et al. 1994) that *TWEAK* did not offer any advantages over the *T-ACE* in identifying risky alcohol use by pregnant women (Chang 2001), although it has been used in later research studies (Ettlinger 2000).

Researchers investigating alcohol use by Northern Plains Indian women in the US developed a self-administered questionnaire (*SAQ*) that included a modified version of the *T-ACE* with further questions interrogating bingeing patterns and use of tobacco and other substances (Bad Heart Bull, Kvigne et al. 1999). The '*how many drinks does it take to make you high?*' question of the *T-ACE* was replaced by '*how many drinks does it take for you to first feel the effects of alcohol?*' while the '*have people annoyed you by criticizing your drinking?*' question was replaced by '*do any friends or family ask you to drink less?*' Both these modifications were believed to be phrased in more appropriate language for the population under consideration. Results of the *SAQ* were compared with results of nurse-interview of the participants and medical record review. The *SAQ* identified over 76% of women who were using alcohol antenatally

and had a specificity of 92.8% (Bad Heart Bull, Kvigne et al. 1999), but its use outside this population has not been investigated.

Russell reviewed the use of several tools in the antenatal population and examined their sensitivity and specificity: *MAST*, *CAGE*, *T-ACE*, *TWEAK*, *NET*, the *4Ps* and the *AUDIT* (Russell 1994), and noted that the *MAST* and *CAGE* were really designed for detecting alcohol dependence and /or significant alcohol-related problems. Hence, alcohol use by pregnant women - even heavy use - may not score as problematic use with these tools. In addition, given the singular situation of pregnant women, use of any alcohol may induce 'guilt', lowering the specificity of *CAGE*. Further, tolerance to alcohol may develop quite quickly, even though alcohol related problems have not as yet emerged (Russell 1994a); this phenomenon is not captured with *CAGE* and *MAST*.

Another screening tool examined was the *NET* (Russell, Martier et al. 1994). Again a questionnaire with only a few items, *NET* - like *T-ACE* and *TWEAK* - incorporates questions from other tools: from the *MAST* (*do you consider yourself a **N**ormal drinker?*), from *CAGE* (do *you ever have an **E**ye opener?*) and from *T-ACE* (the **T**olerance question). Although very simple to administer, evaluation in a sample of 2042 women (of whom 68 reported risky drinking) had shown that, despite high specificity, sensitivity was appreciably lower (at just over 50%) than the *MAST*, *CAGE*, or the *T-ACE* (Russell, Martier et al. 1994).

The *4Ps* is a four question tool specifically designed for pregnant women, with a positive answer to any one of the questions considered indicative of risky drinking (Russell 1994a). The yes/no questions query alcohol problems for **P**arents, for **P**artner, use of alcohol in the **P**ast and in this **P**regnancy (asking about use in the month before the woman knew she was pregnant). Although the focus has been on alcohol, the *4Ps* has potential for interrogating use of

other drugs including tobacco. A 2005 study tested its use in five antenatal populations of diverse ethnicity, in both city and rural areas, and across three US states, and asked about alcohol and tobacco use in the month before the woman knew she was pregnant (Chasnoff, McGourty et al. 2005). The tool was administered to 7,818 women, more than 90% of available women presenting for their first antenatal visit.

Nearly 22% of the women admitted to tobacco use in the month prior to knowing they were pregnant, 20% admitted to alcohol use, and over 9% admitted to both. Follow-up clinical assessment was then performed at four of the five sites for substance use generally, an assessment performed on 1548 women in total. Almost all of the women were continuing to smoke while pregnant; however, only 11% of those interviewed continued to use alcohol, and use of cannabis had declined from 7% pre-confirmation of pregnancy to 3% when pregnant. The study confirmed the value of the *4Ps* tool to identify probable substance use in pregnancy based on a personal profile and previous use, and its ease of incorporation into standard antenatal care. Those with a positive result to the *4Ps* screen could then undergo a more detailed clinical assessment (Chasnoff, McGourty et al. 2005).

In an earlier study, 2,002 women from both urban and rural areas of two states (Washington and South Carolina), were asked questions about substance use via a screening tool which included not only questions similar to the *4Ps*, but also rather less 'threatening' questions related to social functioning and general health, these latter questions being asked first (Chasnoff, Neuman et al. 2001). Although the focus on the substance use questions in this study was solely on the woman herself – past history of use, use in the month before pregnancy, and use at time of interview (Chasnoff, Neuman et al. 2001) – the researchers used classification and regression trees

(*CART*) to identify those variables that could discriminate between women at high risk of substance use from those at low risk. They concluded that interrogation of alcohol and tobacco use only - *Have you ever drunk alcohol? How much alcohol did you drink in the month before pregnancy?* and *How many cigarettes did you smoke in the month before pregnancy?* – enabled identification of risk levels from substance use generally (Chasnoff, Neuman et al. 2001).

Another team of US based researchers (Kennedy, Finkelstein et al. 2004), also adapted the *4Ps* to capture, with their screening tool, the specific issues with pregnant adolescents. A fifth *P* was added - **P**eers, recognizing the significant influence peer use can exert in this group of the population. As with the 2001 Chasnoff study, the substance use questions were preceded by questions assessing social support and health risks more broadly (Kennedy, Finkelstein et al. 2004). In this study, a positive answer to any of the *5P* questions triggered a brief intervention.

In her review cited earlier (Russell 1994), Russell also examined the potential for the *AUDIT* to be used for pregnant women, given its emphasis on harmful drinking rather than alcohol dependence or highly problematic use (Saunders, Aasland et al. 2003).This ten-item questionnaire investigates behaviour typical of alcohol dependence, adverse psychological reactions, and patterns of problematic drinking. Russell concluded that the utility of *AUDIT* for antenatal patients may be limited; the early questions directly relate to alcohol intake and pregnant women drinking at risk levels may deny their level of use, leading to the reduced sensitivity of *AUDIT* in this population (Russell 1994a). Given its well-established use, however, it has continued to be used in both research settings (Goransson, Magnusson et al. 2003) and clinical practice (Western, Cusack et al. 2006).

3.1.2 Tobacco

Quantity-frequency questionnaires have a long history in assessment of alcohol use but have also been used with other substances including tobacco. In a study in North Carolina, 600 antenatal women were randomised to either usual interview in relation to substance use (*yes/no* check boxes for *smoking/alcohol*, *drug use (any)*, and *drug addiction/ alcoholism*) for 200 women, or a more detailed screening for both 'cigarette and alcohol use' and 'illicit drug use' for 400 women. (Clark, Dawson et al. 1999). A significantly greater proportion of women in the second group were detected using substances than through the *yes/no* check box procedure – 21% reported smoking and/or drinking alcohol if the check boxes were used, while 70% of women reported either or both these behaviours with the more detailed quantity and frequency questionnaire. In addition, the more comprehensive questionnaire allowed the distinction to be made between tobacco and alcohol users, not possible with the *yes/no* boxes that had traditionally been used (Clark, Dawson et al. 1999).

A variation on the quantity-frequency method of questioning has been used specifically to assess tobacco use by pregnant women (Kharrazi, Epstein et al. 1999). Four 'maternal smoking questions' were evaluated in Californian studies within a broadly based socio-demographic questionnaire: in the first study, 1171 English speaking women from two antenatal clinics in the north of the state were eligible to participate, by the self-completion of either Question 1 or Question 2: *Question 1 - Tobacco use in pregnancy, yes/no, average number of cigarettes per day* - was part of the *Standard Certificate of Live Birth* and used in most parts of the United States (Ventura, Martin et al. 1998), while *Question 2* (a question assuming that the respondent did smoke) enquired on the *average number of cigarettes per day in (a) the first three*

months of pregnancy, (b) the second three months of pregnancy, and *(c) the third three months of pregnancy.* The response rate to these questions was not determined as the researchers were unsure of the number of pregnant women asked to answer either question (Khazzari, Epstein et al. 1998).

In the second study, 900 women enrolled over a four month period in a state-wide antenatal screening program across 20 hospitals in 4 counties, were asked to self-complete *Questions 3* and *4*, the seeing questions which assumed the behaviour was occurring and queried details of the behaviour (Kharrazi, Epstein et al. 1999). *Question 3* asked which statement *'best describes your smoking'*, with five options that included: *'I quit smoking since finding out I was pregnant'* and *' I wasn't smoking around the time of conception and I don't smoke now'. Question 4 ('How many cigarettes did you smoke each day during the …')* was directed to (a) the 3 months before pregnancy, (b) each individual month until the 6 month of pregnancy, and (c) the final 3 months. Of the 900 women, 774 answered both questions, 125 answered only *Question 3* and one woman answered *Question 4* only.

Self-completers of the questionnaires that included *Questions 1* or *2* were followed through telephone interviews in which women were asked to self-report smoking behaviour; for those women who had self-completed questionnaires involving *Questions 3* and *4*, cotinine (the major nicotine metabolite) was measured in serum samples taken at visits between 15 and 19 weeks' gestation (Kharrazi, Epstein et al. 1999).

After analysis of their data, the researchers postulated that the more complex the question, the lower the response rate. This statement can only be speculative however, given the inability of the researchers to determine the exact number of participants asked either *Question 1* or *Question 2* in the first study (Kharrazi, Epstein et al. 1999). The authors did note, however, that US

national data collection for 1996 indicated that 98.4% of women answered *Question 1*, arguably the simplest question, when asked within the *Standard Certificate of Live Birth* (Ventura, Martin et al. 1998). However, when compared to self-report on telephone interview, Khazzari and colleagues did show that *Question 1* had unacceptably low sensitivity.

In conclusion, the researchers proposed that, in the *Standard Certificate of Live Birth, Question 1* be replaced by a question that assumes the behaviour, a concept first espoused by Dolan-Mullen (Dolan-Mullen, Carbonari et al. 1991). In this questionnaire, respondents were asked about the number of cigarettes smoked in (a) *the three months before pregnancy*, (b) *the first three months of pregnancy*, (c) *the second three months of pregnancy*, and (d) *the third three months of pregnancy*. The researchers acknowledged, however, the space constraints within the *Standard Certificate of Live Birth* and the need to evaluate this expanded question with culturally diverse populations and in groups with differing rates of smoking prevalence (Kharrazi, Epstein et al. 1999).

A Melbourne-based project team, following a literature search and consultation with experts, developed guidelines for promoting smoking cessation that also assumed the behaviour (Project Team Mercy Hospital for Women Southern Health and Women's and Children's Health 2001). It was nominated 'good practice' to ask pregnant women the following question: *'Which of the following best describes your cigarette smoking?'*, with a choice of responses: *I smoke daily now, about the same as before finding out I was pregnant/ I smoke daily now, but I've cut down since I found out I was pregnant/I smoke every once in a while/I quit smoking since finding out I was pregnant/I wasn't smoking around the time I found out I was pregnant and I don't currently*

smoke. No published literature is available reporting implementation of these guidelines.

Arguably however, the gold standard self-report questionnaire for tobacco use is the *Fagerstrom Tolerance Questionnaire (FTQ)* (Fagerstrom 1978) (Miller and Wood 2002), which has undergone extensive validation studies (Prokhorov, Pallonen et al. 1996; Etter 2005; Storr, Reboussin et al. 2005), leading to the emergence of revised versions such as the *Fagerstrom Test for Nicotine Dependence (FTND)* (Heatherton, Kozlowski et al. 1991) and the *Revised Fagerstrom Tolerance Questionnaire (RTQ)* (Tate and Schmitz 1993). The original *FTQ* and other versions investigate not only the amount of tobacco use *('how many cigarettes a day do you smoke?'*) but also domains highly indicative of dependence such as *'how often do you smoke your first cigarette of the day within 30 minutes of waking?'* and *'how often do you smoke when you are sick with a cold, the flu, or are so ill that you are in bed most of the day?'.* Further situational challenges are questioned as in *'how difficult do you find it to refrain from smoking in places where it is prohibited, for example in church, at the library, cinema etc'?'*

Although not validated for use in pregnancy, versions of the *FTQ* have been used in several studies with pregnant women (Albrecht, Cornelius et al. 1999; Roberts-Clarke, Morokoff et al. 2002; Hotham, Gilbert et al. 2006; Handel, Hannover et al. 2009). The original eight item *FTQ,* with some dichotomous and trichotomous variables, has been recognized as having limited ability to detect the known variation in tobacco use behaviours between individuals (Tate and Schmitz 1993). For example, a yes/no response to the question: *'do you find it difficult to refrain from smoking in places where it is prohibited, for example in church, at the library, cinema etc'?'* was not able to capture the range of possible responses.

In their study, Tate *et al* recruited 327 smokers in all: regular smokers not wanting to quit (46), smoking cessation clinic participants (51), outpatients of substance use clinics (182) and inpatients of substance use clinics (48) (Tate and Schmitz 1993). They administered a ten item revised version of the *FTQ*, with the question relating to 'brand' of cigarette dropped and three questions related to inhalation techniques included. All questions had a common factor structure, which allowed 5 responses on a visual analogue scale – a common psychometric technique used in questionnaires (Tate and Schmitz 1993).

Factor and psychometric analyses of the responses led to the conclusion that this revised version of the Fagerstrom Tolerance Questionnaire (the *RTQ*) was able to measure a uni dimensional construct, namely nicotine dependence, a conclusion unable to be drawn from analyses of the original questionnaire. Internal consistency was somewhat lower (0.72) in those attending the smoking cessation clinic while in the other groups of smokers, internal consistency ranged from 0.81 to 0.85. The researchers postulated that this resulted from recent changes in smoking patterns related to attempting cessation (Tate and Schmitz 1993). The test-retest reliability coefficient of 0.88 for the total score, calculated for a sub-sample of the substance use treatment clients who were re-interviewed 4-6 weeks later, indicates a good level of temporal stability. The limitation of including 230 clients undertaking substance abuse treatment in the study sample was identified, namely that these smokers may have different characteristics to smokers without concurrent use of other substances (Tate and Schmitz 1993).

3.1.3 Other Substances

A screening tool that has been used in a number of clinical trial situations in Ohio with the pregnant population is the *Substance Abuse Subtle Screening Inventory (SASSI).* The earlier work focused on comparing results from the

SASSI - a 78 item 'psychologic questionnaire' - with results from urine toxicology (Horrigan, Piazza et al. 1996). As with other such questionnaires with a broad social functioning focus, the 'subtle' questions that do not appear to be asking about problematic substance use are asked first, with questions related to substances (the *Risk Prediction Scale for Drugs*) as well as to alcohol (the *Risk Prediction Scale for Alcohol)* being asked in the second part of the questionnaire.

Of the 560 pregnant women enrolled in the study, 96 women self-reported use of substances while urine screening detected 83 substance users. The *SASSI* identified 95 women as being positive for substance abuse and a further 151 to be 'at risk' of abuse. The toxicological screen allowed for detection of the metabolites of cocaine, opiates, benzodiazepines, amphetamines and barbiturates as well as of cannabinoids, but *SASSI* also enabled detection of alcohol use, absent on the toxicology screen. Following chi-squares analyses of *SASSI versus* self-report, *SASSI versus* urine screening, and *SASSI* plus self-report *versus* urine screening, the researchers concluded that the best results were obtained when *SASSI* was used in combination with standard self-report with only 19 extra women being identified by urine toxicology (Horrigan, Piazza et al. 1996). Toxicological testing is expensive and those tested are able to manipulate their results by refraining from substance use for a few days prior to testing, leading to high false-negative rates (Horrigan and Piazza 1999). With a false-negative rate of over 57% in the 1996 study, Horrigan and his colleagues concluded that the *SASSI* would be a better tool for detection of pregnant substance users in clinical practice.

Similar overall findings in a larger study with 1251 antenatal patients led the researchers to propose the use of *SASSI* to distinguish between those substance users who could be managed within standard antenatal care and

those who would require specialist intervention (Horrigan and Piazza 1999). They determined that urine toxicological screening should be reserved for those women who refused to complete the *SASSI* or those whose broader social situation, past history and general health were suggestive of substance use (Horrigan and Piazza 1999). More recently, the *SASSI*'s value for detecting substance use by using both direct and indirect ('subtle') items has been questioned (Feldstein and Miller 2007) and a meta-analysis of 48 studies reporting its use has highlighted the lack of reliability assessment in 73% of those studies (Miller, Woodson et al. 2009).

3.1.3.1 Cannabis

Determination of cannabis use has generally been acknowledged as complicated by its status as an illicit substance, yet a substance that has greater social acceptance than other illicit substances (Alexander 2003). For care providers in antenatal settings however, this ambivalence is unlikely to exist due to the undisputed harms related to its use, as detailed earlier. Efforts have been directed in the AOD field to the development of a cannabis-specific screening tool (Alexander and Leung 2004), although as yet such a tool has not emerged for pregnant women.

The American Psychiatric Association's *Structured Clinical Interview for DSM-III-R* (Spitzer, Williams et al. 1990; Spitzer, Williams et al. 1990a), superseded by the *DSM-IV* version, retains its position as a gold standard for detection of substance use generally. However, its length and level of complexity, although suited for specialist intervention, make it inappropriate for routine antenatal services.

Antenatal use of alcohol and other substances including cannabis was documented antenatally and at 13 months postpartum in a study of 361 African-American women in inner-city Detroit, (Jacobson, Jacobson et al.

1991). For cannabis, as for the other substances, questions related to the quantity and frequency of use during the preceding fortnight were asked at the time of enrolment (mean of 23.7 weeks) and at each subsequent antenatal visit. At the single postpartum interview, women were asked about quantity and frequency of use in a "*typical week*" while pregnant. The *MAST* (the Michigan Alcoholism Screening Test) and other tests relating to social functioning and psychological well-being were also administered at the enrolment visit and at post-partum interview.

Alcohol, cannabis and cocaine were the most common substances used by this cohort with higher antenatal use reported at the postpartum interview, than declared when interviewed during pregnancy (Jacobson, Jacobson et al. 1991). However, without any measurement of the sequelae of cannabis use *per se,* the researchers were unable to make meaningful conclusions about the validity of their assessment of the participants' cannabis use by this self-report method. A weak correlation was found between maternal depression and the retrospective report of antenatal use of cannabis (Jacobson, Jacobson et al. 1991).

Frequently, cannabis use has been screened for in pregnancy within an 'other drugs' framework. In one US study, 186 women attending a university - based antenatal clinic were administered a questionnaire to determine their mental health status (the *Primary Care Evaluation of Mental Disorders Patient Health Questionnaire*) and *CAGE* questionnaires for both alcohol and for 'drugs' (including cannabis) (Kelly, Zatzick et al. 2001). The latter were modified so that the time frame for questioning was focused on the *'12 months before you found out you were pregnant'.* Results of these screening questionnaires were analysed in relation to medical record documentation by care providers, all

clinical summaries and any visits related to medical ('non-obstetric') complications.

Seventy women (38%) of women screened positive to psychiatric conditions, substance use or both (Kelly, Zatzick et al. 2001). This detection was more than twice that recorded by care providers or documented in clinical summaries. In addition, only one in four of those women who screened positive had any evidence of treatment for either substance use or mental ill-health and only one in three had any documented psychosocial intervention. Despite acknowledged limitations, the researchers concluded that the self-report questionnaires have a clear role in obstetric practice although further investigation was required. In addition, the value of focusing on peri-conceptional substance use as an indicator of antenatal substance use was recognized (Kelly, Zatzick et al. 2001).

Further work on the use of *'drug CAGE'* was conducted within the *California Perinatal Needs Assessment (PNA),* a large multi-site study that recruited 1,147 pregnant women from 19 agencies, including community and public hospital health clinics, nutrition programs, shelters and goals (Midanik, Zahnd et al. 1998). Again, the *'12 months before finding out about the pregnancy'* was used as the period for enquiry of drug use. The *alcohol CAGE* 'eye-opener' question: '*In the 12 months before you found out you were pregnant, did you drink first thing in the morning?'* was replaced by the following: '*Sometimes people feel bad when a drug wears off. Did that ever happen to you in the past year?'* and *'Did you ever take another drug when that happened?'* Positive answers to both these questions were needed to register a 'yes' response to the 'eye-opener' question.

Measures of 'high risk' drug use in the 12 months before pregnancy were based on fulfilment of one of three criteria as descriptors of drug use in that

period, with cannabis allocated a stand-alone category. High risk use was confirmed based on either: (1) five or more times using 'lighter drugs' (exemplified by such as prescription drugs used non-medically or hallucinogens); (2) one or more times using 'heavier drugs' (exemplified by such as cocaine, methamphetamine, or heroin); or (3) five or more episodes of cannabis use to get 'high' and with usual use of at least three days per week (Midanik, Zahnd et al. 1998).

Receiver operating characteristics (ROC) analyses, and sensitivity and specificity tests were performed (Midanik, Zahnd et al. 1998). Sensitivity for cannabis was established as 'low' for both age categories (less than 20 years old and 20 years old and older) and at each of the three cut-points (1, 2 and 3), ranging between 23% and 30%; however, specificity was high for cannabis (ranging between 94% and 99%) (Midanik, Zahnd et al. 1998). The ROC analysis indicated that at a cut-point of 1 (one positive response on the *CAGE*), sensitivity and specificity for cannabis was maximized (area under the curve of 0.67 for those less than 20 years old and 0.83 for those equal to or greater than 20 years old). The researchers concluded however that, in this group of pregnant women - those with low income and accessing publicly funded support and health services - the value of this modified drug *CAGE* lay with identification of use of 'heavier drugs' rather than of cannabis (Midanik, Zahnd et al. 1998), as areas under the curve determined by the ROC analysis were much higher for 'heavier drugs'.

The *Timeline FollowBack (TLFB)* was initially developed to measure alcohol use via self-report (Sobell and Sobell 1992); this was followed by further research into its administration by telephone or using a computer-based version (Sobell, Brown et al. 1996). *TLFB* is a retrospective calendar-based screening tool, that uses a number of techniques to enable quantification of substance use and the

detection of atypical, non-patterned use as well as regular and predictable use patterns (Sobell and Sobell 1992).

However, although there has been increasing application of *TLFB* in both research and clinical settings with users of other drugs, and indeed with clients exhibiting other behaviours of concern (Weinstock, Whelan et al. 2004), its use with women of childbearing age has been focussed on alcohol consumption (Manwell, Fleming et al. 2000; Project Choices Research Group 2002)(pers. comm. Linda Sobell e mail 9th March 2005). Further, its extensive use with pregnant women has also only been for the exploration of alcohol consumption (Chang, Wilkins-Haug et al. 1998; Stoler, Huntington et al. 1998; Chang, Goetz et al. 2000) (Chang 2001) (Goransson, Magnusson et al. 2003).

The initial studies with the *TLFB* were conducted in a variety of populations (alcohol dependent clients in a variety of treatment facilities - inpatient and outpatient, college students and 'normal drinkers'). Correlation between the original use and a later use of the tool (test-retest reliability) ranged between 0.79 and 0.96 for variables including frequency of drinking and level of drinking (Sobell and Sobell 1992). There were also fair to good levels of correlation in the various research settings between 'subject' reports and 'collateral' reports for *days of abstinence* (r values between 0.79 and 0.92), *high alcohol consumption* (r values between 0.59 and 0.82), and for verifiable events such as *hospitalisation episodes* (r values of 0.97 and 0.98) (Sobell and Sobell 1992). Unsurprisingly, the latter data were not available for all populations studied. However, the *TLFB* correlated only moderately with biochemical markers of damage caused by alcohol consumption, such as serum glutamic-oxaloacetic transaminase (SGOT) and serum γ-glutamyl transpeptidase (GGT) (Sobell and Sobell 1992). Further information on such

tests is given in the section of this chapter that outlines biological markers for substance use.

As detailed in the *TLFB Tips and Techniques to Aid Recall* (Sobell and Sobell 1996a), the *TLFB* assessment utilizes the 'anchoring [of] questions on drinking in particular social contexts', thus facilitating a more accurate recall of drinking behaviour. 'Key dates' and 'discrete events', 'black and white days' and other phenomena such as 'drinking boundaries', can all be queried.

Even at the time of development of the tool, the potential of the *TLFB* to be applied to explore use of other substances and indeed other behaviours, for example bulimia nervosa, was noted (Sobell and Sobell 1992). *TLFB* has since been used to detect cannabis use in the population generally (O'Farrell, Fals-Stewart et al. 2003) and for adolescents specifically (Duhig, Cavallo et al. 2005). In the study by O'Farrell *et al* (2003), there were high correlations in the sample of those participants in treatment programs between frequency of drug use (including cannabis use) by self-report and that determined by the TLFB. Further, these results correlated well with collateral reports from the spouses of users. The correlations were also good for these comparable analyses in the community sample used as controls.

In the Connecticut study by Duhig *et al* (2005), the *TLFB* was employed to detect use of both cannabis and alcohol in adolescents recruited from local high schools and via newspaper advertisements. Higher rates of use of cannabis and alcohol were detected in tobacco smokers compared with non-tobacco smokers, with no age or gender differences detectable in use of cannabis by the tobacco smokers. The researchers concluded that the tool was useful to give a more detailed assessment than feasible with other tools (Duhig, Cavallo et al. 2005).

3.2 Screening by Using Biological Markers

Although arguably more definitive than self-report methods for detecting substance use, some limitations become evident when the use of biological markers are examined. Although it is possible for an individual to alter use of a substance prior to a scheduled testing date to manipulate test results, as there is often a narrow 'window of detection' (Horrigan and Piazza 1999; Huestis and Choo 2002), this is not relevant in the context of this study with a non-anticipated single interview. Another possibility is that of minimizing concentration of a substance in urine by ingestion of copious volumes of water (Miller, Cox et al. 1994; Huestis and Choo 2002); certainly this possibility is recognized in another context by the Australian Sports Anti-Doping Authority, which checks the specific gravity of provided urine samples to ensure that the urine is 'normal' (Australian Sports Anti-Doping Authority [ASADA] 2009). This again is not relevant to this study with a non-anticipated single interview.

3.2.1 Biomarkers to Detect Use While Pregnant

Much of the emphasis in the US literature is on using biomarkers of substance use in pregnancy in the overall context of a punitive approach to pregnant substance users (Lester, Andreozzi et al. 2004). This approach is not adhered to in other Western countries. However, some clinicians and commentators in the US recognize the potential for criminalization of a pregnant woman because of her substance use to deter her from antenatal care, to the detriment of both the woman and her baby (Miller, Cox et al. 1994; Huestis and Choo 2002; Lester, Andreozzi et al. 2004).

It has been argued that the use of biomarkers in an effort to prevent fetal harm could only be done effectively by both regular, systematic testing of urine and/or saliva throughout pregnancy and hair sampling every few months (Huestis and Choo 2002). However, even then, the likelihood of being tested

can be influenced by ethnic and socioeconomic considerations (Miller, Cox et al. 1994). Further, such testing focuses on the woman with no acknowledgement of the influence of her partner's substance use on pregnancy outcome and the later wellbeing of the child (Miller, Cox et al. 1994; World Health Organization and Institute for Global Tobacco Control Johns Hopkins School for Public Health 1999; World Health Organization 2003).

The testing of meconium post-delivery has come to be regarded as the best indicator of intra-utero exposure (Ostrea, Brady et al. 1992; Ostrea, Knapp et al. 1994; Bearer, Jacobson et al. 2003; Bearer, Santiago et al. 2005). Such confirmation of maternal substance use heightens the chance of identifying infants at risk of developmental delay and other physical and cognitive deficits. Placental analysis for correlates of tobacco smoking such as presence of heavy metals and increased activity of the enzyme CYP1A1 (Pereg, Lagueux et al. 2001) has also been conducted to confirm maternal smoking. However, meconium analysis has no relevance to this study and researchers of placental biomarkers have often focused their findings on establishing epidemiological data, again outside the scope of this study.

The three substances of focus in this investigation of screening tools in pregnancy are alcohol, tobacco and cannabis, and this review focussed on biomarkers for their use.

3.2.1.1 Tobacco

Many studies have utilized biomarkers of tobacco use during pregnancy (Hughes, Epstein et al. 1982; Woodby, Windsor et al. 1999; Russell, Crawford et al. 2004; Hotham, Gilbert et al. 2006). Carbon monoxide measurement in exhaled breath readily confirms recent tobacco smoking (Benowitz 1983), while cotinine – a long-acting metabolite of nicotine – can be measured in

saliva, urine, or blood to indicate longer-term smoking behaviour (Benowitz 1983).

Use of cotinine as a marker is, however, compromised in pregnancy as the metabolism of both nicotine and cotinine is accelerated, with the half-life of cotinine shortening to 8.8 hours, compared with 16.6 hours in the non-pregnant state (Dempsey, Jacob et al. 2002). Recent research has focussed on establishing appropriate cut-points for non-smokers, passive smokers and active smokers to enable effective use of cotinine as a biomarker in pregnancy (Higgins, Heil et al. 2007). Data for 131 women in a clinic based study showed good agreement (95% sensitivity and 98% specificity) between urinary cotinine (measured by gas chromatograhy) and self-report at the revised cut-point for active smoking of 25ng/mL (down from 50ng/mL for non-pregnant smokers). The researchers recognized that the selected cut-point may need to be even lower in clinical practice to ensure that pregnant smokers did not miss a desirable intervention. There was evidence of some false declarations of abstinence in the study; however, the researchers still affirmed the value of self-report in assessment of smoking status (Higgins, Heil et al 2007).

A recently conducted meta-analysis of cotinine measurement in hair samples also investigated cut-offs for pregnant smokers, women not smoking in pregnancy and those pregnant women exposed to environmental tobacco smoke (Florescu, Ferrence et al. 2007). Using data from six databases (US, Canada and France) for 1746 people (including neonates and children subjected to environmental tobacco exposure), the authors were able to demonstrate that for pregnant smokers, mean cotinine levels in hair ranged from 1.5 to 1.9 ng/mg, while for those exposed, while pregnant, to the smoking of others, mean cotinine levels in hair ranged from 0.06 to 0.09 ng/mg.

However, it has been recognized that, unlike non-pregnant adult smokers who tend to smoke in a predictable pattern, pregnant women often try to cut-down while pregnant and the significant intra-individual cotinine fluctuations in pregnancy make it a less than reliable marker (Pickett, Rathouz, et al. 2005). With a cohort of 287 pregnant smokers, these researchers used a ROC analysis and utilized radioimmunoassay to measure urinary cotinine values. Values were corrected for urine concentration and expressed as ng/mL of urinary creatinine-adjusted cotinine. A cut-off of 200ng/mL allowed the best balance between sensitivity and specificity. This value was then used to indicate current cigarette smoking. While urinary cotinine and self-reported number of cigarettes were highly correlated *across* women (r= 0.70), the correlation within subjects was weak (r = 0.33) (Pickett, Rathouz, et al. 2005). While cotinine with its long half-life (approximately 24 hours) reflects exposure to nicotine over a period of five to seven days, carbon monoxide with its short half-life (of three to four hours) is only indicative of recent exposure to tobacco smoke – up to approximately nine hours (Jatlow, Toll et al. 2008). Expired carbon monoxide, plasma cotinine and self report data (using the *TLFB*) were collected for 207 (non-pregnant) subjects at 6 weeks, 3 months and 6 months. Study results showed that carbon monoxide measurement significantly overestimated abstinence rates compared with cotinine, especially at the earlier collection stages. The authors concluded that cotinine had greater reliability than carbon monoxide, although lack of sensitivity and specificity calculations were admitted as a limitation of their work (Jatlow, Toll et al. 2008). The researchers justified this on the basis of the lack of an independent 'gold standard' on which to assess any of these parameters: self-report, measurement of cotinine, and measurement of carbon monoxide.

As was evident when investigating 'self-report' questionnaires, because of the long-standing and sustained interest in alcohol use during pregnancy, there have been a number of research studies considering the use of biomarkers to investigate alcohol use while pregnant.

3.2.1.2 Alcohol

Research using biomarkers for alcohol use by pregnant women has focused on biomarkers of 'excessive' or 'heavy' alcohol consumption (Budd, Ross-Alaolmolki et al. 2000) (Stoler, Huntington et al. 1998) (Barrison, Wright et al. 1982). The biomarker most used to detect heavy alcohol consumption, and with United States Food and Drug Administration (FDA) approval (Javors and Johnson 2003), is serum carbohydrate deficient transferrin (CDT) - the (abnormal) deglycosylated form of transferrin, a blood plasma protein with a single iron-binding site (Javors and Johnson 2003). It has been recognized however, that CDT may increase in pregnancy unrelated to maternal alcohol consumption as a consequence of an increase in total transferrin associated with gestation and the hormones of pregnancy (Stauber, Jauk et al. 1996). It has therefore been proposed that CDT for pregnant women be expressed as a percentage of total transferrin rather than as the absolute value (Budd, Ross-Alaolmolki et al. 2000; Cook 2003). However, in the general population, CDT has lower sensitivity and specificity for women than for men, making its use for pregnant women even less convincing.

Debate in the literature has also focused on fatty acid ethyl esters (FAEE) as a biomarker for heavy alcohol use, although it currently is not in clinical use (Peterson 2004-2005). FAEE and acetaldehyde are products of alcohol metabolism, and with chronic alcohol use, FAEE accumulate in hair and provide a highly sensitive and highly specific test with the ability to differentiate between heavy, 'social' and non-drinkers (Kulaga, Pragst et al. 2009). The

emphasis in the literature is on the detection of heavy use in pregnancy to facilitate detection and support of children with fetal alcohol spectrum disorders (Kulaga, Pragst et al. 2009). Meconium analysis has been proposed for similar motives (Goh, Chudley et al. 2008). However, as with any biomarker, early detection could be used to avoid further damage related to use of the substance.

Within the general population, liver enzymes can be used to detect heavy alcohol use: γ glutamyltransferase (GGT), aspartate aminotransferase (AST) and alanine aminotransferase (ALT), although these are less likely to be elevated in users under 30 years old (Conigrave, Davies et al. 2003). Mean corpuscular volume (MCV) has also been used as a biomarker for heavy drinking, with women likely to show greater elevation than men (Conigrave, Davies et al. 2003). MCV remains elevated up to three months after heavy drinking (defined as in excess of 60 grams of alcohol per day) has ceased, although it has been proposed that, given the different physiological parameters in women, this definition of 'heavy drinking' should be adjusted downwards (Cook 2003). The mechanism by which MCV is elevated by heavy alcohol use is unclear (Conigrave, Saunders et al. 1995; Humeniuk 2000).

However, no single one of these tests is regarded as reliable enough to give a definitive diagnosis of alcohol dependence or abuse (Neumann and Spies 2003)(Peterson 2004-2005) and many health care providers have little training in using biomarker measurement in primary health care settings (Miller and Anton 2004)(Goh, Chudley et al 2008).

In a study over a three year period in five area hospitals in Boston (Stoler, Huntington et al. 1998), 529 antenatal patients were recruited in a consecutive manner on any particular day, at varying weeks of gestation, to evaluate

screening methods. The researchers administered two self-report questionnaires, *TWEAK* and a modification of the *Timeline FollowBack* (both discussed earlier in this chapter), and obtained blood and urine samples (Stoler, Huntington et al. 1998). Four biomarkers in blood for alcohol consumption were used: whole blood-associated acetaldehyde (WBAA), CDT, GGT and MCV. Reported alcohol intake in the 4 weeks before testing showed a dose - response association with biomarker results (Stoler, Huntington et al. 1998). Of the 46 self-reporting daily users, 15 women (of 32) who reported intake of less than half an ounce (less than 14 grams of alcohol) per day had at least one positive biomarker, seven women (of 10) who reported half an ounce or more had at least one positive biomarker, and all of the four women who self-reported at least one or more ounces (approximately 28 grams or more) of alcohol per day had at least one positive blood marker (Stoler, Huntington et al. 1998).

Overall, the panel of the four biomarkers was found to be more predictive of women drinking a significant amount of alcohol while pregnant than any one marker alone, and more predictive than self-report. This conclusion was also drawn in a review of biomarkers in pregnancy (Cook 2003).

Further, in the Boston study, infant outcomes such as birth weight, birth length and head circumference were also assessed by the researchers, and found to be inversely related to the number of positive maternal biomarkers although not all women with positive markers had infants with detectable deficits at birth (Stoler, Huntington et al. 1998). The analysis by the researchers involved logistic regression to adjust for confounding factors, including tobacco use (measured by serum cotinine) and other substance use (measured by urine toxicology) (Stoler, Huntington et al. 1998).

In a editorial in *The Journal of Pediatrics* (Jones and Chambers 1998) commenting on the above study (Stoler, Huntington et al. 1998), the issue was raised as to whether positive biomarker results would really assist in improving neonatal outcomes, given likely practitioner difficulties in interpretation and communication of such results (Jones and Chambers 1998), an issue highlighted elsewhere (Miller and Anton 2004). At the least, however, the editors concluded that such a result could provoke a patient-practitioner dialogue about alcohol use, a valuable consequence (Jones and Chambers 1998).

3.2.1.3 Cannabis

In contrast to alcohol and tobacco, there is a paucity of studies of biomarkers of cannabis use in pregnancy. However, literature on studies with the general population provides further insight.

In a study with antenatal patients attending a high risk service at a Detroit hospital, 75 women who admitted to use of illicit substances (cocaine, opioids and cannabis) were enrolled and biomarker testing was performed on hair samples and, later, post-birth, on meconium (Ostrea, Knapp et al. 2001). The researchers advised participants prior to the first interview that there would be biomarker testing, a tactic to enhance the veracity of reports. Interviews were repeated every two weeks. Hair samples were taken at enrolment (first visit), at the end of the second trimester, and within 24 hours of delivery. Sixty of the participants completed the study and 58 control women were also enrolled. Hair analysis showed high sensitivity for detecting cocaine use (100%) and opioid use (80%), although false positive rates of 13% for cocaine and 20% for opioids limited the value of these analyses (Ostrea, Knapp et al. 2001). The results for detection of a major metabolite of delta-9-tetra-hydrocannabinol (the main psychoactive chemical in cannabis), carboxy-tetra-hydrocannabinol,

in both hair and meconium, did not correlate well with maternal interview. Hair and meconium analysis had low sensitivity (21%, 22.7%) compared with maternal interview (58%), although higher specificity (90%, 97.3%) compared with specificity of 76.5% for maternal interview. The researchers acknowledged that the cost of hair analysis, when coupled with the unreliable results for cannabis, limits its utility for either research or clinical settings (Ostrea, Knapp et al. 2001).

In an earlier study, each of 302 consecutive antenatal patients attending the Medical College in Virginia was interviewed at her initial visit about past and current substance use by both herself and the father of her baby (Christmas, Knisely et al. 1992). In addition a urine sample was taken and toxicological testing conducted for a range of substances including cannabis. Participants were classified as substance users if they either admitted to use of a particular substance, had a positive toxicological result, or both. Cannabis was the most frequently identified substance by toxicology (29 of 302 women), although only eight women had declared cannabis use at interview. In total, 33 women were current users of cannabis, with some women detected by both methods. However, the sensitivity of urine testing for cannabis is limited by its pharmacokinetics. Metabolites persist in the body and are excreted in urine over several weeks; even in blood, heavy users would be expected to have a background level of 1 to 2 ng/mL, which distorts test results (pers. comm. Peter Felgate, 29th March 2005). Hence, it follows that the most economical biological test for cannabis, a *positive/ negative* test, has poor potential if a user's quantity and/ or frequency of use is the desired outcome for the researcher or the clinician.

The researchers in the Virginian study concluded that a self-report questionnaire, coupled with toxicological screening only for those with a

previous self-reported history of substance use, was the most effective and economical method of screening for use in a woman's current pregnancy (Christmas, Knisely et al. 1992). In this study, excluding nicotine use and inviting only those with self-reported substance use to provide urine for toxicological screening, 40 women would have been identified toxicologically compared to 41 women when toxicological screening was employed universally. Inevitably, with studies with substance users, alcohol and tobacco use, especially the latter, can be significant confounders. In this study, more than half of those admitting to use of 'any (other) substance' also used tobacco.

3.3 Conclusion from Review of Screening Tools for Pregnant Women

Substance use is often a marker for environmental stressors such as poverty, domestic violence and ethnic discrimination, and may be linked with mental ill-health and other disorders in both the pregnant woman and other members of her family (Lester, Bagner et al. 2009) (Goh, Chudley et al. 2008) (Dawe, Atkinson et al 2007) (Tobin 2005). The identification of substance use may well lead to identifying the need for intervention across a number of these significant issues, highlighting the desirability of substance use screening.

This review of both self-report tools and biological markers for substance use indicates that a number of screening tools have been usefully employed in antenatal settings. Further, self-report tools have been the focus of intense research interest, given the demonstrated need to identify substance use by pregnant women and the recognized limitations of testing for biological markers.

However, an inherent shortcoming that became evident is that only a very limited number of self-report tools have both applicability across the spectrum of substances to which the fetus could be exposed and relative ease of administration within demanding and sometimes complex antenatal care. If both present in a screening tool, these attributes could enhance the potential for implementation by obstetric care providers.

3.4 Recent Developments in the Primary Health Care Sector

If attention is shifted to screening instruments in primary health care for the the general population, a newly developed WHO tool - the *ASSIST* - is showing promise as a screening instrument for primary health care (Ward, Mertens et al. 2008; Ndetei, Khasakhala et al. 2009) and with some special populations (Allen, Carey et al. 2003; Holmwood, Marriott et al. 2008; Hides, Cotton et al. 2009). Online adaptations for clinical practice are in use in the United States (Boston University School of Public Health 2009; National Institute on Drug Abuse 2009). Training sessions for health care workers are being rolled out in Australia, across three states, since March 2004 (pers. comm. Rachel Humeniuk 23rd July 2009); in addition, training will take place in Vietnam (for the South-East Asian region) and in Fiji (for the South Pacific region) later in 2009 (pers.comm. Sonali Meena 29th June 2009).

3.4.1 The *ASSIST Version 3.0* (The Alcohol, Smoking and Substance Involvement Test)

A twelve item questionnaire was tested initially in nine countries (including Australia) with 236 volunteers who completed test and retest interviews (WHO ASSIST Working Group 2002). It was designed to cover domains indicative of both abuse and dependence: lifetime and recent use, dependence symptoms, substance–related problems, and use of drugs intravenously. Reliability

coefficients (*kappas*) ranged from a high of 0.90 (reporting '*ever use*' of substances) to a low of 0.58 ('*regretting what was done*' under the influence of drugs).

From this first version, 8 items were chosen to create *ASSIST Version 2* on the basis of: medium to high values for *kappa* coefficients for each item in the substance class (ranging from 0.61 for sedatives and 0.78 for drugs in the opioid class), high correlations between frequency of substance use and frequency of symptoms, strong item to total scale correlations, support from qualitative data and face validity (WHO ASSIST Working Group 2002). The validity of the tool was further strengthened by its administration in different cultural contexts at sites in seven countries including Australia, with Adelaide being the Australian site.

A range of substance users were interviewed, 1147 in all, 697 from primary health care facilities and 350 from specialist drug treatment agencies (Humeniuk, Ali et al. 2008). All participants were administered the *ASSIST* and a battery of other tools: the *Addiction Severity Index-Lite* (the *ASI-Lite*), the *Severity of Dependence Scale (SDS)*, the *Mini-International Neuropsychiatric Interview* (MINI-Plus), the *Rating of Injection Site Condition (RISC)*, the *Drug Abuse Screening Test (DAST)*, the *Alcohol Use Disorders Identification Test (AUDIT)*, the *Revised Fagerstrom Tolerance Questionnaire (RTQ)*, and the *Maudsley Addiction Profile (MAP)* (Humeniuk, Ali et al. 2008). The collated worldwide results confirmed the results from the Australian site (Adelaide) alone (Newcombe, Humeniuk et al. 2005).

There were significant correlations between the *ASSIST* and each of *ASI-Lite* ($r=0.76$-0.88; $p<0.001$), *SDS* ($r=0.59$; $p<0.0001$), *AUDIT* ($r=0.82$; $p<0.0001$) and *RTQ* ($r=0.78$; $p<0.001$), thus establishing concurrent validity. In addition, *ASSIST* scores were significantly greater for all substances for

participants with a *MINI-Plus* diagnosis of either abuse or dependence. There were also positive, although not strongly so, correlations between the *Specific Substance Involvement Scores* of the *ASSIST* and other measures of risky injecting behaviour, health, and social functioning thus strengthening the case for construct validity of the *ASSIST* (Humeniuk, Ali et al. 2008).

Finally, discriminative validity was established by the categorization of participants into high risk (those from specialist treatment services), and by allocating the primary health care clients into moderate risk ('abuse') or low risk ('use') categories based on *MINI-Plus* diagnoses. Further, receiver operating characteristic (ROC) analyses was used to allow determination of cut-off *ASSIST* scores for 'low to moderate' and 'moderate to high' risk.

Following minor modifications subsequent to the validation studies, the *ASSIST Version 3.0* is currently in use.

3.4.1.1 The *ASSIST Version 3.0* in Primary Health Care Settings

The *ASSIST Version 3.0* has a number of key features that make it highly suitable for primary health care settings (WHO ASSIST Working Group 2002): expert training does not have to be undertaken to administer it and its questions are relatively simple and brief. The *ASSIST Version 3.0* questions cover nine substances or substance classes: tobacco, alcohol, cannabis, cocaine, amphetamine-type stimulants, inhalants (such as petrol and glue), sedatives or 'sleeping pills' (such as benzodiazepines), hallucinogens, and opioids. With 'sleeping pills' and opioid drugs, respondents are asked to specify 'non-medical use' only. A tenth category 'other' enables declaration of use of substances such as γ-hydroxybutyric acid (*GHB* or *Fantasy*), which do not fit into any of the previously queried categories.

ASSIST Version 3.0 Question 1 - which of the following have you ever used? (non-medical use only) - queries lifetime use of any substance. The tool then

moves to focus on current use (*in the past 3 months*) of substances nominated as affirmative responses to *Question 1*. Questions 2 through to 5 all have five possible responses on a Likert scale ranging from 'never' to 'daily', responses serving a number of purposes in the assessment of substance use:

- *Question 2- how often have you used the substances you mentioned (first drug, second drug etc)?* - establishes the basic use patterns of the nominated drugs.
- *Question 3 - how often have you had a strong desire or urge to use (first drug, second drug etc)?* - gives a measure of psychological dependence.
- *Question 4 - how often has your use of (first drug, second drug etc) led to health, social, legal or financial problems?* – provides a measure of harmful use leading to the emergence of problems. (Humeniuk, Ali et al. 2008).
- *Question 5 - how often have you failed to do what was expected of you because of your use of (first drug, second drug etc)?* – provides a measure of the capacity, or otherwise, to fulfil role obligations.
- *Question 6 - has a friend or relative or anyone else <u>ever</u> expressed concern about your use of (first drug, second drug etc)?* – gives an assessment of the reactions of others in an individual's life to that individual's use of substances.
- *Question 7 - have you <u>ever</u> tried and failed to control, cut down or stop using (first drug, second drug etc)* – gauges the individual's ability to control his/her use.

Both Questions 6 and 7 allow for three possible responses: either of two positive responses - *in the past three months* or *not in the past three months* - or a negative response, *No, never*.

The final question (Question 8) queries non-medical use of a drug by injection, and again allows three responses: *No, never*. *Yes in the past three months* or *yes, but not in the past three months.*

3.4.1.2 Decision to Investigate the *ASSIST Version 3.0* in Pregnancy

With the established need to find a suitable tool for identification of women whose substance use was at 'risk' levels and the value of the *ASSIST Version 3.0* in primary health care settings as a screening tool for the spectrum of substances, it was determined to investigate its use with pregnant substance users. The methods of this investigation are described in the following chapter.

Chapter 4

Phase II Methods:

Investigation of the *ASSIST Version 3.0 in* Pregnancy

4.1 Hypothesis

That the ASSIST Version 3.0 can be shown to have clinical utility as a screening tool with pregnant women.

4.2 Aims of the Study

- to undertake an investigation of the *ASSIST Version 3.0* to test its ability to effectively identify pregnant women who are using substances and the level of 'risk' of that use.
- to focus that investigation on the use of tobacco, alcohol and cannabis, as these have been shown to be the substances with highest level of use in the population under study.

4.3 Methods

4.3.1 The *ASSIST Version 3.0*

If a respondent answers positively to lifetime use of one or more substances in Question 1 of the *ASSIST Version 3.0*, then the remaining questions only need to be asked with regard to use of named substances in the 3 months prior to interview, the period of interest with the *ASSIST Version 3.0* (Humeniuk, Ali et al. 2008). For pregnant women, this 3 month time-frame encompasses either a period of time when conception took place and the woman moved into early pregnancy or a three month phase of the woman's pregnancy.

If the former, the time frame would also include the time in which she became aware of her pregnancy, an event that could trigger a more cautionary approach to substance use. If the latter, this would, in clinical practice, indicate a woman coming late to antenatal care. For effective intervention, screening for substance use, as with other screening, should take place at the first antenatal visit and ideally this would be in early pregnancy.

There are a number of 'scores' that can be derived from the *ASSIST Version 3.0*. Although these may have relevance for research purposes, the *Specific Substance Involvement Score* (for each substance that has been used in the past 3 months) has greater utility in clinical settings, being reflective of risk attributable to the specific substance under consideration (Humeniuk and Ali 2005). It is calculated for each substance by tallying the scores for that substance for Questions 2 through to 7.

Based on an individual's *Specific Substance Involvement Score,* the clinician using the *ASSIST Version 3.0* is guided as to the appropriate intervention: if 'low' risk - no intervention; if 'moderate' risk - a brief intervention, with the individual seen as using hazardously or exhibiting low dependent use; if 'high' risk - referral to a specialist AOD setting, with the individual seen as exhibiting highly dependent use. The *ASSIST Version 3.0* appears in *Appendix Two* and the 'cut-offs' that designate levels of risk in the general population are shown.

4.3.2 Concept of Risk in Pregnancy

To test the ability of the *ASSIST Version 3.0* to identify pregnant women who are using substances and to identify the level of 'risk' of that use, the concept of risk needs further scrutiny. Risk is broadly defined as 'exposure to the chance of injury or loss' (Yallop, Bernard et al. 2005). Unlike in the population generally, where substance use carries a level of risk to the individual,

substance use by a pregnant woman places not only the woman herself at risk, but also the fetus.

It is plausible that an individual woman who is not pregnant may perceive the risk of experiencing negative outcomes from her substance use as acceptable. Consciously, or unconsciously, she may have decided that the 'benefits' gained from her use of the substance outweighs possible attendant health risks. Further, she may have recognized that the risk is after all a relative risk, even though the statistical term may not have been articulated to her or by her. These perceptions are likely to be magnified when the expert opinion is that there is risk 'associated' with use of a substance, rather than that the risk is absolute or guaranteed, Further, others may be noted as using substances without apparent negative sequelae.

However, if the woman is pregnant, there is a second user - the fetus - and the situation becomes more complex. If there is a conscious or unconscious estimation of risk, it must now encompass a second individual. Again the harms may be seen as only associated with use, not inevitably caused by use, and the risk as relative, not absolute. Even if the risk of a specific harm is strongly associated with use (for example, intrauterine growth restriction and tobacco smoking), the woman may not perceive, or wish to perceive, this as relevant to her personally, or indeed appreciate the impact of these adverse effects. Anecdotes of experiences of known others, or of herself in an earlier pregnancy, may be used to support her decision to continue use (Hotham, Atkinson et al 2002). In addition, ambiguous advice from obstetric care providers (such as 'cut down' tobacco smoking) may be seized on to support her substance-using behaviour (Hotham, Atkinson et al 2002).

The fetus of course is without decision-making power and must contend with the substance use *in utero* and the sequelae which may continue into

adulthood. Therefore the emphasis placed by care providers on the welfare of the fetus can be seen as emanating from recognition of the disempowered status of this patient. This view is in conflict with much of the feminist literature which sees this emphasis as a threat to the autonomy of the woman (Field 1989 cited in Oaks p. 178) and consistent with the values of a patriarchal society (Sha and Kirkman 2009). In this latter analysis, the authors assert that women themselves may be co-opted to support these values and, within that framework, judge and indeed openly criticize the behaviours of other women during pregnancy (Sha and Kirkman 2009).

Certainly, when the 'risk' of substance use by a pregnant woman is canvassed in the medical literature, the focus is generally on risk to the fetus (Armstrong 1998). This focus may not be stated, just as it may not be stated in the obstetric care setting. However, it is implicit. Ideally, the needs of both would be seen as mutual rather than competing (Harris 2000); however, the potential for conflict has been acknowledged (Fasouliotis and Schenker 2000) and was noted in 1.2.

In addition, the concept of fetal personhood, which has arisen in the context of the struggle between the pro- and anti- abortion lobby, has gained some plausibility in other legislative areas, particularly in the US (Paltrow 1999). If in the future, the fetus were to become a 'full person' under the law, then the rights of the fetus could not rationally be subjugated to those of the pregnant woman. These perspectives have already led to pregnant drug users in the US facing discrimination and sometimes prosecution (as noted in 1.2.1); other women have been forced to surrender their infants to welfare authorities (Anderson 2008).

The complexity of the concept of risk is not only clouded by the current lack of definitive thresholds for harm attributable to substance use, but also by the

presence of several confounders which influence risk assessment. These include a myriad of psychosocial factors, genetic variability, and general maternal health including antenatal nutrition (Huizink 2009). Further, the principle of currently unidentifiable mother-infant dyads being at particular risk has been recognized, specifically with alcohol use (Mukherjee, Hollins et al. 2005).

4.3.2.1 Risk to the Fetus

- **Tobacco**

There is a large body of evidence (reviewed in Chapter 1) of the negative impact of substance use on the fetus. Smoking *per se* has detrimental effects on the fetus (Rhainds and Levallois 1997; Lammer, Shaw et al. 2005); in addition, the level of nicotine exposure that could be regarded as 'safe' cannot be quantified, but is increasingly understood to be lower than that previously proposed (Slotkin 2008). Because the threshold for nicotine damage is below that likely to affect intrauterine growth, Slotkin has concluded that the emphasis on growth restriction when considering the effects of maternal smoking is inappropriate (Slotkin 1998; Slotkin 2008).

- **Alcohol**

Alcohol is known to be a teratogen and heavy maternal use is linked to life-long impairment of the offspring (Chiriboga 2003), although it has not currently been proven that infrequent, low levels of alcohol use are harmful in pregnancy (Royal College of Obstetricians and Gynaecologists (RCOG) 2006). However, the public health messages related to alcohol use in pregnancy have become progressively more conservative, with abstinence promoted as the appropriate decision for a pregnant woman to make (Office of the Surgeon General 2005). Although there have been reservations expressed about the abstinence message (Royal College of Obstetricians and Gynaecologists

(RCOG) 2006) and its scientific validity (Armstrong 1998), the difficulty in nominating a level of exposure safe for the fetus has led to its wider adoption (National Health and Medical Research Council [NHMRC] 2009) (National Institute for Health and Clinical Excellence [NICE] 2008).

- **Cannabis**

If cannabis is smoked, many of the risks to the fetus attributable to the smoking of tobacco are present; also, the two substances are often co-administered by that route (Agrawal, Knopik et al. 2008). Twelve thousand women enrolled in the Avon Longitudinal Study of Pregnancy and Childhood. in Britain were questioned on their use of cannabis before and during pregnancy (ALSPAC Study Team, Fergusson et al. 2002). Six hundred cannabis users were identified. The study determined that use of cannabis was independently implicated in reduction in birthweight and birth length, but no threshold level for effect could be established with the numbers under study (ALSPAC Study Team, Fergusson et al. 2002).

Despite a current inability to establish the threshold of risk to the fetus attributable to the use of any of these substances, the concept of being able to categorize the risk level to the fetus as being 'moderate' – one of the levels of categorization of the *ASSIST Version 3.0* - appears incompatible with the biological realities.

4.3.2.2 Risk to the Pregnant Woman

The risks of substance use to the pregnant woman herself are two-fold: the risks to her health, both in the short - and long-term, and the risk of negative impacts on pregnancy outcomes (detailed in Chapter 1).

Risks to the woman's own health due to substance use are reflective of those for any adult substance user, with the level of risk increasing if use escalates through hazardous to harmful use or on to dependence.

However, use of any of the nominated substances in this study could also place the woman at risk from adverse pregnancy outcomes, although the level of use that would be likely to result in compromised pregnancy outcomes is unclear. In addition, the risk of the latter occurring can only be artificially separated from the risk to the fetus; negative pregnancy outcomes are highly associated with negative impacts on the fetus or the neonate.

To investigate the use of the *ASSIST Version 3.0* to identify substance use in pregnancy and the associated levels of risk within the concept of separate entities - the woman and the fetus - it was resolved to adopt a two-pronged approach.

4.3.3 Investigation of the *ASSIST Version 3.0* in Pregnancy

This investigation was carried out by administration of the *ASSIST Version 3.0* to a cohort of pregnant women to test its suitability in this special population group, in which for each individual patient, there is a second patient – the fetus.

It was decided to:

- co-administer selected screening tools that had a history of use in pregnant women
- select a tool for each of tobacco, alcohol, and cannabis. If a pregnancy-specific tool had not been established for the specific substance, the selection would be made from established screening tools that had been used with pregnant women for screening of another substance.
- undertake two sets of statistical analyses, each with a distinct frame of reference, utilizing the *Specific Substance Involvement Score* on the

ASSIST Version 3.0 (for each of the nominated 'focus' substances) and the score generated by the established tool for each of those substances:

(1)

analyses to determine the *ASSIST Version 3.0* score pertinent to the minimum level of use that would be categorized as placing the fetus 'at risk' of short-term and long-term sequelae and that would trigger an intervention if using the nominated established screening tool/s. These analyses will utilize a dichotomous variable: that is, indicate 'risk' or 'no/low risk' to the fetus.

(2)

analyses to determine the *ASSIST Version 3.0* score pertinent to the level of use that would categorize the pregnant woman as being at risk of, damage to her own health in both the short-term and long-term, , and that would trigger an intervention based on those risks. These analyses will be based on the low, moderate and high risk levels inherent in the *ASSIST Version 3.0.* It is acknowledged however that, as the woman is pregnant, considerations of her own health cannot be isolated from the progression of her pregnancy and ultimately, her labour.

- draw conclusions on the v*alue of the ASSIST Version 3.0* for screening substance use in pregnancy based on these findings.

4.3.3.1 Selection of Screening Tools for Co-administration

On the basis of the investigation of screening tools (reported in Chapter 3), the following self-report questionnaires were selected.

- **Tobacco: the *Revised Fagerstrom Tolerance Questionnaire (RTQ)***

The *RTQ* is a short qu*estionnaire (of ten* items) that measures the degree of nicotine dependence (Fagerstrom 1978; Tate and Schmitz 1993). The suite of tools and key questions de rived f rom the o riginal *Fagerstrom Tolerance Questionnaire* are widely used and have been employed in a number of studies with pregnant women (Albrecht, C ornelius et al . 1 999; R oberts-Clarke, Morokoff et al. 2002; Hotham, Gilbert et al. 2006; Handel, Hannover et al. 2009). The question in these tools related to the period of time that elapses before smoking the first cigarette of the day is highly correlated with the level of nicotine dependence (Fagerstrom 1978; Heatherton, Kozlowski et al. 1991; Tate and Schmitz 1993).

The *RTQ* generates five s cores, rangi ng f rom a s core o f *1* (very l ow dependence) to a s core of *5* (severe d ependence). W hen a ttempting t o determine the level of risk attached to a dependence score, the literature does not give much guidance. Clinical trials with pregnant and post-partum smokers tend to f ocus o n tho se wi th hi gh de pendence (Polańska, Hanke et al. 2005; Handel, Hannover et al. 2009), rather than those with lower dependence [as measured by the *Fagerstrom* tools] (Fagerstrom 1978; Heatherton, Kozlowski et al. 1991; Tate and Schmitz 1993).

The existence of a fetal tobacco syndrome was first described over twenty years ago , (Nieburg, M arks e t a l. 1 985) and has had some currency since (Habek, Habek et al. 2002). Its key diagnostic features are: maternal smoking of at least of five cigarettes a day during the pregnancy, no evidence of hypertension during pregnancy, and symmetrical growth restriction at term, with no other obvious cause of the restriction. Although these criteria are only part of the impact of maternal smoking, they are concordant with a score of ≥ 1 on the *RTQ*.

- **Alcohol: the *T-ACE***

The *T-ACE* is a four-item tool that gives a measure of alcohol dependence. It has been shown to be a highly sensitive screen with pregnant women and has been extensively used for over two decades (Sokol, Martier et al. 1989; Chang, Wilkins-Haug et al. 1998). It has in effect come to be regarded as a gold standard for detecting alcohol use by pregnant women.

The first question, related to the number of drinks required to make a person feel 'high', is unlikely to trigger denial of use and is the dominant scoring item(Chang, Wilkins-Haug et al. 1998) (Sokol, Martier et al. 1989). A score ≥ 2 on the *T-ACE* is indicative of a pregnant woman using alcohol at risky levels. The level of alcohol use, regarded as use 'at risk', was set in the original studies with the *T-ACE* at ≥ 1 ounce (28grams) of pure alcohol in a day, and drinking at that level four to five days per week (Sokol, Martier et al. 1989).

- **Cannabis: the *Timeline FollowBack (TLFB)***

The Timeline Follow Back is a calendar-based questionnaire that gives a comprehensive retrospective picture of AOD use over an extended period (Sobell and Sobell 1992). Techniques to enhance recall were originally developed in research settings but have enabled the tool to be used clinically. It allows several dimensions of substance use to be collected, namely: variability, pattern, and extent (amount) of use (Sobell and Sobell 1996a). It has been used extensively with pregnant women and women of childbearing age in the investigation of alcohol use (Manwell, Fleming et al. 2000; Project Choices Research Group 2002; Savage, Wray et al. 2002; Goransson, Magnusson et al. 2003)(pers. comm. Linda Sobell email 9th March 2005)(Dum, Sobell et al. 2009) and with other populations for cannabis use assessment (O'Farrell, Fals-Stewart et al. 2003; Duhig, Cavallo et al. 2005).

No published results on the use of the *TLFB* to screen for cannabis in pregnancy were identified. However, its established value as a screening tool, including extensive use with pregnant women, led to its selection in the absence of a cannabis-specific tool for pregnant women.

Three months was chosen as the period in which retrospective use would be questioned, in concordance with the 3 month period of interest with the *ASSIST.* Determination of level/s of use indicative of 'risk' to a woman based on her *TLFB* report were determined on clinical grounds based on the current state of expert knowledge.

In addition, the decisions were informed by work with *CAGE* screening tools (both alcohol *CAGE* and drug *CAGE*) within the large US study, the Californian Perinatal Needs Assessment (Klein and Zahnd 1997; Midanik, Zahnd et al. 1998). In this study of 1147 pregnant women from 19 agencies, highlighted in Chapter 3, use of cannabis linked to 'risk' was set at use on 3 or more days per week *and* either five or more episodes of cannabis use to get 'high' *or* a positive answer to one of the *CAGE* questions (Klein and Zahnd 1997; Midanik, Zahnd et al. 1998).

These three tools and the scoring that is indicative of levels of 'risk', (1) based on fetal risk assessment and (2) based on risk to the woman's health and to pregnancy outcomes, are detailed in *Appendix Two*.

4.3.4 Biomarkers

In Chapter 3, a review of biomarkers as screening tools for detection of use of alcohol, tobacco or cannabis in this population was reported. Costs of biological testing are high, and unjustified if the findings are not of value.

Biomarkers of tobacco use (carbon monoxide and cotinine) have been widely used in research studies, including with pregnant women, although they are not without limitations (Pickett, Rathouz et al. 2005) (Dempsey, Jacob et al

2002). However, biomarkers of alcohol use by pregnant women are generally inappropriate, as, apart from breath alcohol tests (Heller 2008) which detect recent alcohol use, alcohol biomarkers are only valuable where patterns of alcohol abuse and/or dependence are present (Conigrave, Davies et al. 2003). In addition, one single biomarker may not be enough to give an accurate clinical picture (Neumann and Spies 2003). Women are unlikely to attend antenatal visits having just consumed alcohol; hence breath alcohol tests may be futile. A battery of alcohol biomarkers would confirm those drinking at harmful or dependent levels; however, such women are likely to have been detected on clinical grounds.

With cannabis, both the original *ASSIST* project (Humeniuk, Ali et al. 2008) and other published literature (Ostrea, Knapp et al. 2001) indicates that analysis of hair samples for THC metabolites indicates only whether or not cannabis has been used, but gives no reliable quantification of use. Results of urinalysis for THC metabolites are also liable to distortion (pers. comm. Peter Felgate, 29th March 2005).

Based on this review, biomarkers were not selected as screening tools for this study. Further comment on this decision is made in the final chapter of this thesis.

4.3.5 Sample Size

Tobacco being the most prevalent substance in the Phase I study, the data on tobacco use informed the sample size calculations for the Phase II study.

Of the 748 women in the first study, 209 used at least one substance; of the 209 substance users, 138 had used tobacco – that is 66% (138/209) of those using any substance were users of tobacco.

Thus for the Phase II study, a sample size of 104 participants would allow for the calculation of weighted *kappa* with a standard error of 0.10 or lower with

80% power (when considering tobacco users). That is, on 80% of occasions the standard error based on a sample of 104 women will be less than 0.075 [corresponding to an approximate 95% confidence interval of 0.80 +/- 2x 0.075 = (0.65, 0.95)].

4.3.5.1 Inclusion and Exclusion Criteria

The major inclusion criterion for the Phase II study was reporting use of tobacco, alcohol, and/or cannabis in the last 3 months.

Further criteria were being:

- an antenatal patient of the Women's and Children's Hospital, either as an outpatient attending one of the antenatal clinics or as an inpatient of the antenatal ward
- of any gestation of pregnancy
- over 18 years of age
- able to communicate proficiently in English
- willing to answer questionnaires and respond to screening tools for a period possibly as long as 45 minutes

The exclusion criteria were:

- having cognitive impairment or an intellectual disability
- currently experiencing severe behavioural disturbances or severe mental health problems

Interviewing women from both the 'high risk pregnancy' clinics and the standard antenatal clinics of the hospital enabled the investigation of the *ASSIST* to be performed with a sample which included both women already recognized as having substance use problems or other pregnancy complications (attendees of 'high risk pregnancy' clinics) and women attending the standard clinics.

The sample also included women who were approached for enrolment while inpatients in the ante natal ward of the hospital. These women had been admitted due to complications in their pregnancies, either medical or obstetric.

4.3.6 Sociodemographic Questionnaire

A questionnaire to enable collection of basic demographic details for the women interviewed was developed (see *Appendix Two*). The inclusion of the question: '*How many of your children currently live with you?*' was influenced by the Psychosocial History (PSH) (Comfort and Kaltenbach 1996), the response being regarded as highly indicative of social dysfunction (pers.comm. Karol Kaltenbach, 9th April 2005). The Psychosocial History was developed to supplement the Addiction Severity Index (ASI), with the support of the ASIs creators (McLellan, Kushner et al. 1992), within a comprehensive drug treatment program in Philadelphia for pregnant women and women with children (Comfort and Kaltenbach 1996).

4.3.7 Ethics Approval

The Research Ethics Committee of the Children, Youth and Women's Health Service (CYWHS) granted ethics approval for this Phase II study- REC1813/3/2009 (see *Appendix Two*).

4.4 Recruitment

The intended method of recruitment in the study was to randomly approach antenatal patients in the clinic waiting room and ask the screening question: '*Have you used any of the following: tobacco, alcohol, or cannabis in the last 3 months?*' However, approaching a woman to ask this question almost inevitably resulted in a response of a nod or shake of her head. The response of any woman subsequently questioned could then easily be interpreted by

those women previously approached by the researcher. Hence, this method quickly proved untenable as it could lead to serial breaches of confidentiality.

An alternative method of recruitment was then adopted. The researcher (EH) performed a preliminary 'filtering' of patients by accessing case notes of both clinic patients and antenatal ward patients to check what information was recorded in relation to substance use. This was in accordance with approval granted by the CYWHS Research Ethics Committee and detailed in the Patient Information Sheet (*The researcher may access your case notes. This will only be to confirm what information your doctors or midwives have recorded in relation to alcohol and other drug use and for no other purpose*). Those women with recorded substance use were then approached for interview.

In the antenatal ward, women were again selected for approach after a preliminary perusal of case notes. The implications of this revised method of recruitment on the composition of the study sample is discussed in the last chapter of the thesis.In accord with the design of the study, a woman who fulfilled the criteria was given the Patient Information Sheet (see *Appendix Two*) to read for several minutes, with the opportunity to ask the researcher for any clarification that was needed. Consent was then obtained (see *Appendix Two*) and the interview took place, although this was sometimes delayed to fit with the participant's commitments with her care provider(s), whether in the clinic or the ward setting.

As the interview involved an encounter of possibly as long as 45 minutes, it was possible that subjects could decide to withdraw during the assessment. This was entirely within the rights of the individual involved. However, the payment of an honorarium to compensate a woman for her time was only payable on completion of the interview. This was explained in the Patient Information Sheet (see *Appendix Two*).

4.4.1 Interview

The first questionnaire administered was the *Sociodemographic Questionnaire.* Following this, the *ASSIST Version 3.0* was administered. The *ASSIST Version 3.0* established use of substances in the last 3 months. If alcohol had been used, the *T-ACE* was then administered; if tobacco the *RTQ;* and if cannabis, the *TLFB.* Following administration, the scores for all questionnaires were tallied and classified via a two-pronged approach as described below, using classification criteria detailed in *Appendix Two*.

As an interview of this confidential nature was not able to take place in the antenatal clinic waiting room, a private area within the consulting section of the clinic available for researchers was utilized. In the antenatal ward, the interview took place either in the woman's own room or in the ward's patient lounge, if this was available and preferred.

4.5 Statistical Analyses (1): Risk to the fetus

Based on the concept that substance use is either of '*low/no risk*', or '*risky*', receiver operating characteristics (ROC) curves were prepared for each of the substances under consideration, using scores for the *ASSIST* and the substance-specific tool.

In a ROC curve, *sensitivity* (on the vertical axis) is plotted against *1minus specificity (1-specificity)* on the horizontal axis. The area under the curve for each of the substances will give a measure of the performance of the *ASSIST Version 3.0* in diagnosing the dichotomous risk groups according to the previously established tool (see *Appendix Two*). Further, the substance-specific ROC curve allows calculations of the sensitivity and the specificity of the *ASSIST Version 3.0,* as a predictor of risky use of that substance, at different cut-offs.

Interpretation of the area under the curve as a measure of the performance of

of a diagnostic test can be judged on the criteria shown in Text Box 1 (Simon 1999); other researchers and diagnosticians have nominated similar criteria, although cut-offs between categories vary (University of Nebraska Medical Center undated). An ideal test performance would have an area under the curve of 1; a test which was no more useful than 'flipping a coin' would have an area under the curve of 0.5.

Text Box 1

***Area under the ROC Curve* as a**

Measure of Performance of a Test

Value of Area under the Curve	**Strength of Performance of Test**
0.50 to 0.75	Fair
0.75 to 0.92	Good
0.92 to 0.97	Very good
0.97 to 1.00	Excellent

The determination of the most appropriate *ASSIST Version 3.0* cut-off does, by necessity, involve a trade-off between sensitivity and specificity. At a low cut-off, the sensitivity will be higher; however, there may be too many false positives. As the cut-off increases, however, the false positives will go down, but so will the true positives. In addition, both the true negatives and the false negatives will concurrently increase.

Once the *ASSIST* cut-off was determined, 95% confidence intervals related to the sensitivity and the specificity were calculated. In addition, the positive and negative predictive values were tallied.

4.5.1 Further Consideration of Phase II Sample

By focussing on risk categorization attendant on criteria for the *fetal tobacco syndrome* (Nieburg, Marks et al. 1985), those smokers identified in the Phase I study can be classified as placing the fetus '*at risk* (or not), based on using ≥ 5 cigarettes every day (see Text Box 2).

In the Phase I study, 58.7% of smokers were using tobacco 'at risk' based on this classification. Further, 66% of substance users were tobacco users. Hence, in the sample of 104 anticipated recruits in the Phase II study, it could be expected that 40 would be using tobacco '*at risk'* (since 104 X 0.66 X 0.587 = 40).

Text Box 2

Phase I study: Data on Tobacco Use during Pregnancy

Number of participants: 748		
Number who identified as smokers: 138		
37 women smoking 1-10/day but not every day		'low risk'
20 women smoking 1-4/day every day		'low risk'
That is, total of 57 women		'low risk'
46 women smoking 5-10 /day every day		'at risk'
1 women smoking 11+/day but not every day		'at risk'
34 women smoking 11+ every day		'at risk'
That is, total of 81 women		'at risk'
Of the 138 smokers		
57/138 'low risk'	41.3 %	
81/138 'at risk'/ 'high risk'	58.7 %	

4.6 Statistical Analyses (2): Risk to the pregnant women

For each woman, the scores for each questionnaire were categorised according to *Appendix Two,* with categorizations indicative of '*low*', '*medium*' and '*high*' risk. Associations between each established screening tool and the *ASSIST Version 3.0* was explored using two-way tables of the categorized scores. For each two-way table, the statistics of the *kappa coefficient* and *Bowker's* test of symmetry were calculated.

4.6.1 *Kappa coefficient*

The *kappa coefficient* is a measure of inter-rater agreement and allowed the assessment of association between each of the established tools and the *ASSIST Version 3.0*. The *kappa coefficient* equals +1 when there is complete

agreement of the established questionnaire and the *ASSIST Version 3.0*. Any deviation from this perfect situation will result in a *kappa* less than 1.

When the observed agreement exceeds chance agreement, *kappa* is positive, with its magnitude reflecting the strength of agreement. Calculating *kappa* for each screening tool also allows comparison of the performance of the *ASSIST Version 3.0* across the different tools. The following guideline (Text Box 3) was used for interpreting *kappa* statistics.

Text Box 3

Strength of Agreement between two variables based on *kappa* values

Value of k*appa*	**Strength of agreement**
< 0.20	Poor
0.21 - 0.40	Fair
0.41 - 0.60	Moderate
0.61 - 0.80	Good
0.81 - 1.00	Very good

4.6.2 *Bowker's* test of symmetry

		Established screening tool		
		Low	**Mod**	**High**
ASSIST	**Low**	**X**		
	Mod		**X**	
	High			**X**

Bowker's test of symmetry allows the assessment of symmetry of the two-way table between the *ASSIST Version 3.0* and each of the established screening tools used in the study. The implicit null hypothesis is that the table is

symmetric across the diagonal cells. The table above is an example of a 'perfect' table, representing exact agreement between the *ASSIST Version 3.0* and the specific established screening tool. This test allows assessment of any imbalance in misclassification between the two tools.

If *Bowker's* test returns a statistically significant result, this means that the corresponding two-way table is not symmetric. In reality, this would represent either the *ASSIST Version 3.0* consistently classifying women in lower risk categories than the established screening tool (that is, the *ASSIST* would be too conservative), or the *ASSIST Version 3.0* consistently classifying women in higher risk categories than the established screening tool (that is, the *ASSIST Version 3.0* would be too sensitive).

However, if *Bowker's* Test does not return a statistically significant result, then there is insufficient evidence to conclude that the table is not symmetric, and the null hypothesis cannot be rejected. The P-value is not the probability of symmetry; it is the probability of observing the collected data under the assumption that the underlying process generating the data is one of symmetry.

4.7 Other Statistical Associations

Associations between each of various demographic variables, such as age, socio-economic status, years of schooling, number of previous children and the *ASSIST Version 3.0* scores were also explored. This component of the analysis was regarded as secondary to the associations explored above. Statistical significance was set at 5% and analysis performed using *SAS Version 9.1* (SAS Institute Inc., Cary, NC, USA) through the Faculty of Health Sciences Statistical Service, University of Adelaide.

4.8 Further Exploration of the ASSIST Version 3.0: Qualitative Analysis

In addition to collating respondents' answers to the questionnaires themselves, the researcher documented observations related to the participants' reactions to the questions and any interpretative difficulties that arose, any areas (domains) of the participants' substance use that emerged during interview that did not appear to be adequately assessed by the *ASSIST Version 3.0*, and any questions in the *ASSIST Version 3.0* that seem inappropriate for pregnant women.

Documentation of all observations related to administration of these tools by the researcher enabled the qualitative analysis of the suitability of the *ASSIST Version 3.0* for identification of risk of substance use in the pregnant population. These data are reported in Chapter 6.

Chapter 5

Phase II Quantitative Results:

Investigation of Use of the *ASSIST Version 3.0* in Pregnancy

Recruitment commenced in October 2006 and was completed in December 2007. One hundred and four women were interviewed, with an average interview time of 25 minutes (12-45 minutes). All participants completed all the required questionnaires. Of the participants, 73 women were attendees of one of the antenatal clinics and 31 women were inpatients of the antenatal ward. A total of 46 women refused to participate when approached. The reasons given are shown in Table 12. A further 26 women, when approached, reported cessation of substance use, with no use at all in the last 3 months, making them ineligible for the study.

Table 12

Reasons Given for Declining Participation: n = 46

Reason given	Number
'Not interested'	18
Not interested in research/ *'previous negative experience with research'*	3
'Not interested in quitting' / *'I'm only smoking and that's OK for me'*	5
'Have spoken to the QUIT line and I'm still smoking 10/day. I'm just not interested.'	1
'Trying to quit'	2
Not feeling well today/ not appropriate/ sleep deprived	8
No reason	4
'Would need to speak to my partner'	1
Too busy/ no time/ *'active toddler'*	3
'My husband doesn't know I'm smoking and I don't want to talk about smoking with you'	1

5.1 Analysis of Quantitative Data

Data for the 104 participants were entered into a *Microsoft Office Excel* spreadsheet. These included: all sociodemographic data given by participants in response to the *Sociodemographic Questionnaire* and the tallied scores for each screening tool administered: the *ASSIST Version 3.0* and whichever of the *Revised Fagerstrom Tolerance Questionnaire (RTQ)*, the *T-ACE*, and the *Timeline FollowBack (TLFB)* were applicable to the participant interviewed. All calculations for the analysis of the data were performed using SAS Version 9.1 (SAS Institute Inc., Cary, NC, SA).

5.1.1 Tobacco

5.1.1.1 Statistical Analyses (1): Risk to the fetus

Of the 104 participants in the study, 98 were using tobacco. All 98 were classified as using 'at risk' based on the *RTQ*. Hence, it was not possible to conduct a ROC analysis based on a dichotomous variable for risk according to the *Revised Fagerstrom Questionnaire (RTQ)* and *ASSIST Version 3.0* scores for tobacco.

5.1.1.2 Statistical Analyses (2): Risk to the pregnant woman

A 3X3 table was prepared using scores in the *ASSIST Version 3.0* and the *RTQ* for the participants who smoked tobacco (n=98). The agreement results for the *ASSIST* and the *RTQ* are shown in Table 13.

Table 13

Agreement between *ASSIST Version 3.0* Tobacco and *RTQ* Risk Groups

n = 98

***ASSISTVersion 3.0* Tobacco Risk Group**	***RTQ* Tobacco Risk Group**			**Total**
Frequency Percent	Low Risk	Moderate Risk	High Risk	
Low Risk	0 0.00	0 0.00	0 0.00	0 0.00
Moderate Risk	0 0.00	**39** 39.80	12 12.24	51 52.04
High Risk	0 0.00	16 16.33	**31** 31.63	47 47.96
Total	0 0.00	55 56.12	43 43.88	98 100.00

The tools were in agreement for 70 (39+31) of the 98 tobacco users. No participant was classified as 'low risk' by either the *ASSIST Version 3.0* or the *RTQ*. Hence, the 3X3 table became a 2X2 table. Table 14 shows the *kappa* calculations for this table. For 2X2 tables, *Bowker's* test of symmetry is undefined.

Table 14

Kappa* Statistics: The *ASSIST Version 3.0 and* the *RTQ

***kappa* Statistics**				
Statistic	Value	SE*	95% Confidence Limits	
Simple *kappa*	0.4257	0.0913	0.2467	0.6047
Weighted *kappa*	**0.4257**	0.0913	0.2467	0.6047

* standard error

Simple and weighted *kappa* statistics are the same for a 2X2 table. The value of 0.4257 is indicative of *moderate* agreement between the *ASSIST Version 3.0* and the *Revised Fagerstrom Questionnaire (RTQ).*

5.1.2 Alcohol

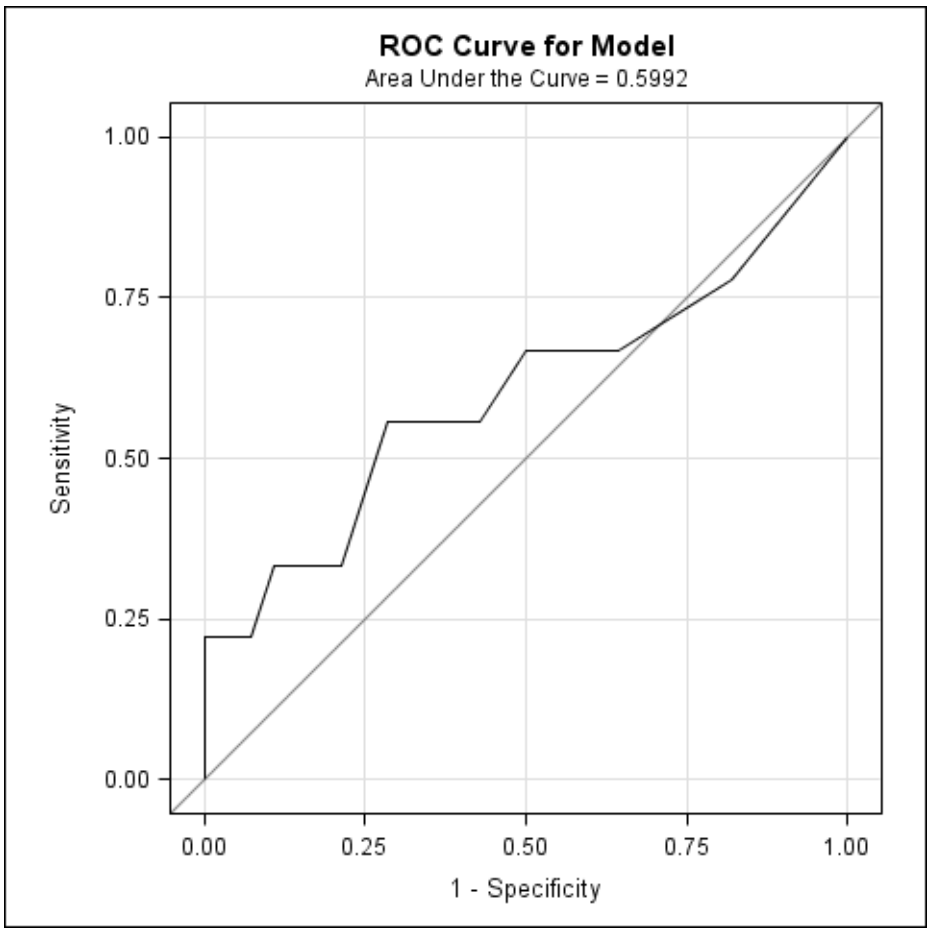
5.1.2.1 Statistical Analyses (1): Risk to the fetus

ROC analysis based on a dichotomous variable for risk according to the *T-ACE* risk group and *ASSIST Version 3.0 score*s for alcohol is shown in Figure 1.

Figure 1

Dichotomous Risk *T-ACE* and *ASSIST Version 3.0* Scores for Alcohol

n = 37



The area under the curve was 0.5992 (≈ 0.6), indicating that the *ASSIST's* performance was *fair* in diagnosing the dichotomous risk groups according to the *T-ACE*.

The sensitivities and specificities for cut-offs (based on each of the data points on the curve) are shown below in Text Box 4.

Text Box 4

Specificity and Sensitivity at Cut-offs (Data Points)

on the ROC Curve (Alcohol)

Cutoff	Sensitivity	Specificity
2	100.00	0.00
3	77.78	17.86
4	66.67	35.71
5	66.67	50.00
6	55.56	57.14
8	55.56	64.29
9	55.56	71.43
10	33.33	78.57
11	33.33	89.29
14	22.22	92.86
18	22.22	96.43
21	22.22	100.00
27	11.11	100.00

Determination of the 'cut point' on the *ASSIST* which could best be used to define the level of alcohol use that would place the fetus 'at risk', necessarily involves a 'trade-off' between the sensitivity of the test [the proportion of those identified as positive ('*at risk*') who are truly '*at risk*'] against the specificity [the proportion of those identified as negative (not '*at risk*') who are truly not '*at risk*'.]

5.1.2.1.1 Choice of cut-point on the ROC curve

At a cut-point of 5, the sensitivity is 66.67% and the specificity is 50%. That is, designating a Specific Substance Involvement Score (SSIS) on the *ASSIST Version 3.0* of 5 as indicative of risk to the fetus would result in identification of 66.67% of the alcohol users who would truly be placing the fetus at risk.

In the sample of 37 alcohol users under study, using the cut-point of 5, 18 would be classified as using alcohol so as to place the fetus 'at risk'.

However, on the standard *ASSIST Version 3.0* classification of risk to the woman herself, a further 8 women would be in the low risk category (*SSIS* score of 10 or under on *ASSIST Version 3.0*). Only 11 women in the study would be regarded as using at levels risky to herself (either at a medium or a high level of risk).

The 50% specificity indicates that at the cut-point of 5 on the *ASSIST Version 3.0*, only half the women who were classified as not placing the fetus 'at risk' would be correctly identified, that is would truly not be placing the fetus at risk.

By attempting to achieve higher sensitivity by lowering the **cut-point to 3**, the sensitivity would be higher (77.78%); however, the specificity would be much lower (< 18%). That is, designating an *ASSIST Version 3.0* score of 3 as indicative of alcohol consumption that would place the fetus 'at risk', would detect over three-quarters of the true positives for fetal risk.

In the sample of 37 alcohol users, using the cut-point of 3, 24 would be classified as using 'at risk' to the fetus, while on the standard *ASSIST Version 3.0* classification of risk to the woman herself, 18 of these women would be assessed as using at low risk to their own health (*SSIS* score on the *ASSIST Version 3.0* of 10 or under).

However, the 17.86 % specificity indicates that, at the cut-point of 3 on the *ASSIST Version 3.0*, fewer than 1 in 5 of the women classified as not 'at risk' would be correctly identified. This would result in a high number of false positive results. Although it has been postulated that false positives are less of a concern than false negatives, since a positive result for 'at risk' alcohol use (even if later determined to be false) could trigger a useful dialogue between practitioner and pregnant patient (Chang, Wilkins-Haug et al. 1998), this is an unacceptably low specificity

In this study, there were a high proportion of women classified by *T-ACE* as using alcohol at a level that would not place the fetus 'at risk'. If this was the situation in the pregnant population generally, it could be interpreted that a low specificity (17.8%) would be unacceptable, resulting in unnecessary counselling interventions.

By contrast, selection of a **cut-point of 6** or higher on the ROC curve would mean a decline in sensitivity values. Hence, it was concluded that a cut-point on the *ASSIST Version 3.0* of 5 was most appropriate as an indicator of alcohol use placing the fetus 'at risk'. The data for the alcohol users in this study are shown in Table 15. Currently, the cut-point for intervention in *ASSIST Version 3.0* is 10, based on risk to the woman herself.

Table 15

***ASSIST Version 3.0* and *T-ACE*: Dichotomous Risk**

n = 37

ASSIST Version 3.0	***T-ACE* dichotomous**		
Frequency (Cut-off Based on ROC analysis)	High risk	Low risk	Total
≥5	6	13	19
< 5	3	15	18
Total	9	28	37

In detail, **at the cut-point of 5**, the sensitivity is 66.67% (95% CI: 29.93%, 92.51%) and the specificity is 50.00% (95% CI: 30.65%, 69.35%). The positive predictive value (PPV) at this cut-point is 30.00% (95% CI: 11.89%, 54.28%) and the negative predictive value (NPV) is 82.35% (95% CI: 56.57%, 96.20%).

The PPV is the proportion of those who are screened as being 'at risk' on the *ASSIST Version 3.0* who are truly 'at risk' (calculated by true positives/ true positives + false positives). The NPV is the proportion of those who are screened as being not 'at risk' on the *ASSIST Version 3.0* who are truly not 'at risk' (calculated by true negatives/ true negatives + false negatives). The relationship between these parameters is illustrated in Table 16, using the example of the *ASSIST Version 3.0* and the *T-ACE*.

Table 16

Relationships between sensitivity, specificity, PPV and NPV

[Shown for the *ASSIST* and *T-ACE* (the 'gold standard')]

Alcohol

	***T-ACE* 'at risk'**	***T-ACE* not 'at risk'**	
***ASSIST Version 3.0* positive**	True positives (TP)	False positives (FP)	**PPV** = TP/ TP + FP
***ASSIST Version 3.0* negative**	False negative (FN)	True negatives (TN)	**NPV** = TN/ FN =TN
	Sensitivity = TP/ TP + FN	**Specificity** = TN/ TN + FP	

PPV: positive predictive value & NPV: negative predictive value

PPV is closely dependent on the 'prevalence' of the condition (here, alcohol use 'risky' to the fetus) in the population. The scarcity of population data relating to use by pregnant women of any substance apart from tobacco makes it difficult to comment on whether the sample in the study (most women not using 'at risk') is representative of the broader pregnant population, either in Australia or more generally. Hence, the ability to interpret the significance of the low PPV (30%) is limited. The significance of the high NPV (82.35%) is again difficult to interpret given this lack of population prevalence data.

5.1.2.2 Statistical Analyses (2): Risk to the pregnant woman

A 3X3 table was prepared using scores in the *ASSIST Version 3.0* and the *T-ACE* for the participants who used alcohol (n=37). The agreement results for the *ASSIST* and the *T-ACE* are shown in Table 17.

Table 17

***Agreement between ASSIST Version 3.0* Alcohol and *T-ACE* Risk Groups**

n = 37

ASSIST Version 3.0 Alcohol Risk Group	**T-ACE Alcohol Risk Group**			**Total**
Frequency Percent	Low Risk	Moderate Risk	High Risk	
Low Risk	**20** 54.05	6 16.22	5 13.51	31 83.78
Moderate Risk	1 2.70	**2** 5.41	2 5.41	5 13.51
High Risk	0 0.00	0 0.00	**1** 2.70	1 2.70
Total	21 56.76	8 21.62	8 21.62	37 100.00

The tools were in agreement for 23 (20+2+1) of the 37 alcohol users. *Kappa* statistics are shown in Table 18 and results for *Bowker's Test of Symmetry* in Table 19.

Table 18

Kappa* Statistics: the *ASSIST Version 3.0* and *T-ACE

***Kappa* Statistics**				
Statistic	Value	SE	95% Confidence Limits	
Simple *kappa*	0.2269	0.1157	0.0001	0.4536
Weighted *kappa*	**0.2513**	0.1172	0.0216	0.4810

The value of weighted *kappa* of 0.2513 is indicative of *fair* agreement between the *ASSIST Version 3.0* and the *T-ACE*.

Table 19

Bowker's* Test of Symmetry: the *ASSIST Version 3.0* and *T-ACE

Bowker's Test of Symmetry	
Statistic (S)	10.5714
Degrees of Freedom (DF)	3
P-value	**0.0143**

Bowker's Test of Symmetry has returned a statistically significant result (P <0.05); that is, Table 19 is not symmetric. Specifically, the *ASSIST Version 3.0* classified women in lower risk categories than the *T-ACE* (that is, the *ASSIST Version 3.0* was too conservative when classifying alcohol users).

5.1.3 Cannabis

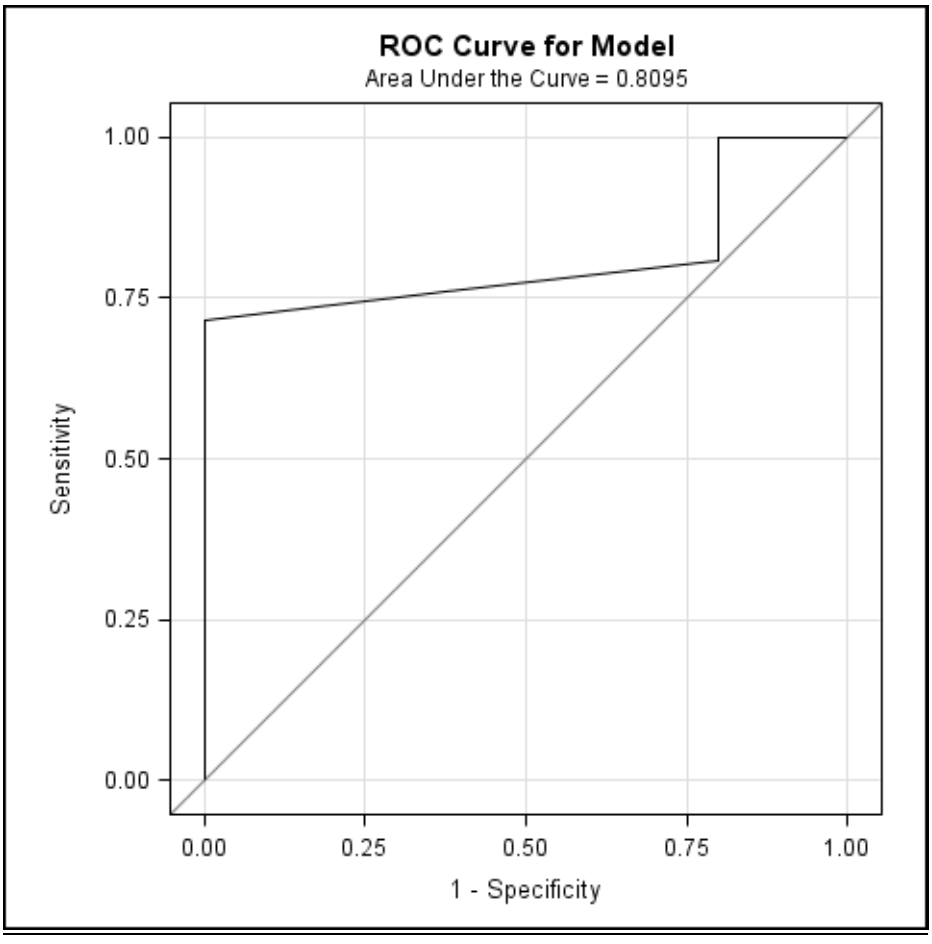
5.1.3.1 Statistical Analyses (1): Risk to the fetus

ROC analysis based on a dichotomous variable for risk according to the *Timeline FollowBack (TLFB)* and *ASSIST Version 3.0* scores for cannabis is shown in Figure 2.

Figure 2

Dichotomous Risk: *TLFB* and *ASSIST Version 3.0* Scores for Cannabis

n = 26



The area under the curve was 0.81, indicating that the *ASSIST Version 3.0* performed well in diagnosing dichotomous risk groups according to the *TLFB*.

The sensitivities and specificities for cut-offs (based on each of the data points on the curve) are shown below in Text Box 5.

Text Box 5

Specificity and Sensitivity at Cut-offs (Data Points) on the ROC Curve (Cannabis)

Cutoff	Sensitivity	Specificity
2	100.00	0.00
4	100.00	20.00
5	100.00	20.00
6	95.24	20.00
12	90.48	20.00
14	85.71	20.00
15	80.95	20.00
16	76.19	60.00
17	71.43	100.00
18	61.90	100.00
21	57.14	100.00
22	52.38	100.00
24	47.62	100.00
25	42.86	100.00
26	38.10	100.00
27	33.33	100.00
28	28.57	100.00
30	23.81	100.00
32	14.29	100.00
33	9.52	100.00
34	4.76	100.00

5.1.3.1.1 Choice of cut-point on the ROC curve

At a cut-point of both 4 and 5, the sensitivity is 100% and the specificity is 20%. That is, designating an *ASSIST Version 3.0* score of 4 or 5 as indicative of risk would identify 100% of those whose cannabis use would place the fetus 'at risk'. In the sample of 26 cannabis users, 24 would be classified as using 'at risk' to the fetus.

On the standard *ASSIST Version 3.0* classification of risk to the woman herself, these women would also be classified as using cannabis at risk to their own health: either at medium or high risk levels (*ASSIST Version 3.0* score of 4 or greater).

The 20% specificity indicates that, at the cut-point of either 4 or 5 on the *ASSIST Version 3.0*, only 1 in 5 of the women classified as not 'at risk' would be correctly identified based on the assessment by the *TLFB.* This would result in a high number of false positive results.

To achieve a higher specificity, the cut-point would need to be increased to 16 (60% specificity, 76.19% sensitivity). **At a cut-point of 16**, 100% specificity is achieved; however, the sensitivity has dropped by more than 24%. Further, given the negative impacts of cannabis use in pregnancy, it would be difficult to justify raising the cut-point to such an extent.

Further, the study sample had a high proportion of women classified by *TLFB* as high risk users for cannabis. If this was the situation in the pregnant population generally, it could be interpreted that a low specificity (even as low as 20%) would be acceptable at the cut-point for which sensitivity was 100%.

It appears most appropriate for a **cut-point on the *ASSIST Version 3.0* of 4** as indicative of cannabis use placing the fetus 'at risk' as this is the cut-off already delineated as indicative of medium risk to the woman herself on the

standard *ASSIST Version 3.0.* The data for the cannabis users in this study based on this cut-off are shown in Table 20.

Table 20

***ASSIST Version 3.0* and *TLFB*: Dichotomous Risk**

n = 26

ASSIST Version 3.0	*TLFB dichotomous*		
Frequency (Cut-off Based on ROC analysis)	High risk	Low risk	Total
≥4	21	3	24
<4	1	1	2
Total	22	4	26

In detail, at the cut-point of 4, the sensitivity is 100.00% ((95% CI: 83.89%, 100.00%) and the specificity is 20% (95% CI: 0.51%, 71.64%). The positive predictive value (PPV) is 84% (95% CI: 63.92%, 95.46%) and the negative predictive value (NPV) is 100% (95% CI: 2.50%, 100.00%). The high values for PPV and NPV, 84% and 100%, appear pleasing. However, as commented with the analysis of dichotomous variable of risk with alcohol users, the lack of population wide data on cannabis use in pregnancy limits the ability to generalize the findings of the PPV and the NPV to the wider population.

5.1.3.2 Statistical Analyses (2): Risk to the pregnant woman

Agreement results

A 3X3 table was prepared using scores in the *ASSIST Version 3.0* and the *TLFB* for the participants who used cannabis (n=26). The agreement results for the *ASSIST* and the *TLFB* are shown in Table 21.

Table 21

Agreement between *ASSIST Version 3.0* Cannabis and *TLFB* Risk Groups

n = 26

ASSIST Version 3.0 Cannabis Risk Group	**TLFB Cannabis Risk Group**			**Total**
Frequency Percent	Low Risk	Moderate Risk	High Risk	
Low Risk	**1** 3.85	0 0.00	0 0.00	1 3.85
Moderate Risk	4 15.38	**3** 11.54	11 42.31	18 69.23
High Risk	0 0.00	0 0.00	**7** 26.92	7 26.92
Total	5 19.23	3 11.54	18 69.23	26 100.00

The tools were in agreement for 11 (1+3+7) of the 26 cannabis users. *Kappa* statistics are shown in Table 22 and results for *Bowker's Test of Symmetry* in Table 23.

Table 22

Kappa* Statistics: the *ASSIST Version 3.0* and the *TLFB

***Kappa* Statistics**				
Statistic	Value	SE	95% Confidence Limits	
Simple *kappa*	0.2057	0.0842	0.0408	0.3707
Weighted *kappa*	**0.2831**	0.1027	0.0819	0.4843

The value of weighted *kappa* of 0.2831 is indicative of *fair* agreement between the two tools.

Table 23

Bowker's Test of Symmetry*: the *ASSIST Version 3.0* and the *TLFB

Bowker's Test of Symmetry	
Statistic (S)	15.0000
Degrees of Freedom (DF)	3
P-value	**0.0018**

Bowker's Test of Symmetry has returned a statistically significant result (P <0.05); that is, Table 15 is not symmetric. Specifically, the *ASSIST Version 3.0* tended to classify women in lower risk categories than the *TLFB* (that is, the *ASSIST Version 3.0* was too conservative when classifying cannabis users).

5.1.4.3 Reconsideration of the ROC Analysis for Alcohol in Light of the Cannabis Findings

A cut-point of 4 has been determined as the most appropriate to delineate fetal risk related to cannabis use. It is therefore compelling to reconsider the ROC analysis findings for alcohol use.

At both the cut-point of 5 (determined earlier) and at a cut-point of 4, the sensitivity was the same: 66.67%. If the cut-point for alcohol was selected as 4, this would align the recommendations for both alcohol and cannabis; however, it would be at the expense of specificity for the alcohol cut-point, which would drop from 50% (at a cut-point of 5) to only 35.71% at the cut-point of 4.

Although this would mean an increase in false positive results, this weakness could be seen as more than compensated by the clear delineation of a score for fetal risk for either of alcohol or cannabis. Table 24 shows the data for alcohol users in this study based on a **cut-off of 4**.

Table 24

***ASSIST Version 3.0* and *T-ACE*: Dichotomous Risk**

(revised)

n = 37

ASSIST Version 3.0	***T-ACE* dichotomous**		
Frequency (Cut-off Based on ROC analysis)	High risk	Low risk	Total
≥4	6	19	25
<4	2	10	12
Total	8	29	37

5.1.5 Sociodemographic Factors and *ASSIST Version 3.0* Scores

ASSIST Version 3.0 scores were compared between the categories of the following variables*:*

- age category:15-24, 25-29, 30-44
- marital status: married/defacto, other
- schooling category:<12 years, >=12 years
- ethnicity: Australian, Aboriginal or TSI, other
- socio-economic status (SES) [continuous variable]
- currently studying: yes, no
- paid work: yes, no
- live births/cohabiting with those children: no live births, live births > children with whom cohabiting, l ive bi rths = c hildren wi th who m cohabiting (noted earlier as a measure of family function/dysfunction)

- all pregnancies resulting in live births: no previous pregnancies, previous pregnancies < live births, previous pregnancies = live births)
- maternal age at birth of first child: 15-24, 25-29, 30-44
- complications in previous pregnancy:yes, no
- complications in this pregnancy: yes, no
- trimester at interview: 1st (0-12 weeks), 2nd (13-27 weeks), 3rd (27-40 weeks)

Independent samples *t-tests* were used to compare *ASSIST* scores according to predictor variables with two levels (for example, comparing *ASSIST* scores between women currently working or not currently working).

For predictor variables with three or more levels, a one-way *ANOVA* (analysis of variance) was used to compare *ASSIST* scores. One such variable was ethnicity and its method of categorization follows.

5.1.5.1 Categorization by Ethnicity

The Australian Bureau of Statistics in its Australian Standard Classification of Cultural and Ethnic Groups (ASCCEG) (Australian Bureau of Statistics 2005) defines ethnicity as the '*shared identity or similarity of a group of people on the basis of a one or more factors*', including shared history, cultural tradition, language, geographic origin and being '*racially conspicuous*'. Further, given the 'self-perceived group identification' involved, the response of 'Australian' has been endorsed as a category ('Australian') in the ASCCEG.

In this study, within the *Sociodemographic Questionnaire*, participants were asked to nominate their 'ethnicity'. Of the 104 women interviewed, 74 described themselves as 'Australian' and a further 10 as 'Aboriginal' or 'Aboriginal Australian'. For the purposes of classification, this category includes

Torres Strait Islanders (TSI), although no women of that ethnicity were participants in the study.

Of the remaining 20, nominated ethnicity allowed categorization within the following nine ASCCEG categories: New Zealander Peoples, British, Irish, Western European, Northern European, Southern European, Eastern European, South-East Asian, Sub-Saharan African. The small number in each of these categories could not allow meaningful analysis in relation to *ASSIST* scores; hence, a category of 'other' was used to describe the ethnicity of these 20 participants.

5.1.5.2 Categorization by Socioeconomic Status (SES)

For socioeconomic status (SES), a continuous predictor variable, simple linear regression models were used. The method of classifying socioeconomic status based on postcode is shown below.

The *Index of Relative Socio-economic Disadvantage* (IRSD) is a continuum of values with low values for disadvantage and high values for advantage, and is derived mainly from Census variables related to disadvantage, such as 'low income, low educational attainment, unemployment and dwellings without motor vehicles' (Australian Bureau of Statistics 2006). The area in which a person lives, not his/her individual socioeconomic situation, determines the index's value. This and three other indexes are used to provide a measure of the welfare of Australian communities through an ABS product termed SEIFA (Socio-Economic Indexes for Areas) (Australian Bureau of Statistics 2006).

In this study, the postcode of residence for each participant was queried; this was then linked to the *Index of Relative Socio-economic Disadvantage.* Values for South Australia range from 659 to 1128; in the study, values ranged from 788 to 1108. Three participants were from interstate - two from Broken Hill, NSW, (with an IRSD of 898) and the third from a location close to Darwin with

an IRSD of 979. These values were obtained from the relevant interstate IRSD rating of postcodes. All calculations were performed using SAS Version 9.1 (SAS Institute Inc., Cary, NC, USA).

5.1.5.3 Sociodemographic Factors as Predictors of the *ASSIST Version 3.0* Scores

This analysis of the sociodemographic parameters pertaining to the Phase II participants showed that a limited number of these factors were predictive of the *ASSIST* scores. Results are shown in Tables 25, 26, and 27.

Table 25

Sociodemographic Factors and *ASSIST Version 3.0* Tobacco Scores

n = 98

Variable	Category	Mean *ASSIST* Version 3.0 Tobacco Score	Standard error	P-value
Age	15-24 (n = 34)	25.4706	1.0098	0.3764
	25-29 (n = 25)	23.4400	1.1776	
	30-44 (n = 39)	25.2308	0.9428	
Marital Status	Married/defacto (n = 63)	24.0952	0.7341	0.0857
	Other (n = 35)	26.2286	0.9849	
Schooling	< 12 years (n = 53)	25.9811	0.7951	**0.0396**
	>= 12 years (n = 45)	23.5333	0.8628	
Ethnicity	Australian (n = 71)	24.7887	0.7036	0.7250
	Aboriginal or TSI (n = 10)	26.2000	1.8749	
	Other (n = 17)	24.3529	1.4379	
SES	Not Relevant	-	-	0.6920

SES quintile	1 (n = 9)	25.2222	1.9978	0.9628
	2 (n = 23)	24.2609	1.2497	
	3 (n = 17)	25.5882	1.4536	
	4 (n = 22)	24.5455	1.2778	
	5 (n = 27)	25.0370	1.1534	
Studying	Yes (n = 16)	23.9375	1.4759	0.4974
	No (n = 82)	25.0366	0.6519	
Paid work	Yes (n = 23)	23.0435	1.2157	0.0914
	No (n = 75)	25.4133	0.6732	
Live births /cohabiting	No live births (n = 28)	24.5357	1.0988	0.3843
	Live births > children cohabiting (n = 16)	26.8125	1.4535	
	Live births = children cohabiting (n = 53)	24.6415	0.7986	
Pregnancies resulting in live births	No previous pregnancies (n =18)	23.9444	1.3982	0.7645
	Previous pregnancies > live births (n = 52)	25.0000	0.8226	
	Previous pregnancies = live births (n = 28)	25.1786	1.1211	
Age at birth of first child	15-24 (n = 56)	25.1607	0.8248	0.6813
	25-29 (n = 7)	26.5714	2.3330	
	30-44 (n = 5)	23.4000	2.7604	
Complications in previous pregnancy	Yes (n = 42)	26.3095	0.9092	0.0555
	No (n = 30)	23.5667	1.0758	
Complications in current pregnancy	Yes (n = 64)	25.8906	0.7177	**0.0163**
	No (n = 30)	22.9118	0.9847	
Trimester at interview	1 (n = 5)	24.8000	2.6412	0.5021
	2 (n = 24)	26.0833	1.2055	
	3 (n = 69)	24.4348	0.7110	

Table 26

Sociodemographic Factors and *ASSIST Version 3.0* Alcohol Scores

n = 37

Variable	**Category**	**Mean *ASSIST Version 3.0* Alcohol score**	**Standard error**	**P-value**
Age	15-24 (n = 12)	9.0833	1.6341	0.2422
	25-29 (n = 6)	4.8333	2.3110	
	30-44 (n = 19)	6.1053	1.2987	
Marital Status	Married/defacto (n = 24)	5.6667	1.1372	0.0842
	Other (n = 13)	9.0769	1.5451	
Schooling	< 12 years (n = 15)	6.6667	1.5013	0.8650
	>= 12 years (n = 22)	7.0000	1.2397	
Ethnicity	Australian (n = 26)	5.8846	1.0819	0.1006
	Aboriginal or TSI (n = 2)	4.0000	3.9007	
	Other (n = 9)	10.3333	1.8388	
SES	Not Relevant	-	-	0.9652
SES quintile	1 (n = 4)	8.2500	2.9137	0.5855
	2 (n = 8)	5.7500	2.0603	
	3 (n = 7)	4.1429	2.2026	
	4 (n = 8)	8.0000	2.0603	
	5 (n = 10)	8.2000	1.8428	
Studying	Yes (n = 7)	10.8571	2.0670	**0.0390**
	No (n = 30)	5.9333	0.9984	
Paid work	Yes (n = 15)	6.1333	1.4934	0.5294
	No (n = 22)	7.3636	1.2331	

Live births /cohabiting	No live births (n = 15)	7.6667	1.5270	0.8116
	Live births > children cohabiting (n = 3)	5.6667	3.4146	
	Live births = children cohabiting (n = 18)	6.6111	1.3940	
Pregnancies resulting in live births	No previous pregnancies (n = 11)	7.0909	1.7773	0.9578
	Previous pregnancies > live births (n = 14)	6.5000	1.5754	
	Previous pregnancies = live births (n = 12)	7.0833	1.7016	
Age at birth of first child	15-24 (n = 16)	6.3750	1.2671	0.9467
	25-29 (n = 3)	7.3333	2.9263	
	30-44 (n = 2)	6.0000	3.5840	
Complications in previous pregnancy	Yes (n = 11)	5.1818	1.5115	0.1245
	No (n = 13)	8.4615	1.3904	
Complications in current pregnancy	Yes (n = 26)	6.6154	1.1382	0.6901
	No (n = 11)	7.4545	1.7499	
Trimester at interview	1 (n = 2)	16.5000	3.7935	**0.0390***
	2 (n = 11)	5.5455	1.6176	
	3 (n = 24)	6.6667	1.0951	

*Scores in trimester 1 were significantly higher than scores in trimester 2 and trimester 3 (**p = 0.0119** and **p = 0.0178** respectively). No differences were found between trimester 2 and trimester 3 (p = 0.5698).

Table 27

Sociodemographic Factors and *ASSIST* Version 3.0 Cannabis Scores

n = 26

Variable	Category	Mean Cannabis *ASSIST Version 3.0* Score	Standard error	P-value
Age	15-24 (n = 11)	23.6364	2.6865	0.1184
	25-29 (n = 8)	15.0000	3.1502	
	30-44 (n = 7)	17.7143	3.3677	
Marital Status	Married/defacto (n = 13)	2.5750	2.5750	0.2324
	Other (n = 13)	2.5750	2.5750	
Schooling	< 12 years (n = 16)	21.8750	2.2478	0.0867
	>= 12 years (n = 10)	15.4000	2.8432	
Ethnicity	Australian (n = 17)	17.8824	2.3018	0.5060
	Aboriginal or TSI (n = 4)	20.7500	4.7454	
	Other (n = 5)	23.4000	4.2444	
SES	Not Relevant	-	-	0.5807
SES quintile	1 (n =1)	15.0000	9.5506	0.7463
	2 (n = 3)	16.0000	5.5140	
	3 (n = 3)	25.6667	5.5140	
	4 (n = 10)	18.8000	3.0202	
	5 (n = 11)	19.8182	2.8796	
Studying	Yes (n = 4)	15.5000	4.7068	0.3785
	No (n = 22)	20.0909	2.0070	

Paid work	Yes (n = 3)	18.0000	5.5172	0.7919
	No (n = 23)	19.5652	1.9926	
Live births /cohabiting	No live births (n = 5)	24.8000	4.1820	0.3599
	Live births > children cohabiting (n = 5)	19.0000	4.1820	
	Live births = children cohabiting (n = 16)	17.8125	2.3378	
Pregnancies resulting in live births	No previous pregnancies (n = 5)	24.8000	3.9569	0.1008
	Previous pregnancies > live births (n = 15)	16.0667	2.2845	
	Previous pregnancies = live births (n = 6)	23.1667	3.6121	
Age at birth of first child	15-24 (n = 18)	18.4444	2.3704	0.9271
	25-29 (n = 2)	16.0000	7.1111	
	30-44 (n = 1)	16.0000	10.0566	
Complications in previous pregnancy	Yes (n = 12)	16.8333	2.8727	0.4780
	No (n = 8)	20.1250	3.5183	
Complications in current pregnancy	Yes (n = 18)	19.7222	2.2523	0.7893
	No (n = 8)	18.6250	3.3785	
Trimester at interview	1 (n = 1)	28.0000	9.3301	0.3416
	2 (n = 5)	23.4000	4.1725	
	3 (n = 20)	17.9500	2.0863	

5.1.5.4 Discussion of Sociodemographic Factors Significantly Predictive of *ASSIST Version 3.0* Scores

- ***Tobacco***
    - ***Years of Schooling***

For tobacco users, only years of schooling [<12 years or >/= 12 years] (p= 0.03960) and complications in the current pregnancy (p= 0.0163) were predictive of the *ASSIST* score (see Table 25).

It is not unexpected that having attended school for less than 12 years was predictive of a higher *ASSIST Version 3.0* tobacco score. The likelihood of engaging in post-secondary education is correlated with socioeconomic status (SES) (Foley 2007; Universities Australia 2008), with those of lower SES less likely to engage. Further, tobacco use in Australia is known to be associated with being of lower socioeconomic status (Turrell, Stanley et al. 2006); this was also confirmed in the Phase I study, in which those attending the Lyell McEwin Hospital in the northern suburbs of Adelaide being significantly more likely to smoke tobacco than those attending the Women's and Children's Hospital in the centre of Adelaide.

- **Medical or pregnancy-related complications in the current pregnancy**

The other predictor of a higher *ASSIST Version 3.0* tobacco score was experiencing medical or pregnancy-related complications in the current pregnancy. The finding is an intuitive one. Phase II data indicated that 64 of the 98 tobacco users reported complications in their current pregnancies, with 16 of these hospitalized for pregnancy complications associated with tobacco use. A further 14 women reported medical conditions likely to be aggravated

by tobacco use. Detail of reported complications associated with tobacco use appears in Table 28.

Table 28

Phase II study: Medical and Pregnancy-related Complications for Tobacco Users in Current Pregnancy [Data shown only for Complications Associated with Tobacco Use]

n= 29

Participant No	Medical condition negatively affected by tobacco use/ associated with tobacco use	Pregnancy complication associated with tobacco use
4	Depression	
7	Depression	
8	Asthma	
12	cardiac condition	
18	Type I diabetes	
19 *	diabetes	preterm premature rupture of membranes
20		threatened preterm labour
24		antepartum haemorrhage
25	Type 2 diabetes	
28	Asthma	
29	Asthma	
30		preterm premature rupture of membranes
35		preterm premature rupture of membranes
40		IUGR
41	Diabetes	
43		preterm premature rupture of membranes
46		threatened preterm labour

47		threatened preterm labour
54	Schizophrenia	
63		threatened preterm labour
64	cardiac condition	
67	Diabetes	
68		threatened preterm labour
71		threatened preterm labour
72		preterm premature rupture of membranes
80		preterm premature rupture of membranes
82	Schizophrenia	
92		threatened preterm labour
97		placenta praevia
***** medical condition likely to be aggravated by tobacco use/associated with tobacco use *and* pregnancy complication associated with tobacco use.		

- ***Alcohol***
    - ***Trimester of Pregnancy***

For alcohol users, the only predictors of the *ASSIST* score (see Table 19) were trimester of pregnancy at interview (p= 0.0390) and whether or not the woman was currently studying (p= 0.0390). Scores for women in the first trimester were significantly higher than scores for women in the second and third trimesters (p = 0.0119 and p = 0.0178 respectively). However, no significant difference was found for the *ASSIST* scores between women in the second trimester and those in the third trimester (p = 0.5698).

Earlier research has indicated decreasing use of alcohol as the pregnancy progresses (Condon and Hilton 1988; Colvin, Payne et al. 2007), with the Western Australian study showing that 14.8% of first trimester women used alcohol outside the then current (2001) NHMRC guidelines, compared with

10% in the second and third trimesters (Colvin, Payne et al. 2007). In contrast to these findings in the Phase II study, the Phase I study detected no significant differences in prevalence of use of alcohol between women in the three trimesters, although the amount of alcohol used was not analysed.

Research supports that being a student in any of a variety of educational settings is associated with problematic alcohol use (Ingersoll, Ceperich et al. 2005; Carvalho, Sant'Anna et al. 2008; Eaton, Kann et al. 2008). However, given the lack of any information regarding the educational settings for the women in the study, further comment cannot be made.

- **Cannabis**

For **cannabis** users, none of the variables measured were predictive of the *ASSIST* score (see Table 20).

5.1.5.5 Further Analyses of the Quantitative Data: *Risk to the Pregnant Woman*

It was anticipated at the commencement of this research project that the investigation conducted to determine associations between the *ASSIST* and the other tools could lead to a re-assessment of the relevance for the study population (pregnant women) of the 'cut-offs' in scores indicative of different levels of risk to the women themselves. The existing 'cut-offs' had been established within the general population for each of the substances/ classes of substances assessed. The lower cut-off - the score which starts the moderate risk category - is currently set at 4 for tobacco and cannabis and 11 for alcohol. The upper cut-off - the score that starts the high risk category for all substances - is set at 27.

The statistical analysis described earlier in this chapter was based on the existing 'cut-offs'. Following this, the association (measured by mean *kappa*)

between the *ASSIST* and the *RTQ* in the study population was calculated using a series of lower and upper cut-offs for risk. These analyses were based on the tobacco tools, given the larger number of tobacco users identified and interviewed in the Phase II study, 98 in all.

In the series of calculations, 630 in all, the lower cut-off ranged in value from 2 to 36 and the upper cut-off ranged in value from 3 to 37. Using all possible combinations of cut-points, the value of *weighted kappa* was no higher than for the initial analysis (reported earlier in this chapter) of 0.4257 (≈ 0.43). Hence, it was concluded that any change to the low/medium/high risk categories based on '*risk to the pregnant woman*' could not be justified and no extension of this analysis was conducted.

5.2 Further Results: Tobacco Use by the Phase II Participants

A feature of the Phase II study was the predominance of tobacco users in the study cohort, with 98 of the 104 interviewees (94.2%) reporting tobacco use. Women were targeted for approach by the researcher (EH) based on case note records of any substance use. For the purposes of the study, it was necessary for women, once questioned, to be users (in the last three months) of at least one of tobacco, alcohol or cannabis, with or without use of other substances. The predominance of tobacco users in Phase II was in marked contrast to the Phase I study, in which 66% of those using substances were using tobacco. This could be related to the different representation of the trimesters in the two cohorts.

Phase I participants were, by design, all women attending for their first antenatal visit. Over half the women (418 of 748 women: 55.9%) were in the first trimester, with 272 women (36.4%) in the second trimester and only 32

women (4.3%) in the third trimester. Twenty-six women (3.4%) did not answer the question related to gestation of pregnancy.

However, in the Phase II study, the higher proportion, 73 of the 104 women (70.2%) were in the third trimester, with 26 women (25%) in the second trimester, and only 5 women (4.8%) in the first trimester. The weighting towards the third trimester is likely to have been at least partly related to the recruitment of approximately one-third of participants from the antenatal ward. This was a deliberate tactic to increase women at 'high risk' in the cohort, by including women with medical or pregnancy-related complications; such complications may be associated with, or exacerbated by, substance use.

Early in pregnancy, many women stop use of tobacco (Fingerhut, Kleinman et al. 1990; Wakefield and Jones 1998) and other substances (Zambrana and Scrimshaw 1997; Chen and Kandel 1998; Ockene, Yunsheng et al. 2002; Ebrahim and Gfroerer 2003). However, it is well-recognized that nicotine is a highly addictive substance (Dempsey and Benowitz 2001; Slotkin 2008); even women who do cease early in pregnancy may resume smoking later (Quinn, Mullen et al. 1991), due, at least in part, to their nicotine dependence (as evidenced by their daily cigarette use) (Quinn, Mullen et al. 1991).

Hence, it is possible that, for some of the women interviewed later in pregnancy for the Phase II study, use of other substances had ceased by the time of interview, while use of tobacco was ongoing or had been resumed.

This is concordant with the other study finding that those participants who were tobacco users were likely to be using at higher levels. A similar pattern for participants' cannabis use (that is, likely to be at the higher risk end) may reflect the reported difficulty experienced by heavier users of cannabis in ceasing use, even though pregnant (Fried, Barnes et al. 1985). Although data from the earlier Phase I study did not show a significant difference in

substance use between participants according to trimester, that analysis was constrained by the limited number of third trimester women in that sample.

Chapter 6:

Qualitative Data related to the *ASSIST Version 3.0: Questions 2 through to 7*, and their Thematic Analysis

Of the 104 women interviewed and administered the *ASSIST Version 3.0* in the Phase II study, all but four chose to expand on their answers to the tool. Qualitative data emerging from the *ASSIST Version 3.0* questions 2 through 7, the scores for which contributed to the *ASSIST's Specific Substance Involvement Score,* were transcribed during the interview. Thematic analysis was later used to determine identifiable themes and the patterns of perspectives, behaviours and experiences reported. These collated findings and the implications that arise from them are reported in this chapter.

6.1 Question 2: *In the <u>past three months</u>, how often have you used the substances you mentioned (first drug, second drug, etc)?*

Eighteen participants added further comments to their responses to this question. Two main themes emerged from these data: that many women found pregnancy a strong motivator for change, and that, if they did continue to use, it was with reservations about the behaviour. For a few women, however, substance use was simply a reality in their lives.

6.1.1 Changes Motivated by Pregnancy

Some women took the opportunity to elaborate on pregnancy-motivated changes to substance use: '*Before my pregnancy was confirmed, I used hallucinogens and opioids …' (*Participant 18); '*… only one drink in the last 3 months*' (Participant 20); '*… cigars but not when I'm pregnant*' (Participant

74); '*Before I … was pregnant, … amphetamines, but not in the last 3 months*' (Participant 88); '*No, not cannabis. I cut down and stopped in the first 8 weeks*' (Participant 102).

For Participant 66, her previous pregnancy had shifted her attachment to drug use. *'Life changes. You hit your 30s. I grew out of it. The year before J. (her son) was born, [I did] no drugs. Just working. Not interested. Now, even tobacco is starting to make me sick. Have had queasiness and was coughy (sic)'.*

6.1.2 Continuing Use, but with Reservations

However, others reported continuing substance use, although with reservations, for example Participant 65: 'Yes. [I'm] *smoking every day and increasing*' while Participant 61 added '*unfortunately*' to her report of daily smoking. Although still smoking daily, Participant 68 declared that: '*I wouldn't use alcohol. Alcohol's worse than anything. And I tell [other] pregnant women not to smoke*.'

6.1.3 Affirmation of Reality

Not all women interviewed regretted their substance use. Participant 80 declared: '*I am a smoker and I smoke very day!',* while Participant 76 reported that she needed '*a session at night [of cannabis use] to relax',* and Participant 99 regarded her daily cannabis use as '*medicinal*'.

6.2 Question 3: *During the <u>past three months</u>, how often have you had a strong desire or urge to use (first drug, second drug, etc)?*

Twenty-two participants elaborated on their responses to this question. A number of themes emerged: that a compulsion to use was strongly linked to specific situations, specific people or to their level of stress; that, particularly

for smokers, such a compulsion was an accepted part of their habit; however, being pregnant could enhance a woman's ability to resist any urges to use a substance.

6.2.1 Situations of Substance Availability

For a number of participants, the urge to use was linked to situations where the substance was available: '[I get an] *urge to use tobacco when I'm with friends*' (Participant 52); while, for Participant 56, the urge to use amphetamines was linked to '*… when I'm around other people who are using*'. Participant 95 described a recent 'strong urge' to use heroin. '*I've been off it for about 11 years, but was offered it the other day*'.

One participant (No.94), having described occasional 'urges' to use amphetamines, took the opportunity to chronicle her treatment by health care providers in her last pregnancy as the reason she had not disclosed amphetamine use this time: *'Last pregnancy, I was open and honest, but [the care providers] didn't understand that I took <u>oral</u> amphetamine. They [always] looked at my arms. I didn't even like to have a blood test. It was high risk. It was overpowering at each visit.'*

6.2.2 Stress Management

Some participants had a 'strong urge' in circumstances of stress: '*…an urge to smoke…depends on how my son is behaving*' (Participant 58); '*It's a reaction to stress*' (Participant 65- a daily tobacco smoker), and for Participants 71 and 104: '*…a strong urge to use cannabis…weekly. It's when I'm really stressed*'.

6.2.3 Acknowledged Part of Drug Habit

For a number of daily tobacco users such as Participant 68 (now 28 years old), a 'strong urge' was a standard aspect of life: '*When I started, I was 8 years old. I pinched one of Mum's. [From] 14 to 16, I had the occasional one. At 17, I started buying. I've been trying to give it up since I started*.' Another

participant (No.94) spoke of a '*constant craving* [to use tobacco]. *But the smell's no good and I'm only smoking in bursts*'.

6.2.4 Enhanced Capacity to Resist Urges

Others resisted urges to consume substances used previously, because, as Participant 76 explained, '*my son is more important now*'. Health issues assisted Participant 88 to resist 'strong urges' to use alcohol: '*I stopped a month prior to pregnancy, Had an op booked in. I had to cut back. I was an alcoholic. I used to binge for a week*.'

6.3 Question 4: *During the <u>past three months</u>, how often has your use of (first drug, second drug, etc) led to health, social, legal or financial problems?*

Half the participants (55 of the 104) enlarged on their responses to this question. The question (as framed) is a complex one with four dimensions. It became clear to the researcher (EH) after prompting by early respondents, such as: '*could you please repeat the question?*' (Participant 5), that it would be more appropriate to query each of the dimensions separately. The score is a global one so that the highest scoring dimension determines the score for the question.

6.3.1 Health Problems

Tobacco and cannabis were most likely to be reported as implicated, although some women voiced scepticism about the negative effects of tobacco use. Respondents generally focussed on their own health; however, although a number of women were conscious of the impact of their substance use on the baby *in utero*, for example '*Are you talking of the health of me or my baby?*' (Participant 64 reporting daily health problems with tobacco).

- ***Tobacco***

Most participants reported conditions such as '*breathlessness*' (Participant 21); '[regular] *chest and throat infections*' (Participant 42); '*…coughing for the first month* [of pregnancy]… e*very night*' (Participant 68); '*…my lungs. Especially if I haven't slept well*' (Participant 76); '*…asthma, and I have found out that it's linked to high blood pressure*' (Participant 103); '*… my heart*. [The problems] *coincide with doctor's visits*' (Participant 63).

Some participants voiced concern about their baby's health, given their tobacco use: '*….tobacco? Yes. My baby. It's just rammed down your throat. As a mother-to-be, you're letting down the team*' (Participant 39), while Participant 95 commented: '*I am worried about the baby. I know that I shouldn't be doing it and I'm conscious about others' views'.*

However, a few participants were less certain: '[I've spoken to] *half a dozen people who have opinions. I've had a mixture of responses*' (Participant 82). Participant 38 was highly sceptical: '*The doctors tell me that the miscarriages* [I've had seven] *were due to smoking, but this can't be true as I am four months* [pregnant] *now and I am still smoking.*'

A number of women reported cutting down tobacco use because of health problems themselves or concerns about their baby's health: '*I have gone from 50 a day to 5 a day now, and not smoking at the moment*' (Participant 103), and Participant 60 explained that: '*I cut down if I get a cough. I'm only using a pouch- that's about 20 cigarettes- in a fortnight now.*'

By contrast, the tobacco use of one participant (No 65) had accelerated, but she did not perceive that as a problem: '*I got married in February and I've gone from half a pack a day to a pack a day.* [However], *six to nine months like that is not a* [health] *problem. It would be an issue if it continued longer-term.*'

If a woman did 'cut down', it was not always sustained. As Participant 82 reported: '*…early in pregnancy, I got down to three a day. But I'm back to 20 or 25 a day now. I've been smoking since I was 13 or 14* [now 33 years old], *and smoking more now as I get older*.'

- ***Cannabis***

A number of participants reported health problems caused by their cannabis use, for example: '*When I smoke [cannabis], I end up sick and that's when I know I shouldn't be doing it*' (Participant 71). Another participant (No 45) explained that: '*…if I have a cone of cannabis, then I may cough 2 or 3 times,* [and this happens] *about twice a week. Since I have quit* [cannabis], *I've been bringing up lots of phlegm and I'm feeling better. Not feeling lazy and not drugged up. My body can do more than it used to.*' However, Participant 56 found that stopping use was not helpful: '*I stopped* [but] *I was very sick, vomiting. And mentally - well, it didn't make me feel any better*'.

A few participants believed that their cannabis use was impacting on the baby's health: '*Yes, weekly* [problems]. *Probably with the baby. I've got mental guilt* [about using cannabis]' (Participant 66). Another participant (No 94) reported that there had been no health problems with cannabis use, but then followed that with: '*I feel silly saying no, because I know it is a problem* [for the baby]'.

- ***Alcohol***

Health problems related to alcohol were only reported by one participant (No 76): '*It affects my appetite and general well-being. My sister-in-law is a bad influence*.'

- ***Other Substances***

One participant (No.42) detailed health problems 'in the past 3 months' with opioids: '*I'm taking Panadeine Forte®* -eight to twelve a day for the past 2*

months. I'm worried about the paracetamol and my liver. I don't want to come off at this stage but I am wondering about my labour. My mother-in-law will be there. She's a retired midwife and I've been reading about NAS [neonatal abstinence syndrome] on the internet. I'm worried she'll notice the baby is affected.' The researcher (EH) referred this patient to one of the obstetricians, without disclosing the reason, so that she could access the appropriate care.

*each tablet contains paracetamol 500mg and codeine phosphate 30mg

6.3.2 Social Problems

Problems in social settings were detailed by a number of participants. Even participants who had not personally experienced such problems, such as Participant 102: '*it never happened to me*', were conscious of the potential for such experiences: '*People who (sic) you know that smoked in pregnancy say that people look at you differently when they know you're pregnant*' (Participant 21). Another woman, Participant 66, commented that: '*I wouldn't smoke in public*', while Participant 29 recognized that, although '*I haven't had a problem myself … you shouldn't drink while you're pregnant, so that could be a problem when you're out*'.

Often the social problems arose from encounters with strangers, most commonly in relation to tobacco use: *'…a woman in a restaurant said it's none of my business but…'* (Participant 65), while Participant 30 reported that: '*…some people look at me weird…*'. Another participant (No 29) reported being ' … *spoken to by a stranger in the train* [about smoking].'

Social difficulties did not only arise from approaches by strangers: *'I get lectures from people at work. I'm under scrutiny. It forces you to be secretive* [about tobacco use]' (Participant 37). Further, even if the approach is friendly, a woman may find it socially problematic: '*An old fellow came up to me and said nicely….I don't want you to get sick like me'* (Participant 77).

6.3.3 Financial Problems

A recurring theme explored by participants was financial problems related to their substance use. This was mentioned in relation to tobacco most often, to cannabis at times, but not at all in relation to alcohol.

- ***Tobacco***

'I was advised to give up tobacco in '95. I use tobacco now [rollies] to save money' (Participant 19 – now 36 years old); although, as another participant (No.31) noted: '*… cheaper but tougher on the lungs*'. Participant 53 described 'daily' financial difficulties and '*… trying to cut down because of the cost*.' Another participant (No.85) was '*… noticing* [the cost] *now while I'm in hospital. My partner can't work. He's got to look after the kids*.'

- ***Cannabis***

'*We spend $125 a week on cannabis and we've been putting our stuff in hock*' (Participant 43), while Participant 45 reported that: '*It was costing me about $50 a week and I had to sell some of my stuff to buy it* [cannabis]. *I've stopped now and getting back on track. I've disposed of my bong*.' However, for one participant (No 67), there were no such financial issues: '*my friend grows it*'.

6.3.4 Legal Problems

The legal impacts of substance use were only commented on by a few participants using cannabis, with one participant (No.18) commenting '*I was [recently] busted* [in relation to cannabis],' and another (Participant 103) that she '*was busted in 2006*'. Pregnancy and parenthood was again reported as a motivator for change, this time by Participant 66 (now 34 years old): '*yes…when I was younger, I would have driven and used cannabis. No way I'd do that now*'. This sentiment was reiterated later in her interview: *'I've got a baby now. A bit more responsibility and guilt'.*

No mention was made of legal problems related to driving a motor-vehicle under the influence of either alcohol, cannabis or other drugs.

6.4 Question 5: *During the <u>past three months</u>, how often have you failed to do what was normally expected of you because of your use of (first drug, second drug, etc)?*

Fourteen participants elaborated on their answer to this question. There were a number of recollections of incidents when they had failed to live up to their responsibilities because of use of substance/s. Despite the *ASSIST* not demanding a response to this question for tobacco, the researcher was prompted to ask it by one of the early interviewees (Participant 17).

- ***Tobacco***

Her comment on family duties was typical of the eight participants who answered this question in the affirmative: '*I can avoid responsibilities by taking time out to smoke*'. However, one participant (No 57) described how '*my supervisor is down on me. He may see me as wanting to smoke first, then do* [my] *work*.'

- ***Cannabis***

'*Yes…definitely. I have missed a few appointments with Job Network and my social worker*' (Participant 43); '*Doing no housework, my partner got grumpy, just cruising about, and I realized that this was crap.*' (Participant 45); and Participant 56 reported that '...[cannabis] *puts you out of it*'.

- ***Alcohol***

"Yes…once or twice. I was late to pick up the kids from arrangements with my ex-husband. Nothing major.' (Participant 74).

- ***Other Substances***

'Yes…I can't get motivated until I get my methadone' (Participant 56), while Participant 95, an ATS user, reported: '*Once or twice. Was linked with the kids. Had guilt, a conscience about it. Was supposed to do shopping but I lost track of time.'*

6.5 Question 6: *Has a friend or relative or anyone else <u>ever</u> expressed concern about your use of (first drug, second drug, etc)?*

Most pregnant substance users do receive expressions of concern, often from several people in their lives: '*…my midwife bugs me every time I come in, my aunt says just stop when you're pregnant, and my mother says you know you shouldn't be doing it…*' (Participant 96, tobacco user).

6.5.1 Friends

Fourteen women elaborated on friends' expressions of concern in the past three months and a further 15 of their concerns at earlier times. For three participants, concern had been expressed by friends both recently and in the past: '[In the past 3 months], *my friends count the cigarettes or if I have a glass of alcohol*' (Participant 65), while earlier: '…yes, *concern or criticism from friends of friends of friends*…' [regarding her use of a number of substances]. For Participant 71, friends had said:'…*you shouldn't be smoking while you're pregnant*…', while [not in the past 3 months], in relation to her use of ATS: '*Everyone - friends, family, the local GP. I used I/V [intravenously]. Went from size 12 to size 6 in three weeks. After five months of using, I faced it* [the reality of the situation].'

Although the friends of Participant 30 were currently expressing concern '*more than ever'* about her tobacco use, in the past friends had voiced concerns about her use of ATS, and '*pushy friends still check* [regarding this]'. For Participant 47, friends had recently expressed concern about her smoking, but '*I hide it from my family. I've had a mini-stroke. Everyone I know smokes and I don't think I smoke much compared to other people'.*

Although another participant (No 80) had her friends '*… concerned about the cannabis'* [in the past 3 months], she explained that '*... it helps me with the depression. The doctors and midwives respect that* [and do not express concern]. *However, I underestimate my use to them. Say a half instead of a full bag.'*

6.5.2 Relatives

Sixty-two women described how one or more family members had voiced concern [in the past 3 months], and forty-three that concern by family members had been voiced earlier – [not in the past 3 months]. These two sets of responses are not mutually exclusive; that is, for some participants, family members had voiced concern both 'in the past 3 months', and earlier.

Many of the concerns were expressed in relation to tobacco use, this being the substance of which use was most commonly reported while pregnant. However, for any one participant, over her lifetime, concern had sometimes been expressed by family members about use of a number of substances. For example, one participant (No.104) reported being 'nagged' by her sisters: '*I've managed to stop other substances. In my second pregnancy, I did cut down tobacco. But when things get on top of me, I smoke more. People should get off my case.'* The concept of a family member being '*on [her] case*' was echoed by another participant (No.76), who reported in relation to her cannabis use: *'The child's father [has expressed concern]. He's on my case*

daily. Worried about disability in his family', while participant No 45 concluded that '*my whole family is on my case - teenage nephews and nieces, my boyfriend, sisters and Mum'*.

This woman was not the only participant who listed a number of family members concerned about her substance use. Another was Participant 30 who reported '*Mum, Dad, sister, brother, boyfriend, Auntie*' as all being concerned about her smoking. For Participant 68, her mother, father and grandfather were all concerned about her tobacco use, and '*Grandpa offered me money to quit*.' For some women, it was their children who voiced concern: '*My 21 year old… he smokes himself*' (participant 65) and for another (Participant 102), '*…just in the last couple of days. My 9 year old daughter'*.

Women may face more concern from others at times of crisis. For Participant 49, family expressions of concern became more intense [not in the past 3 months] when '*my grandmother died of lung cancer. I quit for 2 weeks after her death. That's the longest time.'* Participant 76 reported concern expressed '… a*bout my amphetamine use* [not in the past 3 months]…e*specially friends and my sister. Soon after her friend died from heroin*'.

Family members were sometimes moved to intervention due to their concern. One woman (Participant 103) described how, earlier, '*All my family [were concerned]. I was using meth[amphetamine] for two and a half years. And anything else. My family sent me to London and I went cold turkey.'*

6.5.3 Anyone Else

Five women reported that concerns had been expressed 'in the past 3 months' at work in relation to their substance use, three by work colleagues, one by her supervisor, and the fifth by her '*female boss*.' In all instances, the substance use that drew concern was that of tobacco. However, apart from friends and family, it was health care providers who were most likely to

express concern. Seventy-two participants nominated care providers as 'expressing concern' in relation to their substance use, 58 'in the past 3 months' and 14 'previously'.

Participant 80 reported that: '*Doctors and midwives are always on my case. [But] not my family. They mostly smoke*', while Participant 69 commented that: '*The doctor at the hospital is always telling me about my smoking'.* Participant 66 reported that: *'One of the nurses spoke to me today.* [However] *my family don't know. They'd be the ones to criticize. My husband. Yes. He's using patches and giving up. Friends? No. I have the odd drag with them',* and for Participant 56, the doctors had expressed concern: '*…I've had whooping cough*'.

Women reported varying messages from different health care providers as to their tobacco use. While participant 63 had been told: *'You should quit smoking while you're pregnant',* another participant (No 72) reported that: '*My GP said to cut back but don't quit [smoking]. That causes more stress.* [But] *he knows I cut down my drinking and stopped while I'm pregnant*'. The 'cut down' message was given by other care providers also, for example: '*Both my doctor and the midwife. Stop is better, but cut down'* (Participant 53).

Women had often been using a number of substances and this was highlighted when care provider advice was being discussed. Participant 95 commented: '*The GP, yes...give up smoking. At the hospital? Not much. They're more interested in the methadone*', and another participant (No.60) reported praise from her health care providers: '*The Warinilla people* [from drug and alcohol services] *were pleased that I'm cutting down on cigarettes and that I'm off morphine and on to methadone'.*

Although another participant (No.39) appreciated the concerns expressed by the doctors and midwives, in this instance to her tobacco use, she suggested

that the concern should have been more definite: '*They've only mentioned it once. They're very sensitive about it. Maybe that's why I trust them. But had they expected it more, I might have made more of an effort'.* However, advice when given was not always heeded: '*My GP in L.* (South Australian country town) *said I should stop cannabis and referred me to the mental health worker. I stopped going*' (Participant 35).

Four participants had been referred to the South Australian Cancer Council's *QUIT* line by the health care providers at the hospital and all commented negatively on its value. Participant 37 reported that: '*QUIT rang and suggested positive strategies [but] I'm in the hard basket. They suggested I try a counsellor, but no advice about where. It doesn't lead anywhere',* while, for Participant 46: '*The QUIT line hasn't been useful. They ring. Sound like my Dad. Then I smoke. It's a different person each time*.'

6.5.4 Response if Negative Response to Question 6 Followed Up

If participants responded 'no' to this question, the researcher (EH) queried whether 'anyone at the hospital' had expressed concern. Eighteen participants then responded '*no*' or '*not at all*'. As Participant 31 noted: '*Well, I have given up on the other stuff* [apart from tobacco].' However, Participant 52's situation was that: '*No-one here [at hospital] knows. Haven't told the doctor or midwife. This is my third visit'.*

6.6 Question 7: *Have you <u>ever</u> tried and failed to control, cut down or stop using (first drug, second drug, etc)?*

This was a question that the researcher (EH) found had to be carefully explained to participants as there are multiple possible situations, making the question somewhat complex for respondents to grasp.

6.6.1 No, Never ('tried and failed')

Nineteen participants reported that they had 'never' tried and failed to control their drug use. However, for several of these, they had never failed because they had never tried: '*No, never. Any of the drugs I use* [tobacco, alcohol, cannabis] *I believe I could stop if I needed to. If I had to*' (Participant 87). Participant 65 had also '*…never tried. Been smoking since I was 12 or 13* [now 38 years old]. *I'm down now from 16mg to 12mg.*' Another participant (No 101) was somewhat defiant: '*No, never. Any substance I use, I can quit. But I refuse to quit'*, while Participant 43 disclosed that: '*I've never tried to quit cannabis. I am obsessed with it.*'

Despite her use of ATS, Participant 94 had, however, assessed that: *'I'm not feeling out of control* [with drugs]', so had not tried to stop. However, she admitted that: '*I know that the amphetamine is linked with depression, but I'll seek treatment after the pregnancy'*.

By contrast, a number of participants had tried and had been able to control or stop their substance use. Participant 41 commented that: *'It's a good incentive to cut down with the baby. I've gone from 10 [cigarettes] a day to 3 or 4'*, while another participant (No 14) was pleased to be '*… more under control now. Almost three months clean* [from ATS]*'.*

There were a few reports of success with stopping substance use leading to other problems. An example of this occurrence was detailed by participant 95 who had ' *… given up [tobacco] twice* – [first time] *12 or 13 years ago. I substituted with cannabis, then went cold turkey for 4-6 weeks. I should have been in a health service. I was paranoid and scared. I was getting very anxious, had breathing difficulties and couldn't get out what I wanted to say. Then my weight. I've put on a lot of weight over the years. I'm so frustrated and angry, I'm still anxious*'.

6.6.2 Yes, (have tried and failed), in the past 3 months

Thirty-five participants elaborated on this response to the question. For many, the focus was the intense difficulty in cutting down or stopping tobacco use: *'I try not to smoke. Early in pregnancy, I didn't smoke, but later on, it picked up again… since about half way'* (Participant 61), while Participant 80 reported that she had tried in a number of ways to stop smoking: *'… patches, the QUIT line and cold turkey. Nothing helped'*. For another participant (No 29), she had *'… cut down while I had morning sickness but now I'm too stressed'.*

Failure to cease use of other substances was also described: *'Tried to give up prescription drugs - morphine slow release tablets* [without success].*'* (Participant 14), and for Participant 79: *'Cannabis. Have tried for 5 or 6 months. I need will–power.'*

6.6.3 Yes, (have tried and failed), but not in the past 3 months

Thirty-seven participants detailed the experiences linked to this response. Again, a major focus was the difficulties inherent in tackling tobacco use. As participant 96 commented: *'Other drugs I've been able to control',* while another participant (No 43) reported that: *'I've tried too hard and got angry in the past when I tried to quit* [tobacco]. Again, a participant (No 49) reported trying a number of cessation methods: *'Had hypnotherapy in February 2007* [5 months ago] *and lasted 6 days. I had 20 cravings an hour and became rather aggressive.* [Before that] *I tried the patch. I'm allergic to the patch. It burnt holes in me, and I had nausea and vomiting and was dizzy. Even the lowest strength, actually burnt the skin. But it did reduce the craving'.*

Experiences with other substances were also described, with reference to the environment of use. Participant 68 reported that she had *'…had trouble with cannabis - and other substances. It depends on who* (sic) *you are with. When*

I left the city, it was an easier environment', while for Participant 84: '*…other substances? Yes. But we were all doing it together*.'

One participant (No.66) spoke of her inability earlier in her life to control her alcohol use with the description of '*… depressive tendencies through my family. Blur or block.'* However, '*… getting pregnant, you have to think more about what you put into your body.'* The same participant described her earlier difficulties in stopping use of other substances: *'When you're growing up, you go through certain stages of life. It's now about where I'm at myself. I'm searching for the meaning of spirituality. You're not going to find that in a nightclub'.*

6.7 Discussion on Qualitative Findings

6.7.1 Suitability of the Questions to this Cohort

Most questions required no interpretation for the interviewees. However, both Question 4 [*During the <u>past three months</u>, how often has your use of (first drug, second drug, etc) led to health, social, legal or financial problems?)*] and Question 7 [*Have you <u>ever</u> tried and failed to control, cut down or stop using (first drug, second drug, etc)?*] necessitated meticulous interrogation due to their complexity.

6.7.1.1 Question 4

For pregnant women, the domains of Question 4 of 'health' and 'social' have particular poignancy. For the 'health' domain, this is because not only is a woman's own health being investigated, but also, potentially, the often hidden aspect of the health and well-being of the fetus. Most women took the question at face value and discussed their own health (for example '*asthma*' or '*breathlessness*' related to tobacco use). However, other participants

elaborated on the '*guilt*' attached to their substance use due to possible or probable negative impacts on the health of the fetus.

With regard to the 'social' domain, pregnant women are particularly vulnerable to social intrusion in their lives attendant on their substance use (Oaks 2001; Hotham, Atkinson et al. 2002). Comments on their substance use are likely to be made not only by people known to them - family, friends, acquaintances - but also, specifically in relation to the highly visible behaviour of smoking tobacco, by strangers encountered in settings such as shopping centres (Oaks 2001; Hotham, Atkinson et al. 2002).

6.7.1.2 Question 7

The concepts behind the question are not of themselves complex, viz whether an interviewee has tried, either in the 'past 3 months' or previous to that, to control or cease substance use, and has experienced difficulty in doing so. The subtleties arise in that an interviewee may have not experienced difficulty because she has not 'tried'. Hence, the question has inherent limitations to assess dependence on a specific substance.

Certainly, a number of participants in the Phase II study articulated a situation in which lack of failure to control use was correlated with absence of attempts. However, with this acknowledged limitation, the question is still of consequence for assessment of pregnant women. Failure to control substance use '*in the past 3 months*' equates, for a pregnant women, with failure to control use in the peri-conceptional period or whilst pregnant. Failure at a time when the majority of women are not only concerned themselves about their substance use but are also subject to a coterie of family, friends, health care providers and others '*on* [their] *case*' is unarguably indicative of a level of dependence on the substance under consideration.

6.7.1.3 Question 5

The researcher (EH) decided, after one of the early interviews of the project, to ask participants whether they had failed to fulfil role obligations due to tobacco use [Question 5: *During the past three months, how often have you failed to do what was normally expected of you because of your use of (first drug, second drug, etc)?*], this being a question which was not incorporated in the *ASSIST Version 3* following the validation studies on the earlier version. Although pregnant women with small children do have unique responsibilities which they can avoid by '*taking time out to smoke*', the limited affirmative response to this question - only 8 of the 98 participants using tobacco - does not justify its re-inclusion in the *ASSIST*.

6.7.2 The Role of Health Care Providers

In elaboration on their responses to Question 6 [*Has a friend or relative or anyone else ever expressed concern about your use of (first drug, second drug, etc)?*], 72 of the 104 participants nominated health care providers as '*anyone else'.* Most of these concerns had been expressed 'in the past 3 months'. If participants responded 'no' to this question, the researcher (EH) queried whether '*anyone at the hospital*' had expressed concern: 18 participants responded in the negative.

The value of intervention by care providers in promotion of cessation of substance use has been established (Corse and Smith 1998; Manwell, Fleming et al. 2000; Sobell, Agrawal et al. 2003; Lumley, Oliver et al. 2004). However, these qualitative data linked to the *ASSIST* administration support earlier findings that health care providers do not always intervene (Hotham, Atkinson et al. 2002; Cook 2003; Moran, Thorndike et al. 2003). The situation is complex and many reasons have been proferred for lack of intervention. This will discussed further in the concluding chapter.

6.7.3 The 'Quit or Cut Down' Message

'*Quit or cut down*' as a message given by health care providers is dissonant with the serious impact of tobacco smoking in pregnancy. It was reported by women in this study and it is a common care provider practice known from earlier research (Hotham, Atkinson et al. 2002; Tappin, Lumsden et al. 2005; Chang, Dado et al. 2008). It is possible that care providers believe that many of their patients have a compromised capacity to stop smoking due to their complex psychosocial circumstances. As one woman reported: '*They're more interested in the methadone*'. One participant in this study blamed her lack of cessation on her care providers: '*… had they expected it more, I might have made more of an effort'.* This is a difficult situation to disentangle, since had the care providers 'expected more', the woman may have become resentful or defensive.

The overall deterrence to behaviour change due to the lack of a definite injunction to cease tobacco use remains unclear. Recent work gives some credence to gradually 'cutting down' as a means to control intake of nicotine without significantly increasing exposure to the many toxic components of tobacco smoke (Benowitz, Hall et al. 2007). However, the typical pattern reported in the Phase II study was that of vacillating tobacco use with an inability to sustain any reduction.

6.7.4 Discussion on Referral to External Treatment Services

The most common 'addiction' service alluded to by the interviewees in the Phase II study was the government-subsidized *QUIT* line. However, a few participants referred to engagement with Drug and Alcohol Services of South Australia when they elaborated on their answers to the *ASSIST* questions: '*The Warinilla people were pleased that I'm cutting down on cigarettes and that I'm off morphine and on to methadone*' (Participant 60).

The negativity expressed by participants to the *QUIT* line program, instituted at the hospital within a *Smoke Free Pregnancy* project promoted by the South Australian Government (Stevens 2005), may be associated with the recalcitrance of women smoking in pregnancy to cessation initiatives. It may also be reflective of the special needs of this cohort, which a generic service such as the *QUIT* line struggles to fulfil. This issue will be further addressed in the final chapter.

Chapter 7:

Conclusions

7.1 Investigation of the ASSIST Version 3.0 in Pregnancy

This investigation of the *ASSIST Version 3.0* with pregnant women was conducted based on the need to find a suitable tool for identification of women whose substance use was at 'risk' levels and the increasing application of the *ASSIST Version 3.0* in primary health care settings as a screening tool for substance use. It is evident that the health of the pregnant woman would benefit from screening, identification of substance use and instigation of treatment for her current pregnancy. Often benefits extend to the woman's life postnatally (Mulhuri and Gfroerer 2009). However, for some women using substances problematically, particularly illicit substances, deleterious social and environmental factors weaken their capacity to effect sustained positive changes (Keenan, Dorman et al 1993).

From this perspective, the pregnant woman can be regarded as part of the general population for which the *ASSIST Version 3.0* was developed and in which it is now finding clinical application. However when a pregnant woman seeks care, there is a second patient - the fetus. Its health is vulnerable to maternal substance use not only while in *utero* but continuing through childhood to adulthood (Barker 1990; Barker 2008). While the concept of levels of risk resonates with an adult substance user, it is far less tenable when the fetus is under consideration.

By a series of statistical analyses, it was determined that an *ASSIST* score of 4 was consistent, for each of alcohol and cannabis, of a level of use at which other established screening tools (*T-ACE* for alcohol and *TLFB* for cannabis)

would require intervention for the health and well-being of the fetus. Both these tools had previously been used to screen pregnant women for use of a specific substance or substances.

However, the study was unable to determine a 'cut-off' *ASSIST Version 3.0* score commensurate with fetal risk due to tobacco use owing to the absence of 'low risk' use (as identified by both the *RTQ* and the *ASSIST*) among the study participants, of whom 98 of 104 used tobacco at high risk levels. Current comment on a likely 'cut-off' score for fetal risk due to tobacco use would only be speculative.

These analyses are discussed below for each of the substances.

7.1.1 Limitations of these Analyses

The reliability of the reported determinations of 'cut-offs' commensurate with fetal risk for alcohol and cannabis is limited by the absence of good agreement of the *ASSIST Version 3.0* with existing tools in most of the analyses conducted. Characteristics of the study sample may have contributed to this lack of strength in both the *ROC* and *weighted kappa* analyses. Participants were recruited from both the antenatal clinic and the antenatal ward, with an expectation that reported use would be reflective of the patterns in the Phase I study: of declared substance users in the Phase I study, 66% (138/209) were users of tobacco. These patterns informed Phase II sample size calculations.

However, the Phase II sample was heavily weighted to tobacco users, with lower rates of alcohol use and cannabis use than expected. In addition, only five alcohol users were not using tobacco and all but one cannabis user also used tobacco. Co-administration of the latter two substances is a well-recognized behaviour and has been noted previously (Agrawal, Knopik et al. 2008).

The method of recruitment in both the antenatal clinic and ward (detailed in Chapter 4) resulted in participant selection only from those women who had documented use of substances in their ante natal records. It has been recognized in studies elsewhere that it may be more disadvantaged women and women of certain ethnicity who are singled out for screening by care providers (Miller, Cox et al. 1994). Hence, this selection method possibly had a lowered potential to select women across a broader range of socioeconomic groups. This is likely to be a contributor to the lack of strength in several of the analyses.

The original recruitment method could have been maintained, adding to the randomness of the sample, by asking the screening question only in relation to tobacco use. This would be unlikely to have aroused the same sensitivity (despite the harms of maternal tobacco use during pregnancy) as do questions related to use of the other substances, alcohol and cannabis. Questions related to these substances are sensitive differentially to each other as noted later in this chapter.

The predominance of late trimester women in the study was discussed in Chapter 5; this feature may well have skewed the study sample towards women using substances, particularly tobacco, at more risky levels.

A further consideration, however, is that the patterns of alcohol and tobacco use in the Phase II study may be typical of the ante natal population in Australia: women using alcohol at low levels or not at all, and those still using tobacco as the pregnancy progresses, using it at higher levels. A similar situation may prevail with respect to cannabis use (Fried, Barnes et al. 1985). The results related to tobacco use in the Phase II study may be reflective of a combination of initiatives in Australia directed to the population generally, including mass media campaigns promoting awareness of the health

implications of tobacco use and legislation to ban smoking in indoor areas and in sporting and entertainment venues. With the impact of these initiatives on prevalence rates in Australia - now less than one in five adult Australians are smokers (Scollo and Winstanley 2008) - it has been acknowledged that those who continue to smoke are those that are most dependent and least able to quit (Cancer Council of New South Wales, undated). This phenomenon has also been identified with pregnant women (McBride 2000).

It is of note that the pattern of daily use of tobacco, often at high levels, and infrequent and lower levels of alcohol use, was also evident for those declaring substance use during pregnancy in the Phase I study, even though this study had a very different participant composition, with nearly sixty percent of participants in the first trimester and a low proportion of third trimester women.

7.1.1.1 Analyses of Data on Alcohol Use

Lack of good agreement was most obvious with the *ASSIST Version 3.0*'s use with alcohol users: in the *ROC* analysis, the area under the curve was ≈ 0.6, indicative of only fair performance of the *ASSIST Version 3.0* against the *T-ACE*, and in the value of *weighted kappa* based on the 3x3 table there was only fair agreement between the *ASSIST Version 3.0* and the *T-ACE*. These limitations are explained at least in part by the predominance of 'low risk' alcohol use (based on both the *ASSIST Version 3.0* and the *T-ACE*) by the study participants. Reasons for this phenomenon have been proffered earlier in this thesis.

A further complexity is that the level of alcohol use identified by the *T-ACE* as 'risky' (to the fetus) has been set as use of the equivalent of ≥ 1 ounce (28grams) of pure alcohol in a day (Sokol, Martier et al. 1989; Chang, Wilkins-Haug et al. 1998); even at the time of development of the *T-ACE*, this level

was recognized as having the potential to attract controversy, being likely to be seen by some as too high (Sokol, Martier et al. 1989). Changing approaches through the intervening years to the current climate of encouraging pregnant women to be abstinent from alcohol use are likely to be in accord with that view and it may be that the 'gold standard' for 'risky' alcohol use in pregnancy does itself need modification.

7.1.1.2 Analyses of Data on Cannabis Use

The analyses with cannabis users showed stronger agreement than for alcohol based on the *ROC* analysis: an area under the curve of 0.81, indicative of good performance of the *ASSIST Version 3.0* against the *TLFB.* However, in the value of *weighted kappa* based on the 3x3 table, agreement was only fair between the *ASSIST Version 3.0* and the *TLFB*. Only one participant used cannabis at low risk (as measured by both the *ASSIST Version 3.0* and *TLFB*); all other cannabis users were identified as using at moderate or high risk, a pattern discussed earlier (Fried, Barnes et al. 1985).

7.1.1.3 Analyses of Data on Tobacco Use

Comment on the absence of low risk tobacco users and the inability to define an *ASSIST Version 3.0* score commensurate with fetal risk was made earlier. In addition, the value of *weighted kappa* showed only moderate agreement between the *ASSIST* and the *RTQ* in the investigation of risk to the pregnant woman.

7.2 Key Issues Impacting on Screening Pregnant Women for Substance Use

The motivation for women to cease use of substances when pregnant has been described elsewhere (Wakefield and Jones 1998; Ockene, Yunsheng et al. 2002), and was evident in both phases of this research. For some pregnant

women however, factors such as their level of dependence on the substance and their social environment (particularly the substance use by significant people in their lives) militated against expressed interest in effecting change. For a minority, substance use was perceived as a fact of life and accepted pragmatically.

7.2.1 Care Provider Intervention

The somewhat ambivalent attitudes adopted by care providers to their pregnant patients' substance use were also highlighted. Despite substance use being a well-documented risk factor for both fetal harm and negative impacts on pregnancy outcome, care providers often appear reluctant to tackle this issue, while zealously monitoring physiological parameters such as blood glucose and blood pressure that also place the fetus and the woman's pregnancy at risk. A number of barriers have been identified, all of which should be addressed within health professional education (Holland Lussky 2003; Gunn, Hegarty et al. 2006; Iannucci, Sanders et al. 2009).

7.2.1.1 Barriers to Screening

Negative attitudes held by care providers to pregnant women who use substances have been recognized as influencing the likelihood of intervention (Weir, Stark et al. 1998), although it was espoused over twenty years ago that the building of mutual trust can ensure continuity of care and a reduction in the incidence and severity of prematurity and perinatal morbidity in the infants of substance-using women (Rodgers and Lee 1988). Substance-using women may perceive care providers as hostile or punitive in their approach and antenatal services as generally unsupportive (Jones, Svikis et al. 2004). Prejudicial care provider attitudes, or fear of them, may lead to women not attending for antenatal care (Hepburn 1990; Broekhuizen, Utrie et al. 1992). Significantly, a lack of attendance at antenatal care has been suggested to be

more damaging than the substance use *per se* and often a marker of social chaos (Broekhuizen, Utrie et al. 1992). It has been proposed that the social conditions of antenatal substance users, often adverse and likely linked with compromised health more broadly, could be the focus of management of that use (Huizink 2009).

One of the participants (No 94) in the Phase II study would not disclose her amphetamine use, as doing so in her previous pregnancy had resulted in stigmatization by care providers; another participant (No 43), although in extreme distress undergoing cannabis withdrawal as an inpatient, had not asked for assistance as she was worried that 'people will judge [her]'. These reports resonate with other findings (Jacobson, Jacobson et al. 1991; Lester, Andreozzi et al. 2004; Tobin 2005).

Reluctance to disclose substance use has also been identified in the United States to be linked to the fear of intervention by child protection services and possibly by the criminal justice system (Lester, Andreozzi et al. 2004); this fear can also be a significant issue in Australia (Tobin 2005). It seems unlikely that pregnant substance users would perceive child protection services as a 'resource' to support them and their children, although this view has been proffered (McCance-Katz 1991).

Deficiency of knowledge of substance use and its treatment has been reported by obstetric care providers (McCance-Katz 1991; Diekman, Floyd et al. 2000; Holl and Lussky 2003) although this would not be tolerated in other aspects of antenatal care, in which care providers would attest to keeping attuned with evidence based approaches and adopting clinical practices that improve outcomes (Barash and Weinstein 2002). Screening and treatment of substance use disorders should be handled with the same level of professionalism.

However, there may exist a generally pessimistic view among care providers of the value of addiction treatment (Svikis and Reid-Quinones 2003).

It is possible that care providers perceive substance use as a 'choice' by a pregnant woman and not as deserving of care provider attention, while other health issues of concern such as elevated blood glucose, although likely to be influenced by dietary 'choice', are regarded as legitimate grounds for intervention (Schneiderman 1994; Corse and Smith 1998; Kennedy, Finkelstein et al. 2004).

Care provider perceptions of the lack of an effective screening tool to detect substance use may also pose a significant barrier. Several useful tools have been developed over recent decades, although implemented inconsistently. A question that expects a simple yes/no response is poor screening. Closed questions almost demand a 'no' response, especially in pregnancy, when women often experience guilt and may have to cope with prejudicial attitudes.

7.2.2 The Veracity of Self-Report

The reliability of self-report screening tools such as the *ASSIST* is inevitably limited by any failure to disclose substance use (Jones 2005). In the realm of substance use as with other personal behaviours (Heitmann 1996; Matt, Garcia et al. 1999), care providers often perceive that their patients may give the socially desirable response rather than the accurate one (Babor, Brown et al. 1990; Jacobson, Jacobson et al. 1991). Further, the study by Jacobson and colleagues found that recall of pregnancy-related substance use by women interviewed post-pregnancy was higher than that reported while they were pregnant, particularly if a woman had delivered an apparently healthy infant (Jacobson, Jacobson et al. 1991).

Intuitively it is probable that a pregnant substance user's recall of her substance use would be an underestimate rather than an overestimate,

although in some populations it has been found that recall of substance use may be at a higher or lower level than biochemical screening would indicate (Akinci, Tarter et al. 2001).

Fear of stigmatization was raised earlier in this thesis and guilt was discussed in relation to the Phase I study results (Jacobson, Jacobson et al. 1991; Poole and Dell 2005). A number of women in the Phase II study spoke of their guilt at using substances and the possibility of fetal harm due to that use. Poor recall has been identified as a factor limiting self-report accuracy (Jones 2005). Recall can also, perhaps subliminally, be affected by guilt.

The South Australian Government's ongoing campaign promoting a zero tolerance approach to alcohol in pregnancy (Children Youth and Women's Health Service 2004) was noted earlier. As one respondent (No 86) commented: *'[I] feel guilty about [even] having one [drink]. More posters around about alcohol and pregnancy than about tobacco and pregnancy…'*. Further, the NHMRC have revised their guidelines on alcohol use in pregnancy in line with guidelines in several other countries (Office of the Surgeon General 2005; National Institute for Health and Clinical Excellence [NICE] 2008) and abstinence is now promoted for pregnant women (National Health and Medical Research Council [NHMRC] 2009).

These are ongoing factors that may continue to affect the veracity of women's self-reports of alcohol use. However it may be that the majority of women will cease use and that the limited number of alcohol users identified in both phases of the research exemplifies this occurrence. In addition, the binge drinking episodes reported in data from the US (Tsai, Floyd et al. 2007) were not evident here, perhaps reflective of the relatively small number of alcohol users identified.

7.2.2.1 Possibility of Differential Self-Reporting of Focus Substances

Alcohol use in pregnancy is now 'under the spotlight'; interrogating cannabis use given its illicit status could also potentially generate less than accurate reports (Harrison, Haaga et al. 1993). However there was no suspicion on the part of the researcher (EH) of differential barriers to self-disclosure of use of any substance by study participants, or indeed of any barriers at all. This included a lack of reluctance to disclose tobacco use despite its undoubted potential to negatively impact on the fetus and the outcome of the pregnancy. Comments such as *'everyone I know smokes. I don't think I smoke much compared to everyone else'* (participant No 47) and '*I'm only smoking and that's OK for me'* (a woman who declined to be interviewed) were typical of the approach of some participants to their tobacco use. Interestingly, it has been found that care providers also feel more comfortable with acknowledging their patients' tobacco use, despite its negative impacts, than their use of alcohol or illicit substances (Chang, Dado et al. 2008).

Of the three focus substances in the study, tobacco use at interview could have been more effectively assessed biochemically than either of the other two substances, via measurement of cotinine, a long-acting nicotine metabolite (Benowitz 1983; Pickett, Rathouz et al. 2005). However, cotinine is affected by ethnic and environmental differences (Benowitz, Hukkanen et al. 2009), may fluctuate during pregnancy (Pickett, Rathouz et al. 2005), and is highly influenced by the increased metabolism in pregnancy of both nicotine and cotinine itself (Dempsey, Jacob et al 2002).

Yet despite these limitations it is still regarded broadly as a useful measure and may have provided a level of validation of self-report and of the researcher's belief in an apparent lack of barriers to disclosure of use in the study environment. However, it was originally believed that there would be

inherent limitations in extrapolating assessment of the veracity of self-report of tobacco to either alcohol use or cannabis use, due to the possible different perceptions held by the women of the 'acceptability' of the three substances. The decision was therefore made not to utilize the biochemical validation of tobacco use via cotinine.

Accuracy of participants' self-reporting has been recognized as more likely in research studies than in clinical practice (Chang, Wilkins-Haug et al. 1998); indisputably, doubt as to the veracity of patients' self-reports will endure in clinical practice whilst negative, unhelpful attitudes are held towards substance users.

7.3 The Way Forward

Substance use in pregnancy contributes to a significant burden of disease throughout the world. While the WHO has identified the use of alcohol, tobacco and other substances (AOD use) as one of the top 20 risk factors for ill-health in the global population (World Health Organization [WHO] 2002), the burden of disease attributable to substance use by pregnant women is less well-documented, although a 1995 estimate indicated that between 12 and 14 million women world-wide smoked in pregnancy (Windsor 1999). There has been a focus on the changing social mores in developing countries leading to an increased acceptance of tobacco use by women (World Health Organization and Institute for Global Tobacco Control Johns Hopkins School for Public Health 1999; World Health Organization 2003). However, patterns of consumption of alcohol and illicit substances are also shifting with increased use reported (World Health Organization 2003).

With pregnancy rates typically higher in developing countries, substance use in pregnancy is poised to become a significant public health issue globally. In

addition, use of tobacco and other substances by the partners of pregnant women also impacts on women's health, their pregnancies and the health of their children (Wakefield, Reid et al. 1998; World Health Organization 2003). Although passive smoking has remained somewhat under-acknowledged as a health issue globally (World Health Organization 2008), the overall impact of substance use on families, and on children particularly, is increasingly being recognized (Wagner, Katikaneni et al. 1998; Huestis and Choo 2002; Kissin, Svikis et al. 2004; Dawe, Atkinson et al. 2007).

Programs such as community-based folic acid supplementation (World Health Organization 2009) and administration of Rh (D) immunoglobulin to at-risk individuals (The Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG) 2007) have been successfully implemented in developed countries (Barash and Weinstein 2002) and have gained some momentum globally (Vidyasagar 2002). However substance use screening still continues to lag behind other initiatives in antenatal care (McPherson and Hersch 2000; Hunt and Lumley 2002) despite the evidence that dedicated screening for substance use and subsequent instigation of treatment (Daley, Argeriou et al. 1998; Comfort and Kaltenbach 2000) can have a positive impact on the disease burden of pregnancy-related substance use (Manwell, Fleming et al. 2000; Ingersoll, Floyd et al. 2003; Jones, Svikis et al. 2004; Floyd, Ebrahim et al. 2006).

Other markers of psychosocial distress often co-exist with substance use (Schulman, Morel et al. 1993; Howell and Chasnoff 1999; Bessant 2004; Harrison and Sidebottom 2008); ideally, all domains of concern would be addressed. Further, the focus of substance use screening needs to vary throughout the world according to local conditions (Bergsjo and Villar 1997; Gilligan, Sanson-Fisher et al. 2009; Lewis, Hickey et al. 2009). It is important

in treatment settings that respect for the pregnant woman is not subverted by concern for the fetus, though the latter concern is rational and significant (DeVille and Kopelman 1998; Pollard 2000; Roberts and Dunn 2003); neither should women of lower socioeconomic or certain ethnic backgrounds be singled out for attention (Miller, Cox et al. 1994).

7.3.1 Tobacco Use as a Key Target for Intervention

Tobacco use is clearly a good indicator of use of other substances (Christmas, Knisely et al. 1992; Marcenko, Spence et al. 1994; Svikis, Henningfield et al. 1997; Burns, Mattick et al. 2008; Ethen, Ramadhani et al. 2009), and the predominance of tobacco use by the substance users identified in the Phase II study is concordant with multiple other research studies and clinical data generally (Shiono, Klebanoff et al. 1995; Noble, Vega et al. 1997; Burns, Mattick et al. 2006; Burns, Mattick et al. 2008; Slotkin 2008).

Resources directed to treating nicotine dependence would not only improve the chances of cessation of other substances (Tough, Tofflemire et al. 2006; Hjerkinn, Lindbaek et al. 2007; Harrison and Sidebottom 2008a) but also have the potential to have a major public health impact due to reduction in tobacco use (World Health Organization and Institute for Global Tobacco Control Johns Hopkins School for Public Health 1999; Slotkin 2008; World Health Organization 2008).

Guidelines have been formalized in the United States for care provider engagement with pregnant smokers through individual psychosocial interventions that 'exceed the minimal advice to quit' (Fiore, Jaen et al. 2008). Reservations expressed by some study participants about the Cancer Council of South Australia's *QUIT* line service also suggest a need for more intensive interventions for pregnant smokers.

If the emphasis on screening for substance use were to be placed on screening for tobacco use, then, within a comprehensive tobacco cessation program of screening and treatment, use of other substances would likely be identified, and treatment programs for these substances could also be implemented if needed. A recent review by US researchers confirmed common associated factors, such as lower socioeconomic status, in populations of pregnant smokers and those pregnant women using other substances. They concluded that existing effective interventions for pregnant women with substance use disorders could have a place in the treatment of pregnant smokers, a group likely to have higher nicotine dependence and to be in need of 'more intensive and comprehensive treatments' (Heil, Linares Scott et al. 2009).

The political philosophy towards pregnant substance users in countries such as Australia, Canada and the UK favours treatment over incarceration but this is not the situation elsewhere, including in parts of the US. The latter pathway is unlikely to be helpful, deterring women from seeking antenatal care (Oberman 1992; DeVille and Kopelman 1998; Lester, Andreozzi et al. 2004) and should be abandoned.

Identification of substance use requires an environment of honesty and trust (Jones 2005). These cannot co-exist in antenatal settings alongside fear of stigmatization and experiences of negative and prejudicial attitudes from care providers. Attitudinal change must be accompanied by the enhanced capacity of providers to perform primary health care level screening as the first and highly significant step in engaging women in smoking cessation treatment, and, if appropriate, in treatment for other substance use also (McPherson and Hersch 2000; Potter and Fleming 2003; Svikis and Reid-Quinones 2003).

The selection of a screening tool for the identification of tobacco use could well be the *Revised Fagerstrom Questionnaire (RTQ)* (Tate and Schmitz 1993) or

one of its modifications. The key question *'how often do you smoke your first cigarette of the day within 30 minutes of waking?'* is highly indicative of nicotine dependence and this as a stand-alone question would be a good point to start a dialogue between care provider and antenatal patient about their substance use. The only Australian screening tool for smoking cessation, The Three Centres Consensus Guidelines, may also be an option (Project Team Mercy Hospital for Women Southern Health and Women's and Children's Health 2001), although no published literature is extant evaluating its use.

7.3.2 Clinical Utility of the *ASSIST Version 3.0* for Pregnant Women

A number of good self-report tools have been tried with pregnant women but implementation has been inconsistent at best. The results of this investigation highlighted the value of detection of tobacco use as the primary screening focus. Currently, the place of the *ASSIST Version 3.0* is equivocal as the statistical analyses did not uniformly show good agreement. There was no evidence from this study to support changing the cut-offs between low, medium and risk use for the woman as an individual patient.

However, a cut-off score for use indicative of fetal risk has been determined for both alcohol and cannabis: a Specific Substance Involvement Score of 4. Further research could be undertaken to determine the cut-off for tobacco use, although careful sampling would be required to capture both low risk and high risk smokers. This may be best achieved by recruitment targeted to first trimester women.

One future scenario for screening for substance use in pregnancy may be the implementation of the *ASSIST Version 3.0* to screen for other substances if initial screening for tobacco use conferred a positive result.

What is without doubt is that screening must occur consistently and currently does not. The need for research into how best to engage care providers,

through early educational activities and later through professional societies and bodies developing institutional guidelines, is certainly justified. Universal screening for substance use generally, and tobacco use in the first instance, is an urgent priority and a change of practitioner culture needs to occur for this to eventuate.

***Appendix One*: Phase I Study**

(pages 196-201)

Government of South Australia
Children, Youth and Women's Health Service

Research Secretariat
Level 2 Samuel Way Building
72 King William Road
North Adelaide SA 5006
Tel 08 8161 6521
08 8161 6930
Fax 08 8161 8177

28th June 2005

Ms E Hotham
School of Pharmacy & Medical Sciences
University of South Australia
Frome Rd
ADELAIDE SA 5000

Dear Ms Hotham

Re: Validation of the Alcohol, Smoking and Substance Involvement Screening Test (ASSIST) in pregnant women: Phase I – Prevalence. REC1713/5/2008

Thank you for your response to matters raised by the CYWHS Research Ethics Committee at its May 2005 meeting. All matters have been addressed and final approval is given for the study to proceed.

I remind you approval is given subject to:
- immediate notification of any serious or unexpected adverse events to subjects;
- immediate notification of any unforeseen events that might affect continued ethical acceptability of the project;
- submission of any proposed changes to the original protocol. Changes must be approved by the Committee before they are implemented;
- immediate advice, giving reasons, if the protocol is discontinued before its completion;
- submission of an annual report on the progress of the study, and a final report when it is completed.

Please note it is your responsibility to provide these reports – without reminder from the Ethics Committee.

Approval is given for three years only, and if the study is more prolonged than this, a new submission will be required. Please note the approval number above indicates the month and year in which approval expires and it should be used in any future communication.

Yours sincerely

TAMARA ZUTLEVICS (DR)
CHAIR
CYWHS RESEARCH ETHICS COMMITTEE

Cc: A/Prof R Ali, University of Adelaide

Use of Drugs in Pregnancy

Prevalence Study

Women's and Children's Hospital and Lyell McEwin Health Service

Information Sheet

This survey is being conducted to find out how many pregnant women in South Australia are using drugs (such as alcohol, tobacco, cannabis or speed), how much they are using and at what times they use. The survey is being conducted by researchers at the University of Adelaide because, at the current time, there is very little information available about drug use by Australian women while they are pregnant.

We appreciate your taking time to fill in this questionnaire. Your name does not appear anywhere on the questionnaire.

When you have completed the questionnaire, please place it in the envelope provided, seal the envelope and hand it back to clinic staff.

This study has been approved by the Research Ethics Committee of the Women's and Children's Hospital. Please contact Ms Brenda Penny, Research Secretariat on (08) 8161 6521* if you have any queries, or the Chief Investigator, Associate Professor Robert Ali, ph. (08) 8274 3349.

SUB CRUCE LUMEN

DRUG & ALCOHOL SERVICES SOUTH AUSTRALIA

* These details were amended for the Lyell McEwin Hospital arm of this study.

Study Number: ☐☐☐☐

Question 1: Your date of birth

☐☐ ☐☐ ☐☐

Day Month Year

Question 2: Total number of <u>previous</u> pregnancies (do not include this pregnancy, but do include all miscarriages)

☐☐

Question 3: Number of live births

☐☐

Question 4: Pregnancy complications in <u>previous</u> pregnancies: please specify.

.....

.....

Question 5: Pregnancy complications in <u>this</u> pregnancy: please specify.

.....

.....

Question 6: This pregnancy

Date of last menstrual period

☐☐ ☐☐ ☐☐

Day Month Year

Question 7: Think about your drug use *in a typical month when you were not pregnant, not trying to become pregnant, and not breastfeeding*

For each drug, write

Column A: the number of days of use

Column B: maximum amount used per day

	Column A	Column B
	Number of days of use (write 0 if no use)	Maximum amount used in any one day or session (specify the amount as you would describe, e.g. 4 cones, 20 cigarettes, 3 caps heroin)
Tobacco products (cigarettes, cigars etc)		
Alcoholic beverages (beer, wine, spirits)		
Cannabis (marijuana, pot, grass, hash etc)		
Cocaine (coke, crack, etc)		
Amphetamine type stimulants (speed, diet pills, ecstasy etc)		
Inhalants (e.g. nitrous oxide, amyl nitrate)		
Sedatives or sleeping pills (Valium, Serepax, etc)		
Hallucinogens (LSD, acid, mushrooms, PCP, Special K etc)		
Opioids (heroin, morphine, methadone, codeine etc)		
Other- specify		

Question 8: Think about your drug use *in the last month*

For each drug, write

Column A: the number of days of use

Column B: maximum amount used per day

	Column A	Column B
	Number of days of use (write 0 if no use)	Maximum amount used in any one day or session (specify the amount as you would describe, e.g. 4 cones, 20 cigarettes, 3 caps heroin)
Tobacco products (cigarettes, cigars etc)		
Alcoholic beverages (beer, wine, spirits)		
Cannabis (marijuana, pot, grass, hash etc)		
Cocaine (coke, crack, etc)		
Amphetamine type stimulants (speed, diet pills, ecstasy etc)		
Inhalants (e.g. nitrous oxide, amyl nitrate)		
Sedatives or sleeping pills (Valium, Serepax etc)		
Hallucinogens (LSD, acid, mushrooms, PCP, Special K etc)		
Opioids (heroin, morphine, methadone, codeine etc)		
Other- specify		

Thank you very much for completing this survey. Please place in the envelope and return to clinic staff.

Appendix Two: **Phase II study**

(pages 202- 224)

Government of South Australia
Children, Youth and Women's Health Service

Research Society Of
Level 7 Samuel Way Building
72 King William Road
North Adelaide SA 5006
tel 08 8161 6521
08 8161 6930
fax 08 8161 8177

10th April 2006

A/Prof R Ali
WHO Collaborating Centre, Discipline of Pharmacology
University of Adelaide. 5005

Dear A/Prof Ali

Re: Exploration of the use of the World Health Organization's ASSIST (Alcohol, Smoking and Substance Involvement Screening Test) with pregnant women (Phase II). REC1813/3/2009

Thank you for your letter dated 5th April 2006 in which you responded to matters raised by the CYWHS Research Ethics Committee at its March 2006 meeting. All matters have been addressed and final approval is given for the study to proceed.

I remind you approval is given subject to:
- immediate notification of any serious or unexpected adverse events to subjects;
- immediate notification of any unforeseen events that might affect continued ethical acceptability of the project;
- submission of any proposed changes to the original protocol. Changes must be approved by the Committee before they are implemented;
- immediate advice, giving reasons, if the protocol is discontinued before its completion;
- submission of an annual report on the progress of the study, and a final report when it is completed. Please note it is your responsibility to provide these reports without reminder from the Ethics Committee.

Approval is given for three years only, and if the study is more prolonged than this, a new submission will be required. Please note the approval number above indicates the month and year in which approval expires and it should be used in any future communication.

If University of Adelaide personnel are involved in this project, you, as chief investigator must submit a Human Research Approval notification form (available at: http://www.adelaide.edu.au/research/ethics/human/guidelines/) within 14 days of receiving this ethical clearance to ensure compliance with University requirements and appropriate indemnification.

Yours sincerely

TAMARA ZIVLEVICS (DR)
CHAIR
CYWHS RESEARCH ETHICS COMMITTEE

Cc: Ms E Hotham

The Alcohol, Smoking and Substance Involvement Screening Test

(the *ASSIST*) *Version 3.0*

Question 1

(if completing follow-up please cross check the participant's answers with the answers given for Q1 at baseline. Any differences on this question should be queried)

In your life, which of the following substances have you <u>ever used</u>? *(NON-MEDICAL USE ONLY)*	**No**	**Yes**
a. Tobacco products (cigarettes, chewing tobacco, cigars, etc.)	0	3
b. Alcoholic beverages (beer, wine, spirits, etc.)	0	3
c. Cannabis (marijuana, pot, grass, hash, etc.)	0	3
d. Cocaine (coke, crack, etc.)	0	3
e. Amphetamine type stimulants (speed, diet pills, ecstasy, etc.)	0	3
f. Inhalants (nitrous, glue, petrol, paint thinner, etc.)	0	3
g. Sedatives or Sleeping Pills (Valium, Serepax, Rohypnol, etc.)	0	3
h. Hallucinogens (LSD, acid, mushrooms, PCP, Special K, etc.)	0	3
i. Opioids (heroin, morphine, methadone, codeine, etc.)	0	3
j. Other - specify:	0	3

Probe if all answers are negative:

"Not even when you were in school?"

If "No" to all items, stop interview.

If "Yes" to any of these items, ask Question 2 for each substance ever used.

Question 2

In the <u>past three months</u>, how often have you used the substances you mentioned* (FIRST DRUG, SECOND DRUG, ETC)*?	**Never**	**Once or Twice**	**Monthly**	**Weekly**	**Daily or Almost Daily**
a. Tobacco products (cigarettes, chewing tobacco, cigars, etc.)	0	2	3	4	6
b. Alcoholic beverages (beer, wine, spirits, etc.)	0	2	3	4	6
c. Cannabis (marijuana, pot, grass, hash, etc.)	0	2	3	4	6
d. Cocaine (coke, crack, etc.)	0	2	3	4	6
e. Amphetamine type stimulants (speed, diet pills, ecstasy, etc.)	0	2	3	4	6
f. Inhalants (nitrous, glue, petrol, paint thinner, etc.)	0	2	3	4	6
g. Sedatives or Sleeping Pills (Valium, Serepax, Rohypnol, etc.)	0	2	3	4	6
h. Hallucinogens (LSD, acid, mushrooms, PCP, Special K, etc.)	0	2	3	4	6
i. Opioids (heroin, morphine, methadone, codeine, etc.)	0	2	3	4	6
j. Other - specify:	0	2	3	4	6

If "Never" to all items in Question 2, skip to Question 6.

If any substances in Question 2 were used in the previous three months, continue with Questions 3, 4 & 5 for <u>each substance</u> used.

Question 3

During the <u>past three months</u>, how often have you had a strong desire or urge to use* (FIRST DRUG, SECOND DRUG, ETC)*?	**Never**	**Once or Twice**	**Monthly**	**Weekly**	**Daily or Almost Daily**
a. Tobacco products (cigarettes, chewing tobacco, cigars, etc.)	0	3	4	5	6
b. Alcoholic beverages (beer, wine, spirits, etc.)	0	3	4	5	6
c. Cannabis (marijuana, pot, grass, hash, etc.)	0	3	4	5	6
d. Cocaine (coke, crack, etc.)	0	3	4	5	6
e. Amphetamine type stimulants (speed, diet pills, ecstasy, etc.)	0	3	4	5	6
f. Inhalants (nitrous, glue, petrol, paint thinner, etc.)	0	3	4	5	6
g. Sedatives or Sleeping Pills (Valium, Serepax, Rohypnol, etc.)	0	3	4	5	6
h. Hallucinogens (LSD, acid, mushrooms, PCP, Special K, etc.)	0	3	4	5	6
i. Opioids (heroin, morphine, methadone, codeine, etc.)	0	3	4	5	6
j. Other - specify:	0	3	4	5	6

Question 4

During the <u>past three months</u>, how often has your use of *(FIRST DRUG, SECOND DRUG, ETC)* led to health, social, legal or financial problems?	**Never**	**Once or Twice Monthly**	**Weekly**	**Daily or Almost Daily**
a. Tobacco products (cigarettes, chewing tobacco, cigars, etc.)	0	4	5	6	7
b. Alcoholic beverages (beer, wine, spirits, etc.)	0	4	5	6	7
c. Cannabis (marijuana, pot, grass, hash, etc.)	0	4	5	6	7
d. Cocaine (coke, crack, etc.)	0	4	5	6	7
e. Amphetamine type stimulants (speed, diet pills, ecstasy, etc.)	0	4	5	6	7
f. Inhalants (nitrous, glue, petrol, paint thinner, etc.)	0	4	5	6	7
g. Sedatives or Sleeping Pills (Valium, Serepax, Rohypnol, etc.)	0	4	5	6	7
h. Hallucinogens (LSD, acid, mushrooms, PCP, Special K, etc.)	0	4	5	6	7
i. Opioids (heroin, morphine, methadone, codeine, etc.)	0	4	5	6	7
j. Other - specify:	0	4	5	6	7

Question 5

During the <u>past three months</u>, how often have you failed to do what was normally expected of you because of your use of *(FIRST DRUG, SECOND DRUG, ETC)*?	**Never**	**Once or Twice Monthly**	**Weekly**	**Daily or Almost Daily**
a. Tobacco products				
b. Alcoholic beverages (beer, wine, spirits, etc.)	0	5	6	7	8
c. Cannabis (marijuana, pot, grass, hash, etc.)	0	5	6	7	8
d. Cocaine (coke, crack, etc.)	0	5	6	7	8
e. Amphetamine type stimulants (speed, diet pills, ecstasy, etc.)	0	5	6	7	8
f. Inhalants (nitrous, glue, petrol, paint thinner, etc.)	0	5	6	7	8
g. Sedatives or Sleeping Pills (Valium, Serepax, Rohypnol, etc.)	0	5	6	7	8
h. Hallucinogens (LSD, acid, mushrooms, PCP, Special K, etc.)	0	5	6	7	8
i. Opioids (heroin, morphine, methadone, codeine, etc.)	0	5	6	7	8
j. Other - specify:	0	5	6	7	8

Ask Questions 6 & 7 for all substances ever used

(i.e. those endorsed in Question 1)

Question 6

Has a friend or relative or anyone else <u>ever</u> expressed concern about your use of *(FIRST DRUG, SECOND DRUG, ETC.)?*	**No, Never**	**Yes, in the past 3 months**	**Yes, but not in the past 3 months**
a. Tobacco products (cigarettes, chewing tobacco, cigars, etc.)	0	6	3
b. Alcoholic beverages (beer, wine, spirits, etc.)	0	6	3
c. Cannabis (marijuana, pot, grass, hash, etc.)	0	6	3
d. Cocaine (coke, crack, etc.)	0	6	3
e. Amphetamine type stimulants (speed, diet pills, ecstasy, etc.)	0	6	3
f. Inhalants (nitrous, glue, petrol, paint thinner, etc.)	0	6	3
g. Sedatives or Sleeping Pills (Valium, Serepax, Rohypnol, etc.)	0	6	3
h. Hallucinogens (LSD, acid, mushrooms, PCP, Special K, etc.)	0	6	3
i. Opioids (heroin, morphine, methadone, codeine, etc.)	0	6	3
j. Other – specify:	0	6	3

Question 7

Have you <u>ever</u> tried and failed to control, cut down or stop using *(FIRST DRUG, SECOND DRUG, ETC.)?*	**No, Never**	**Yes, in the past 3 months**	**Yes, but not in the past 3 months**
a. Tobacco products (cigarettes, chewing tobacco, cigars, etc.)	0	6	3
b. Alcoholic beverages (beer, wine, spirits, etc.)	0	6	3
c. Cannabis (marijuana, pot, grass, hash, etc.)	0	6	3
d. Cocaine (coke, crack, etc.)	0	6	3
e. Amphetamine type stimulants (speed, diet pills, ecstasy, etc.)	0	6	3
f. Inhalants (nitrous, glue, petrol, paint thinner, etc.)	0	6	3
g. Sedatives or Sleeping Pills (Valium, Serepax, Rohypnol, etc.)	0	6	3
h. Hallucinogens (LSD, acid, mushrooms, PCP, Special K, etc.)	0	6	3
i. Opioids (heroin, morphine, methadone, codeine, etc.)	0	6	3
j. Other – specify:	0	6	3

Question 8

	No, Never	Yes, in the past 3 months	not in the past 3 months
Have you <u>ever</u> used any drug by injection? ***(NON-MEDICAL USE ONLY)***	0	2	1

IMPORTANT NOTE:

Patients who have injected drugs in the last 3 months should be asked about their pattern of injecting during this period, to determine their risk levels and the best course of intervention.

PATTERN OF INJECTING	*INTERVENTION GUIDELINES*
Once weekly or less **or** *Fewer than 3 days in a row*	*Brief Intervention including "risks associated with injecting" card*
More than once per week **or** *3 or more days in a row*	*Further assessment and more intensive treatment**

HOW TO CALCULATE A SPECIFIC SUBSTANCE INVOLVEMENT SCORE

For each substance (labelled a. to j.) add up the scores received for questions 2 through 7 inclusive. Do not include the results from either Q1 or Q8 in this score. For example, a score for cannabis would be calculated as: Q2c + Q3c + Q4c + Q5c + Q6c + Q7c

Note that Q5 for tobacco is not coded, and is calculated as: Q2a + Q3a + Q4a + Q6a + Q7a

THE TYPE OF INTERVENTION IS DETERMINED BY THE PATIENT'S SPECIFIC SUBSTANCE INVOLVEMENT SCORE

	Record specific substance score	**no intervention**	**receive brief intervention**	**more intensive treatment ***
a. tobacco		0-3	4-26	27+
b. alcohol		0-10	11-26	27+
c. cannabis		0-3	4-26	27+
d. cocaine		0-3	4-26	27+
e. amphetamine		0-3	4-26	27+
f. inhalants		0-3	4-26	27+
g. sedatives		0-3	4-26	27+
h. hallucinogens		0-3	4-26	27+
i. opioids		0-3	4-26	27+
j. other drugs		0-3	4-26	27+

NOTE: FURTHER ASSESSMENT AND MORE INTENSIVE TREATMENT may be provided by the health professional(s) within your primary care setting, or, by a specialist drug and alcohol treatment service when available.

Preliminary Screening Questions

- Hello. I am Libby Hotham and I am conducting research in the antenatal clinic around social drug use. This is a University of Adelaide project. I am wishing to identify potential participants. Would I be able to ask you a simple question related to social drug use?

- If *Yes*, the question is:

Have you used any of the following: tobacco, alcohol, or cannabis in the last 3 months?

- If *Yes*, are you interested in information about a research study we are doing?

INFORMATION SHEET

Use of Drugs in Pregnancy

Women's and Children's Hospital

This project is being conducted to explore the use of the World Health Organization's *ASSIST* (the Alcohol, Smoking and Substance Involvement Screening Test) with pregnant women.

It is expected that this will take between 30 and 45 minutes, although it may take as little as 20 minutes. We will pay you $30 cash to reimburse you for travel and other costs. You are free to withdraw from the project at any time during the interview; however, as you would expect, we cannot pay you the $30 unless all the questionnaires are completed.

We would like you to answer these questions honestly as this will make the research findings more useful.

Question 1:

What is the *ASSIST*?

The *ASSIST* is a screening questionnaire that has been developed by the World Health Organization to enable health care providers to easily and quickly decide whether people are using alcohol, tobacco and other drugs.

Question 2:

What has this to do with pregnant women?

It is well understood by health authorities that the use of alcohol and other drugs in pregnancy can adversely affect the health of pregnant women and of their babies.

A number of other conditions/ behaviours are screened for in pregnancy, such as diabetes and Hepatitis C. However, researchers have found out that very few maternity hospitals or health care providers are routinely asking pregnant women about their use of alcohol, tobacco and other drugs.

Question 3:

Why can't the *ASSIST* be used for pregnant women now?

It cannot be used until a study such as this takes place. In this study, each participant will be asked to answer the *ASSIST* questionnaire at the same time as other questionnaires that have been used extensively with pregnant women in the past.

If the answers these questionnaires give about a woman's alcohol and other drug use are similar to the answers from the *ASSIST*, then, because we know that the other questionnaires give accurate answers (because they have been used extensively with pregnant women), then it can be concluded that the *ASSIST* is giving accurate answers.

Question 4:

Why not just use questionnaires you already have?

A number of these questionnaires are quite long and require special training for health care providers to use them. The *ASSIST* is a short instrument and does not require special training for health care providers.

However, it has been shown in the general population to give a very accurate and comprehensive picture of the person's drug use.

Question 5:

If I agree to be in the study, what will I have to do?

You will be asked to answer the *ASSIST* questionnaire and other questionnaires as discussed above (Question 3). You may find that some of these questions sound rather similar, but we need you to answer all of them so that we can determine how the *ASSIST* measures up against the other questionnaires.

Question 6:

Do I have to do anything else?

Yes. We will also ask you some details about your pregnancy and medical history, also some information about you such as your ethnic background and your years of schooling. The researcher may access your case notes. This will only be to confirm what information your doctors or midwives have recorded in relation to alcohol and other drug use and for no other purpose.

Question 7:

How will my participation benefit me?

There may be no specific benefit to you, although you could benefit by gaining an awareness of your patterns of use of alcohol, tobacco and other drugs, and whether this substance is having an effect on your life.

However, your participation will help us in the development of a questionnaire that will be used to identify pregnant women who may have problems caused by their use of alcohol or other drugs.

Question 8:

Is everything I tell you kept confidential?

Yes, definitely.

Your name will not be recorded on the questionnaires and therefore, your name cannot appear on any publication from this research.

In order to preserve confidentiality, only a participant number will be associated with the information that you provide.

Any information you give us will not be given to the doctors and midwives in the clinic. It will be kept confidential and locked in a cabinet at the University of Adelaide. Any computer files relating to the project will be protected by password known only to the researcher that you spoke to today and the Chief Investigator of the project.

However, there are limits to the confidentiality that you should be aware of:

- If you provide information that suggests that you are abusing or neglecting your children, the researchers are required by law to report this to the appropriate authorities.
- If you are a danger to yourself or others, we are required to take whatever action is necessary to protect you or them.
- We are also required by law to cooperate if we receive a subpoena for information concerning you.

If you would like further information, you can direct enquiries to the Chief Investigator, Associate Professor Robert Ali, ph. (08) 8274 3349.

If you would like to speak to someone not directly involved in the study, please contact Ms Brenda Penny, Research Secretariat, ph. (08) 8161 6521.

If you are concerned that you may have a problem with drugs, the confidential Alcohol and Drug Information and Referral Service is available 24 hours of the day by telephoning 1300 131 340.

Consent Form

WOMEN'S & CHILDREN'S HOSPITAL RESEARCH ETHICS COMMITTEE

CONSENT FORM

I _____

hereby consent to my involvement in the research project entitled:

Investigation of the Alcohol, Smoking and Substance Involvement Screening Test (the *ASSIST)* with pregnant women

1. The nature and purpose of the research project described on the attached Information Sheet has been explained to me. I understand it, and agree to taking part.
2. I understand that I may not directly benefit by taking part in this study.
3. I acknowledge that the inconvenience (a half an hour or more of my time), as outlined in the Information Sheet, has been explained to me.
4. I understand that while information gained in the study may be published, I will not be identified and information will be confidential.
5. I understand that there will be a payment to me of $30 to reimburse me for travel and other costs.
6. I understand that I can withdraw from the study at any stage and that this will not affect medical care or any other aspects of my relationship with this hospital. However, I will not be paid the financial compensation unless I complete all the questionnaires.
7. I have had the opportunity to discuss taking part in this research project with a family member or friend and/or have had the opportunity to have a family member or friend present whilst the research project was being explained by the researcher.

8. I am aware that I should retain a copy of the Consent Form, when completed, and the Information Sheet.

Signed: .....

Full name of patient: .....

Dated:.....

I certify that I have explained the study to the patient and consider that he/she understands what is involved.

Signed: .....

Name: .....

Title: .....

Dated: .....

Sociodemographic Questionnaire **Date: ……**

Study Number: ☐☐☐

Question 1: Your age (in years)

……

Question 2: Current marital status

Married / De-facto ☐ **Widowed** ☐

Single ☐ **Divorced / Separated** ☐

Question 3: What is your ethnicity?

……

Question 4: Postcode

☐☐☐☐

Question 5: Number of years of formal schooling

☐☐

Question 6: Are you currently studying?

☐ **Yes** ☐ **No**

Question 7: Are you currently employed?

☐ **Yes** ☐ **No**

Question 8: Total number of <u>previous</u> pregnancies

(do not include this pregnancy, but do include all miscarriages and terminations)

☐☐

Question 9: Number of live births

Question 10: How many of your children currently live with you?

Question 11: Your age at birth of first child

Question 12: Pregnancy complications and medical conditions in <u>previous</u> pregnancies: please specify. (e.g. pre-eclampsia, high blood pressure, diabetes)

.....

Question 13: Pregnancy complications and medical conditions in <u>this</u> pregnancy: please specify. (e.g. pre-eclampsia, high blood pressure, diabetes)

.....

Question 14: Do you take any regular medication for these conditions?

Yes **No**

Question 15: This pregnancy: estimated due date of baby's birth

Year		**Month**		**Day**	

Established Tools for Use in the Investigation of the *ASSIST*

Alcohol: The *T-ACE* **Study No:** | | | |

***T*= Tolerance**

***A*= Annoyed**

***C*= Cut Down**

***E*= Eye-opener**

How may drinks does it take to make you feel high? (TOLERANCE)

Have people ANNOYED you by criticizing your drinking?

Have you ever felt you ought to CUT DOWN on your drinking?

Have you ever had a drink first thing in the morning to steady your nerves or get rid of a hangover (EYE-OPENER)?

SCORING : Possible scores (*T-ACE*): 0-5

T- answer of ≥ 2 drinks considered positive: scores 2

A - positive answer: scores 1

C- positive answer: scores 1

E- positive answer: scores 1

(1) Analyses to determine *ASSIST* score pertinent to minimum level of use placing the fetus 'at risk'	**(2) Analyses to determine *ASSIST* score/s pertinent to level of use placing the pregnant woman at risk of compromised pregnancy outcomes/ damage to her own health.**
T-ACE: score of ≥ 2 (Sokol, Martier et al. 1989; Chang, Wilkins-Haug et al. 1998)	*T-ACE* : score of ≥ 2 (high risk) score of 1 (moderate risk) score of 0 (low risk)

Tobacco:

***Revised Fagerstrom Tolerance Questionnaire* (*RTQ*) Study No:** | | | |

1 How many cigarettes a day do you smoke?	10 or less	11 – 15	16 – 20	21 – 25	26 or more
2 How deeply do you inhale?	1 I do not inhale	2	3 Moderately	4	5 Very deeply
3 *How often do you smoke more in the morning than during the rest of the day?*	1 Never	2	3 About half the time	4	5 Always
4 How often do you smoke your first cigarette of the day within 30 minutes of waking?	1 Never	2	3 About half the time	4	5 Always
5 How difficult would it be for you to give up your usual first cigarette of the day?	1 Not Difficult	2	3 Somewhat Difficult	4	5 Extremely Difficult
6 How difficult do you find it to refrain from smoking in places where it is prohibited (eg. in church, at the library, cinema, etc.)	1 Not Difficult	2	3 Somewhat Difficult	4	5 Extremely Difficult
7. How often do you smoke when you are sick with a cold, the flu, or are so ill that you are in bed most of the day?	1 Never	2	3 About half the time	4	5 Always
8 On average, about how much of each cigarette do you smoke?	1/3 o r less	½	2/3	¾	All
9 On average, how often do you inhale?	1 Never	2	3 About half the time	4	5 Always
10. On average, how often do you hold cigarette smoke in your lungs for a moment or two before exhaling?	1 Never	2	3 About half the time	4	5 Always

All items are scored on a 5-point Likert scale. The five anchors are assigned numbers.

eg. Question 1: "26 or more" cigarettes per day is assigned a score of 5.

The total score is calculated as the mean rating across all 10 items, and can range from 1 to 5, i.e. Sum of 10 item scores (range 10-50): _____

Total score (range 1-5): _____(Mean score of all 10 items)

SCORING: Possible scores (*RTQ*): 1-5

Dependence rating: Very low 1

Low 2

Medium 3

High 4

Severe 5

(1) Analyses to determine *ASSIST* score pertinent to minimum level of use placing the fetus 'at risk'	**(2) Analyses to determine *ASSIST* score/s pertinent to level of use placing the pregnant woman at risk of compromised pregnancy outcomes/ damage to her own health**
RTQ: score of > 1 (Nieburg, Marks et al. 1985)	*RTQ* : score of 4-5 (high risk) score of 2-3 (moderate risk) score of 1 (low risk)

Cannabis: *Timeline FollowBack (TLFB)*

Study No: | | | |

The calendar (on page 224) is representative of one month in a 3-month period retrospective to interview. For each participant, the 3-month calendar was prepared, according to the date on which the interview takes place.

Using the calendar, all participants were asked:

- on which of the days in the past 3 months cannabis was used?
- when cannabis was used on a day, how many joints or cones were used?

Following established techniques for *TLFB*, the inclusion of key dates were used to aid recall, such dates being influenced by the time of the year in which the interview occurs. Examples include birthdays and other anniversaries, paydays (including days on which social security benefits are paid), Christmas, New Year, and other dates such as football finals.

Emphasis was also directed to weekends versus weekdays and indicators of usual patterns of socializing (such as Friday and Saturday nights). Days of abstinence were also recorded.

SCORING

- Complete the 3-month calendar retrospective interview.
- Measure the number of days of use and calculate the average number of days per week of use.
- Measure the number of joints/cones each day and calculate average number of joints/cones per day

Cannabis: Possible scores (*TLFB*): 1-3

Quantification of use	**Score**
1 joint /cone per day on < 5 days/week	1
2 joints /cones per day for <5 days/week	2
> 1 joint/cone per day for > or = 5 days/ week	3

(1) Analyses to determine *ASSIST* score pertinent to minimum level of use placing the fetus 'at risk'	**(2) Analyses to determine *ASSIST* score/s pertinent to level of use placing the pregnant woman at risk of compromised pregnancy outcomes/ damage to her own health**
TLFB: report of use on ≥ 3 days per week Informed by:(Klein and Zahnd 1997) (Midanik, Zahnd et al. 1998)	*TLFB* : score of 3 (high risk) score of 2 (moderate risk) score of 1 (low risk)

Calendar for February 2007

Sun	Mon	Tue	Wed	Thu	Fri	Sat
				1	2	3
4	5	6	7	8	9	10
11	12	13	14	15	16	17
18	19	20	21	22	23	24
25	26	27	28			

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