

INTRODUCTION

Early diagnosis of women with various types of drug problems is difficult to achieve within maternity care services. The problems may be concealed or unknown, or only known to other services, e.g. social services. Co-operation problems between primary care, social services and health care can be another reason why the patient is not identified at the antenatal clinic (ANC). Furthermore, identification is made more difficult in that a substance dependency develops gradually. By dependency is meant a group of physiological, emotional and behavioural phenomena in which alcohol consumption has a much higher priority for the individual than other behaviours that were previously of great importance. A change of lifestyle takes place. That the development occurs gradually means that the symptoms change as the alcohol abuse progresses.

Within maternity care, whose area of responsibility is a healthy pregnancy, these women, often with multiple problems, are unable to receive the help and care they need. To achieve this, they need to be referred to specialist maternity services when available.

In present day Sweden, women drink greater amounts of alcohol, and do so more frequently than before. This may result in a depreciation of the risk of alcohol consumption. With the knowledge available today it is important to bring to public attention the long documented harmful effects of fetal alcohol exposure, as well as emerging findings in this field, so that more women are informed about the real risks caused by drinking during pregnancy.

The idea of developing, evaluating and implementing improved methodology for detection of alcohol use and alcohol related problems during pregnancy grew out of my clinical experience that very few women with these problems are identified in regular ANC.

Outline of the thesis

The work began with a questionnaire survey at antenatal care clinics, in which midwives were asked if and how they managed cases in which alcohol abuse problems were present or suspected. The results (**Study I**) suggested that the midwives mostly attempted to manage these problems themselves, and were convinced that most women gave up alcohol during pregnancy. This provided the rationale to proceed with **Study II**. In **Study II** an established screening instrument (AUDIT) was employed to screen for hazardous alcohol use before pregnancy, and alcohol consumption frequency during pregnancy. The results showed that considerably more women than expected had a hazardous alcohol consumption the year prior

to pregnancy. Furthermore, a large number of women continued some alcohol use during pregnancy, although the quantitative extent of that could not be determined based on the AUDIT instrument. However, this result lent support to the idea that there was a need for a more effective tool to help the midwives identify women in the risk zone as well as an instrument that facilitates a dialogue about these issues. Screening in **Study II** was anonymous and in **Study III** the question of whether this screening could be conducted during face-to-face registration at the ANC was examined. Screening instruments were used (AUDIT, TLFB) and blood samples were taken in connection with admission at the ANC. The results show that it is possible to use screening instruments without any major problems and that these identify considerably more women than the questions routinely asked by the midwives based on the ANC medical records. As this more effective method identified more women at risk, it was implemented and evaluated among regular antenatal care staff in **Study IV**. Midwives participated in a short training course in the use of the method whereas a comparison group continued to work as usual. Finally **Study V**, it was shown that an alcohol consumption among women in Sweden is on the rise. The anonymous screening study was therefore repeated 5 years after the original AUDIT-survey, in order to establish whether this development also affects pregnant women.

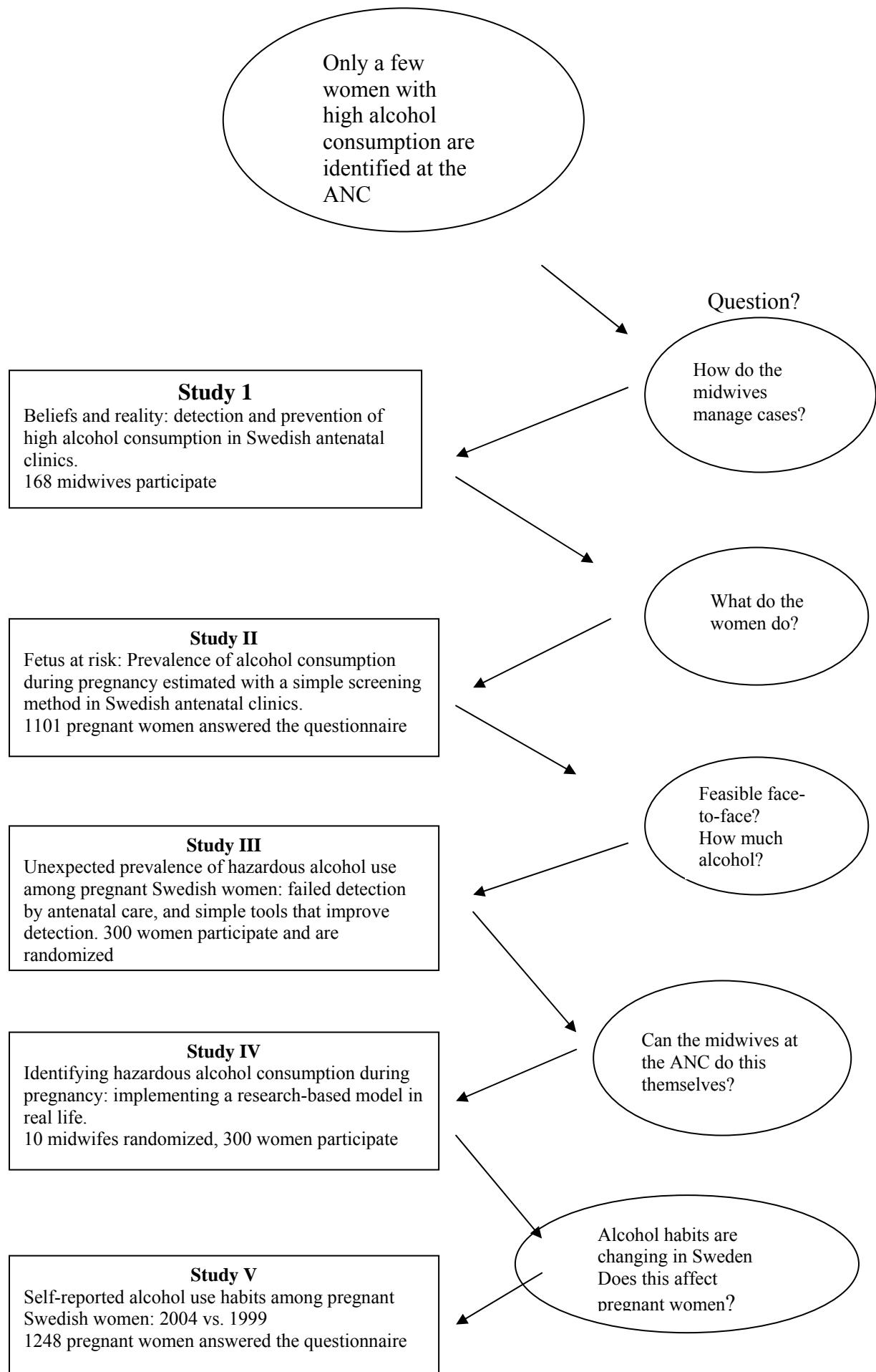


Fig 1: Development of the research process

BACKGROUND

Antenatal Health Care

Since the 1930s, perinatal morbidity and mortality for both children and mothers has been declining in Sweden (2;3). To a large extent, this positive development can be attributed to an increasingly professional antenatal care, which, with its focus on the monitoring of the normal pregnancy and preparation and training for delivery, screens for pregnancies that might be “at risk”. Delivery wards are equipped with increasingly more advanced monitoring technology, so that in most cases delivery complications can be avoided or predicted in time.

Modern antenatal care as it is currently conducted in Sweden was organised during the 1950s, when all pregnant women were offered free antenatal care. The aim of this care was specifically to prevent mortality and morbidity among mothers and children. In 1955 the Swedish National Board of Health and Welfare suggested that this care should also adopt a psychosocial perspective (4). In 1970, antenatal care further expanded its focus to include the entire family, and in 1978 also included parent training (5).

An increasing proportion of the work focuses on health information, which aims to prevent complications during pregnancy for both the mother and the expected child. The aim is also to generate a positive long-term effect on the women’s health by providing information about nutrition, exercise and other life style issues. According to the National Board of Health and Welfare’s ANC report, the chief aim of care delivered through this system is to reduce mortality, morbidity and handicap among expecting and new mothers and children (6;7).

Many ANCs have also worked with expecting mothers who smoke in order to help them try and stop. New goals for the ANC were formally developed in 1977, and emphasised that care is to focus on the pregnant woman and her family and that the primary task is to support the family’s own resources (8).

Due to this development, the ANC has been given an increasing number of areas to address. A further goal is to provide expecting parents with support and help to promote their own development, as well as that of their children (6). The pregnant woman and her psychosocial situation are to be highlighted so that help can be offered as required. The midwife at the ANC is to adopt an holistic view in her work (7).

Midwives at antenatal clinics today have clear guidelines regarding which conditions/complications pregnancy controls should focus upon. Most of these controls focus on physical complications specific to pregnancy, e.g. eclampsia. The difficulty for the ANC

midwives in identifying and managing psychosocial problems is that these are seldom specific to pregnancy or parenthood (2). This increases the risk that they are overlooked by the midwives who are trained to monitor pregnancy.

Women and alcohol

Historically, women have had a restrictive attitude to alcohol. More recently, however, women's consumption and drinking patterns have changed. In particular among young women, consumption has increased, and alcohol use habits are becoming more similar to those of men (9). Alcohol consumption is generally increasing in Sweden, the number of teetotallers is declining and the proportion of women who consume alcohol is rising. Every report that attempts to measure Swedish alcohol consumption consistently indicates it to be on the rise (10;11); www.sorad.su.se.

Young Swedish women typically start consuming alcohol at approximately 13 years of age, and choose to give birth to their first child when they are 30 years old on an average. This means that most women have been consumers of alcohol for more than 15 years when they enter their first pregnancy. This is probably the first time they are confronted with questions about their own alcohol consumption and from most midwives receive the recommendation to refrain from drinking alcohol during pregnancy for the sake of the expected child.

Are the midwives currently working at the ANC ready to meet this new generation of expecting mothers, i.e. young women who increasingly regard themselves as equals to men also in terms of alcohol consumption? Will these women have other questions about complications during pregnancy and if so, what will this mean for the midwives' preventive work at the ANC? Will the midwives require more and deeper knowledge about the harmful effects of alcohol on women and the expected child? Is there an increased need for knowledge regarding raising the issue of alcohol and its consequences, and do the midwives need to learn other working methods in order to identify women who run the risk of harming themselves or the expected child?

These questions initiated this work and the results obtained along the way spurred me on.

Alcohol and pregnancy

It has been known since ancient times that alcohol has a harmful effect on the fetus. In Carthage and Sparta, laws forbade newly married women and men under the age of 30 to drink alcohol in order to prevent “damaged” children. In the Bible’s Old Testament, Judges 13:3-4, the angel came to Samson’s mother and exhorted her to refrain from wine and strong drink while she is expecting her son. Also in the Jewish Talmud it is stated that one should not drink alcohol during pregnancy: “She who uses intoxicating drinks during pregnancy has strange children”.

In more modern times there were alarming reports from England during the “gin epidemic” of 1720-1750, when the flow of cheap gin led to a dramatic increase in the number of children with fetal damage (12). This knowledge was gradually lost as various restrictions were imposed on the sale and use of alcohol. Instead poor home environment and poor nutritional habits of the alcoholic mother during pregnancy were discussed as causes of adverse pregnancy outcomes (13;14).

The discussion of the potential role of alcohol gained new momentum when Lemoine examined a large number of children in alcoholic families and found an increased rate of congenital malformations, neurological disorders and retardation of both growth and development. It was concluded that the damage was been caused by exposure to alcohol (15).

At the beginning of the 1970s, Ulleland described the connection between growth retardation and alcohol exposure during pregnancy (16). In a classic article from 1973 Jones and Smith described the damaging effects of alcohol on the fetus and the term fetal alcohol syndrome (FAS) was introduced (17). Since then, our knowledge of the relation between alcohol use and fetal effects has developed rapidly. Today, there is solid scientific support that alcohol disturbs the complicated process of fetal development.

Since the beginning of the 1980s, guidelines from the National Board of Health and Welfare have charged ANC midwives with maintaining patient records (18). These medical records are standardized throughout Sweden and used at all antenatal clinics. They are structured and pre-printed, and provide an excellent help for the midwife to obtain a medical history, including alcohol use. The records prompts questions about the woman’s alcohol consumption, referring to three time intervals: 3 months before pregnancy, at admission, and in week 32 of pregnancy. For each of the intervals, there are three response alternatives: “seldom/never”, “less than once per week” and “more than once a week” (appendix 1; (19)). While the general perception in Sweden has long been that women essentially abstain from

alcohol use during pregnancy, clinical experience indicated that in fact a considerable fraction of pregnant women in Stockholm continue to drink during pregnancy. Similar results can be found in North American studies (20;21).

How the ANC works with information about alcohol during pregnancy and the staff's attitudes are decisive for the quality of the alcohol history obtained and how the pregnant woman behaves with regard to alcohol during the remainder of the pregnancy (11). The Swedish antenatal clinic patient records contain standard information about the woman's alcohol consumption as well as a wealth of information about her mental and physical status. Some of the information is reported to the National Board of Health and Welfare, e.g. information about tobacco consumption. However, information about alcohol consumption is not reported which means that even if the validity of the data present in the ANC records could be established, there are no reliable data about pregnant women's alcohol consumption.

The charge of the ANC is not to treat alcohol abuse and dependency, but to inform the expecting mother about alcohol and its consequences for pregnancy. Furthermore, the midwives are to identify women with problems as early as possible and refer them to appropriate services (22).

Why ANC?

Almost all pregnant women in Sweden come into contact with the ANC which therefore is uniquely positioned to play a central role in preventing or minimising fetal damage due to alcohol use. To fulfill this mission, midwives should ideally have adequate knowledge of facts about alcohol and pregnancy, possess expertise in using tools to identify risk cases, and be prepared to act. The potential to be successful is considerable. Women have great confidence in Swedish maternity care, and many would like more visits than the number routinely offered (23). Furthermore, pregnancy is a period of high motivation for change. Pregnant women have a strong desire to give birth to a healthy child. A pregnancy forces the woman to shift the focus from herself to the expected child. Studies show that it can be easier for the woman to change her habits during this time than otherwise (24). The fact that pregnant women give priority to the child's health and to the monitoring of the child's health (23) means that the ANC is ideally suited for providing health information and carrying out preventive work related to these issues. Accordingly, it has been shown that limited interventions during this period can result in reduced substance abuse (24).

Finally, it can be noted that risk behaviors of the parents are related to each other, pointing to the role potentially played by the expecting fathers. Government policy

mandates that these should also be involved, as a support or to receive help with their own problems if required (19). Far less empirical data are available on the role of the father, and the feasibility of targeting paternal behaviors in order to reduce risk for the fetus.

Alcohol as a teratogen

How then can exposure to small or moderate amounts of alcohol affect the fetus? Are there any “safe” levels? Is binge drinking on a few occasions more dangerous than “drinking a little all the time”?

The methodological difficulties in providing authoritative, quantitative answers to these questions are enormous. However, a relatively consistent picture, reviewed in the following, is beginning to emerge from a number of available studies employing different approaches. It is important to understand that, just like in any other area of toxicology, relations that emerge are statistical in nature. Rather than concluding that “alcohol causes XXX”, the conclusion will be that a certain level of exposure does – or does not – significantly increase the probability of a certain adverse outcome vs no consumption, or vs a lower level of use. Prediction in the individual case is virtually impossible. Apart from the amount of alcohol consumed and the mother’s drinking pattern, the individual risk to the fetus is related to other risk factors such as differences in the mother’s metabolism, genetically determined vulnerability, and the precise time point of fetal development at which exposure occurs, in particular the various developmental phases of the brain.

A commonly encountered position states that warning against, and screening for low – moderate levels of alcohol consumption can not be justified, since most women who consume alcohol at these levels and their offspring are “just fine”. This position fails to understand the fundamental, stochastic nature of toxicology and teratology.

How is alcohol absorbed and how is it eliminated by the fetus?

If a pregnant woman drinks alcohol the level of alcohol in the blood peaks after approximately fifteen minutes and then drops at a constant rate. The alcohol in the woman’s blood passes freely via the placenta to the fetus. Furthermore, the alcohol passes into the amniotic fluid where it is trapped and remains for a longer period than in the blood, which could mean that the amniotic fluid becomes a reservoir for alcohol (25). As the fetus’ brain is completely unprotected from alcohol this can have serious consequences (26). While the fetus’ liver is capable of producing blood cells already in the fifth to sixth week of pregnancy, its function to break down toxins does not mature until the end of the pregnancy. This means

that the fetus has a much poorer capacity than the mother to break down alcohol, which therefore can only be eliminated by recirculation into the mother, and metabolism by her liver (27).

When the fetus' brain is exposed to alcohol, formation of brain cells is partially arrested, and the final number of neurons may be decreased. Furthermore, the fine-tuned wiring pattern of nerve cells is affected as they migrate out from the subventricular zone where they originate, and they innervate the cortex in a less well organized manner. This means that the child can be born with a decreased brain size, and / or with a brain that functions less effectively (26).

The neurotoxic effects of alcohol are mediated through several different mechanisms. Studies in rodents have shown that the emergence and new formation of synapses is interrupted by ethanol. Alcohol is well known to inhibit glutamatergic signalling through NMDA receptors, and potentiate GABA signalling through GABA-A receptors. For a long time, knowledge was lacking how these effects could lead to inhibition of neuronal formation, since these actions (acutely, and in a non-dependent state) in the adult brain would not be expected to lead to neurotoxicity, but rather protect against it. In an pivotal recent discovery, it was shown that the actions of glutamate and GABA during fetal development are opposite those in adult life. Alcohol mediated inhibition of glutamate NMDA signalling deprives neurons of a signal essential for their survival. Likewise, GABA-ergic inhibition of neuronal firing inhibits the very activity which induces synapse formation, and cells that fail to form synapses are eliminated. In both cases, programmed cell death, apoptosis, is the mediating process (28).

In vivo studies have also shown that ethanol disturbs the migration of neurons by affecting the support tissue glia cells, as well as via the myelination of the nerve cells (29;30). A further mechanism seems to be that ethanol interacts with growth factors, which also influence the cell maturity and the migration of the brain's neurons (31).

Alcohol and the central nervous system

The brain arises in the third/fourth week of pregnancy. The nerve cells divide and grow in number to migrate out towards the brain's cortical layer. The growth of the nerve cells is most rapid between the 10th and 20th week of pregnancy when 100,000 nerve cells are formed every minute.

Different regions in the brain can be more or less sensitive to alcohol during different periods of pregnancy depending on cell type, amount of alcohol and method of exposure. Nevertheless, the brain's development is affected by alcohol during the whole of the pregnancy(32;33). Microcephaly (small brain) and reduced brain stem are described as specific findings when the mother has drunk alcohol during pregnancy(34;35).

It has been shown that when the fetus is exposed to alcohol the respiratory movements usually seen in the fetus in the uterus cease almost completely. This effect can be registered 30 minutes after the mother has drunk a glass of wine. The significance of this effect on the fetus is difficult to assess, but the pattern of fetal breathing is considered to reflect the fetus' well-being (36).

Fetal Alcohol Syndrome (FAS) - Fetal Alcohol Effects (FAE)

FAS refers to the characteristic abnormalities that affect children of mothers who have drunk a large amount of alcohol during pregnancy and where the damage to the fetus has been so substantial that the child can be given a diagnosis. The current criteria for FAS are:

1. Pre- and / or post natal growth retardation with respect to height, weight and head circumference.
2. Facial malformation that gives a characteristic appearance with among other things short palpebral fissures, sunken nasal bridge; flat or absent groove between nose and upper lip; thin upper lip, and low-set ears.
3. Manifestations from the central nervous system (CNS), in the form of developmental disorders, learning difficulties, concentration difficulties, memory problems and / or structural abnormalities such as microcephaly or brain malformation.

To establish the diagnosis FAS, it is necessary that there is at least one symptom from each of the three groups in combination with alcohol abuse by the mother (37). There is a lack of simple and objective clinical tests for the diagnosis of FAS and FAE. What contributes to the difficulties in establishing the diagnosis is that individual symptoms and signs are not specific for this condition, and may arise at different age. A number of other factors such as other drugs or pharmaceuticals, use of nicotine, infections, malnutrition, the mother's standard of living etc. are of significance for the child's well-being and how it develops. The influence of these factors makes the diagnosis even more difficult.

Streissguth has shown that the characteristic features of FAS become less prominent when the child grows up. Even if it were possible to propose clearer diagnostic criteria and train paediatricians in establishing the FAS diagnosis there would still remain the difficulty of diagnosing those children who have only the mental effects of alcohol but who are without the morphological features (32). The prevalence of FAS in France is indicated to be 1/300 birth (38), in Sweden 1/600 birth (27) and in USA 1/750 birth (39), but these are old reports and the results could be considered unreliable. The national incidence of FAS is probably in the 1 to 4,8 per 1000 range and the combined incidence of FAS and FASD increased the prevalence of alcohol-related affected individuals to 9,1 per 1000 (nearly 1 in 100 birth)(40). Knowledge of the incidence of FAS and FASD is limited and involves estimates because no large-scale national incidence studies have been undertaken(35).

FAS is the result of the highest levels of alcohol consumption during pregnancy, and as such the tip of the iceberg. During recent years, an increasing number of studies has demonstrated the significance of more moderate levels of alcohol use during pregnancy. The knowledge that exposure to even small amounts of alcohol can affect the outcome of pregnancy and harm the fetus has also led to a discussion in which changes to the nomenclature in the field have been suggested. Instead of using the categories Fetal Alcohol Syndrome (FAS) and Fetal Alcohol Effects (FAE), the term "Fetal Alcohol Spectrum Disorder" FASD (35) has been introduced to cover the whole spectrum of damage that can arise as a result of exposure to alcohol. These effects are reviewed below.

Miscarriage

Several studies show an increasing risk for miscarriage with increasing alcohol consumption (27;41-43). Almost all these articles raise the issue of uncertainty with regard to the amount of consumption that would significantly increase the risk. Available reports do not find a significant increase below average consumption of less than five drinks per week(60 g pure alcohol/week). No connection has been established between alcohol consumption later in pregnancy and miscarriage (41;44;45), In more recent findings Olsen et al. showed that high alcohol consumption can cause reduced fertility (46). An interesting and plausible explanation for this could be that women with high alcohol consumption and alcohol abusers often experience very early miscarriages that are not registered as such with healthcare, as they can be so early that they are regarded as a delayed menstruation (47).

Intra-uterine growth retardation and effect on birth weight

One of the best established effects of high alcohol consumption during pregnancy is to impair the child's growth (27;48-56). Whether or not a more moderate consumption has the same effect remains uncertain, and different results have been obtained (32;53-60), with several studies failing to find a connection (48;50;52;56-60). There are many potential reasons for these conflicting data, since intrauterine growth and birth weight are likely to be differentially affected depending on the time point during pregnancy when consumption occurs, and other partly correlated variables contribute to the outcome, e.g. smoking, genetics, prematurity etc. In summary, available data support the conclusion that an average alcohol consumption of appr. 100g alcohol /week leads to a considerable risk for growth retardation (61).

The risk for intra-uterine growth retardation and low birth weight increases with increased alcohol intake. At very low levels during the first trimester (less than half a glass of wine/daily) a reduced risk for growth retardation has in fact been described compared with teetotal controls (a so-called J-formed curve). However, the same consumption in the 7th month of pregnancy increased the risk of low birth weight and premature birth (62;63). With average consumption of 1 standard drink (10 – 12g, equalling 1 glass of wine or 1 drink) daily during the first trimester, one study reported a risk of reduced birth weight among male infants (61). With consumption of 1-2 glasses/day in the first trimester, several studies show an increased risk for intra-uterine growth retardation and low birth weight (62-65).

Less information is available regarding the effects of binge drinking, but the risk for growth retardation appears to rise (59;62;63;66;67). In one study the greatest risk for intra-uterine growth retardation and doubled risk for low birth weight was found in children exposed to 5 glasses or more on the same occasion (62).

Premature delivery and stillbirth

Approximately the same levels of alcohol use as those increasing the risk of growth retardation and miscarriage are also thought to increase the risk for premature delivery. Also in this respect boys appear to be more sensitive. During the first trimester, average use of one - three drinks/day leads to an increased risk, while considerably lower levels of alcohol are thought to increase the risk during the seventh month of pregnancy. Just as has been shown with growth retardation, a reduced risk for premature delivery has been observed with low weekly consumption, i.e. 2-4 drinks / week early in pregnancy (44;62;68;69).

The risk of stillbirth increases with increasing alcohol consumption. Women with an alcohol consumption of at least 5 drinks per week ran 2-3 times higher risk of having a stillborn child. No association was found with neonatal death (44).

Alcohol-related fetal damage and neuropsychiatric disorders

The characteristic structural malformations of FAS are likely to require consumption of large amounts of alcohol during pregnancy. This is clearly less common than more discreet FASD manifestations. However, it deserves mention that this type of effect may theoretically be caused inadvertently before a woman knows that she is pregnant, since e.g. the typical facial changes of FAS can result if the fetus is exposed to alcohol during a very limited period early in the pregnancy(70). Epidemiologically, an increased risk of structural malformations is not found after a moderate alcohol consumption of max. 2 drinks per day (70;71).

On the other hand, many studies have shown that moderate alcohol consumption can lead to neuropsychiatric disorders. Attention deficits and hyperactivity have been observed in pre-school children (35). Streissguth et al. have carried out several studies showing that children of alcohol abusing mothers have a lower intelligence quotient, learning difficulties and concentration difficulties (70;72). Swedish studies support these results, although these were conducted with a group of children born to women with substance abuse and social problems (73). All these studies are made difficult by the complex and multifactorial nature of the outcomes which are studied, with contributions of genetic factors and an impoverished environment potentially confounding the effects of alcohol use.

Detecting functional nervous system consequences of maternal drinking also requires long term follow up to an extent which is rarely available. In a comprehensive study, Streissguth and colleagues followed a group of children up to their teenage years. On follow-up at 7 ½ years, maternal consumption of 2 drinks / day or more on an average during pregnancy led to a 7 point decrease of IQ scores even when adjusting for appropriate covariates. On follow up at age 14, both verbal and numerical performance was dose-related to the mothers' self-reported alcohol intake. Children of teetotalers achieved the best results. These effects were robust when considered in relation to a wide variety of potentially confounding variables, such as prenatal exposure to tobacco and other drugs, sociodemographic characteristics, and traumatic postnatal events. A variety of alcohol scores were related to the measures of intellectual performance, but those involving a massing of drinks on a given occasion had the strongest association. The higher the average number of drinks/occasion, the poorer the offspring performance on tasks thought to underlie numerical

problem solving and reading proficiency. (74;75). Memory functioning also showed a negative correlation with increasing alcohol intake. Exposure to alcohol during the first trimester increased the risk for learning problems and had effects on both short- and long-term memory (76).

Finally, increased behavioural problems have also been described among children exposed to 1 drink/day (77).

The most thoughtful and best summary of how these associations should be interpreted is provided by Streissguth. It deserves to be quoted here: *“...alcohol use patterns within the social drinking range can have long lasting effects on IQ and learning problems in young school aged children. These patterns should not be interpreted as biologic thresholds. It should also be noted that these are group effects of prenatal alcohol exposure, not necessarily predictable in the individual child, and that for the most part these children were functioning within the normal range of intelligence.”*

Significance of binge drinking for mental development

Binge drinking may carry risks of its own, independent of overall consumption level (78). Animal studies using rats showed an almost linear connection between alcohol intake and the total weight of the brain. If the rats received alcohol in a binge pattern, i.e. as large amount on one occasion, the damage appeared to be more serious than if the amount was distributed equally over time. That alcohol can be harmful during the first trimester emerged from a study of monkeys exposed to alcohol for intoxication purposes once or twice a week, in different periods of pregnancy. Monkeys that were only exposed to alcohol in early pregnancy showed largely the same extent of brain damage and impaired cognitive functioning as those that had received alcohol during the whole pregnancy.

In the previously mentioned study of Streissguth and colleagues it was observed that the children of mothers who engaged in binge drinking before they knew they were pregnant had attention disorders, cognitive deficiencies and difficulties with problem solving. Binge drinking in early pregnancy has also been shown to significantly affect learning and memory functions. Even single occasions affected the children's results (78;79).

What levels of consumption can entail risk for the child?

Nyberg and Allebeck in ” *Ett glas eller två kan väl inte vara farligt*” (Can one or two drinks be harmful ?) (80) have carried out a major review of studies concerning this question. The authors repeatedly review and acknowledge the difficulty with this type of research, i.e. that it

requires a great number of studies and large groups. There are difficulties in obtaining correct information about alcohol intake even if reasonably reliable methods are now available that with the help of questionnaires or interviews can establish the individual's alcohol consumption. Despite this there can be difficulties in establishing alcohol's role when a multitude of confounding factors must be considered. The existence of various measures of consumption further complicates any conclusions.

However, available studies overall show that binge drinking (more than five drinks on one and the same occasion) is more harmful for the fetus than consumption of the same amount evenly distributed over time (78).

Fetal alcohol spectrum disorders: Summary

Numerous human epidemiological studies prompt the conclusion that average consumption of approximately one or two drinks (10 – 20 g pure alcohol) per day during pregnancy is associated with adverse effects on the fetus and the outcome of pregnancy. Animal models, and a smaller number of human studies indicate that a rapid heightening of blood alcohol levels, as in binge drinking, can be particularly hazardous for the developing brain and result in learning problems and behavioural disorders. There is much less evidence that binge drinking affects the child's growth, premature delivery etc. This should be interpreted with caution, since it may be related to methodological problems in the design of these studies rather than with its real significance (79).

The time when alcohol intake occurs also seems to be of importance. Several studies have indicated the significance of alcohol intake during early pregnancy, even before the woman knows for certain that she is pregnant, which supports the advice that women who consider having children should reduce their alcohol consumption and avoid drinking several glasses on one and the same occasion. Most researchers who have conducted studies that form the foundation of this summary advise pregnant women to refrain from drinking alcohol and not to put their trust in any "safe levels".

Identification of pregnant women with hazardous alcohol consumption

Against the background of the studies reviewed above, it is obviously important to identify women who drink during pregnancy, and to do so as early as possible.

In general, primary healthcare is an important and well studied arena for identifying alcohol related health risks. The prevalence of alcohol use disorders is significantly higher among patients visiting a primary care practitioner than among the

general population (81;82). For this reason, clinicians in primary care have an opportunity to play a key role in detecting alcohol problems and in initiating prevention or treatment efforts. A variety of relatively brief screening instruments are available for this purpose (83-85). These instruments do not provide a diagnosis. Instead, they help identify patients who might benefit from a more thorough assessment of their drinking behaviour (86). They screen not only, and not even primarily for alcohol use disorders, but rather for drinking patterns or behaviours that may place the subject at increased risk for developing adverse health effects or alcoholism, so called “hazardous drinking” (85). Hazardous drinkers who have not yet become alcohol dependent often can be treated successfully within a primary care setting (87).

Although to some extent applicable, it is not possible to directly transfer this knowledge to women attending the ANC. First, it is well-established in Sweden that all women who are pregnant and who intend to carry their pregnancy to term also contact the ANC. Therefore, they do not comprise a selected group other than they are pregnant, and it is not to be expected that hazardous alcohol use is enriched in this population in a way similar to general primary healthcare setting.

Furthermore, the objectives of screening during pregnancy differ from those in general primary care. Pregnant women should be screened not only for alcohol use disorders, but also for drinking patterns or behaviours that would otherwise be entirely acceptable, but that during pregnancy may adversely affect the fetus. Screening pregnant women for alcohol use in this way has become increasingly important in light of the research showing that even low levels of prenatal alcohol exposure can harm the fetus.

Through screening at the ANC it is possible to identify groups in which there is an elevated risk that the woman will expose the fetus to alcohol but also groups in which there is very little risk of alcohol exposure during pregnancy (88). This is of importance in the design of care at the ANC.

Screening is the first step in a process that can lead to a continued examination for diagnostic purposes. A positive screening result does NOT provide a diagnosis. A woman who screens positive should be followed-up and possible interventions discussed. These will vary depending on whether the reason for screening positive is the presence of hazardous alcohol use habits, or “only” otherwise normal consumption which exposes the fetus to risk. Conversely, the fact that a woman screens positive for hazardous alcohol use habits does not necessarily mean that the fetus has been exposed to alcohol. The woman may have engaged in

hazardous use or even have alcohol problems, but may also have succeeded in refraining from drinking because of pregnancy.

It is thus important that the midwife at the ANC tries to identify which children are exposed to alcohol and to what amounts. This implies the use of instruments that screen for hazardous alcohol use habits in general, but also specifically for actual alcohol use during pregnancy, which may be at levels which would otherwise not be relevant to detect. For this reason, over the course of this thesis we perceived a need for two screening instruments. In order to identify possible hazardous alcohol habits the Alcohol Use Disorders Identification Test was used (AUDIT appendix 2). To screen for amounts of alcohol to which the fetus has been exposed during pregnancy we used Timeline Followback (TLFB appendix 3). The use of these two instruments together help the midwives achieve two different goals:

- To help women with a moderate alcohol consumption avoid harming their fetus because they underestimate the risks with alcohol consumption. These are the cases where the amounts consumed do not involve a risk for the adult woman, but can pose a significant risk for a fetus during its development.
- To identify those women who have hazardous consumption, and should reduce their alcohol consumption both for their own sake and for that of the fetus.

Since it has not been possible to establish safe levels of alcohol consumption during pregnancy, professional care staff regularly recommend total abstinence during pregnancy (89;90). However, studies show that a considerable proportion of women continue with some alcohol intake during pregnancy (90-92). No reliable statistics are available on this sensitive issue, and underreporting clearly is a problem (93;94). Unfortunately, although some estimates indicate that approximately 20 per cent of women consume some alcohol during pregnancy, maternal drinking is difficult to detect in regular clinical settings (95).

Questionnaires / screening instruments that have been validated to possess a reasonable degree of sensitivity and specificity offer an approach that reduces the risk for underreporting. A well-designed questionnaire can also facilitate clinical work and reduce obstacles such as denial in the woman and staff resistance to working with these issues (96).

Screening instruments

A number of screening instruments is available for identifying alcohol related problems.

Several of these have been used in academic dissertation theses in Sweden to identify alcohol

consumption in various populations. Spak screened women in Gothenburg (97), Österling used screening with both men and women in Malmö (98) and Hermansson screened men and women at various work places in Stockholm (99). Dejin-Karlsson asked pregnant women in Gothenburg about their alcohol consumption and showed that more than 30% of the women continued to drink during pregnancy (100).

Before initiating screening efforts, it is important to be clear about their purpose. This is also important when choosing the type of screening instrument. As discussed above, screening is normally aimed at identifying which patients that are in the risk zone for developing alcohol related problems (101). In contrast, in all the studies included in this thesis the aim has been to screen healthy women in order to identify both those who drink in a way that is hazardous to their own health, as well as those who not will be at risk themselves, but who expose their expected child to alcohol during pregnancy.

Connors (102) suggests that three important issues should be addressed when selecting screening instruments:

1. The aim of the screening.
2. The study's aim and questions and how much time has been allocated for screening.
3. What resources are available to offer the patient in the form of information, feedback, and follow-up and interventions for those who screen positive.

Many screening instruments have been developed in order to identify patients with harmful alcohol consumption within primary care or in hospital. Most of these questionnaires can be used by all staff categories or can be completed by the patient him/herself (103). The performance and properties of several available screening instruments has been discussed extensively (104-107). Many screening instruments are designed for men, such as MAST and Short-MAST (108;109), CAGE (110;111) and MALT (112). Most instruments are also constructed to identify patients with abuse or dependency problems, which was not the purpose of our screening.

Several screening instruments are also available for the more specific purpose of detecting maternal alcohol problems, although few of these allow the midwives to detect fetal alcohol exposure in the absence of maternal alcohol abuse or dependence (113). Sokol and colleagues developed the T-ACE questionnaire to identify pregnant women who consumed quantities of alcohol that can potentially damage the fetus (114). At the end of the 1980s

screening instruments were tested that were designed to identify alcohol consumption, abuse and dependency among fertile or pregnant women. Examples of such screening instrument are: Ten Question Drinking History (115), the TWEAK (116), the T-ACE (114) and the Pregnancy Alcohol Consumption Indicator (117). These instruments were developed for their special target populations based on other instruments developed to screen for alcohol dependence in the general population, such as CAGE and the Addiction Severity Index (ASI) (103;116).

Most of these screening instruments are centered on questions concerning physical and mental problems as well as psychosocial consequences of alcohol consumption. Questionnaires have from 4 to 200 questions and can be used as self-report questionnaires or in an interview situation. Not all have been tested on pregnant women, and none of them directly addresses the issue of fetal exposure to alcohol during pregnancy. The most common items are questions about frequencies and quantities of drinking, but use a global approach to each of these dimensions rather than tracking them over time (101). These questions can be found in many variants, e.g. *How often do you have a drink containing alcohol? How many glasses do you drink? How many drinks containing alcohol do you have on a typical day when you drink alcohol?* (AUDIT).

The validity, sensitivity and specificity of most available instruments have generally been measured in relation to how well they identify a person who meets criteria for alcohol dependency or abuse according to the International Classifications of Diseases, Tenth Edition (ICD 10; World Health Organization 1990) or the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV; (1)).

An important study at the University of Mississippi Medical Center in Jackson, Mississippi, compared the sensitivity and specificity of CAGE, BMAST, AUDIT and TWEAK in identifying patients who had fulfilled the ICD-10 diagnostic criteria for alcohol dependence and/or harmful drinking during the previous 12 months. The study separately compared the instruments' performance in men and women, and in African-American and Caucasian patients (118-121). For the entire study group, AUDIT and TWEAK demonstrated greater sensitivity (85 and 87 %) than CAGE (75 %) or the BMAST (31 %).

However, these measures were of limited use to guide our choice of instruments in the present line of studies. The aim of these was not primarily to identify women with dependency or abuse problems, as the amount of alcohol that is harmful for the fetus is substantially lower than the amount a woman can consume without medical or mental health

risks. In the context of antenatal care, it is meaningful to identify all alcohol consumers and give them adequate alcohol information about the risks of alcohol for pregnancy at their respective level of consumption. Along the same line, when balancing sensitivity vs specificity in screening for alcohol use during pregnancy, high sensitivity takes priority over high specificity. Because of the potentially grave consequences for the child, it is important that the midwives identify all or as many as possible of the women with a hazardous use; false positive cases can be excluded in subsequent assessment, while false negative results are difficult to address.

When choosing a screening instrument to be used at antenatal clinics, it is equally important to consider that it is practical to use for the midwives, and easy to score and interpret. Direct as well as indirect costs should be minimal.

Several instruments potentially meet these requirements, e.g. CAGE (111), TWEAK (21;116), MAST (Michigan Alcoholism Screening Test; (108;109;122)) and SWAG (Screening Woman and Alcohol in Gothenburg; (97;123)). Most of these instruments are constructed to identify alcohol abuse or dependency whereas AUDIT is the only test designed to identify hazardous and harmful drinking (124).

AUDIT

Definitions: A “harmful” drinker is a person with alcohol dependence and/or alcohol related problems, whereas a “hazardous drinker” is someone whose pattern or amount of drinking place them at risk for (future) alcohol problems (125). In all the studies, the use of AUDIT (Alcohol Use Disorders Identification Test) was chosen as it is vital as early as possible to identify women with an alcohol consumption that can be considered harmful to the expected child. A further reason is that since 1997 Bergman and colleagues have used AUDIT to study the alcohol habits of the Swedish population (9). This gave the opportunity to use their population data on women in the same age group as the pregnant women for comparison purposes. Assessment and feedback of the results in the study are facilitated if there are reference data from the general population with which to compare.

AUDIT is recommended by the World Health Organisation (WHO) and has generated a great deal of research in a short period of time (126). It consists of ten questions, each of which is scored between 0 and 4, yielding a possible maximum of 40 points. There are three questions on consumption patterns, three concerning alcohol dependency and four about alcohol-related damage or problems. On the form, a “standard drink” is defined as 12 g pure

alcohol. This can be consumed in the form of beer, spirits, or wine which is clearly stated on the form.

Cut-off for screening positive: In order to operationalise "hazardous or harmful" alcohol habits in a screening instrument like AUDIT it is necessary to define a cut-off, or threshold. A threshold of 8 points has been shown to give the best combination of sensitivity and specificity among primary care patients (127). With this threshold AUDIT has a good reliability and validity for identifying patients who have a hazardous alcohol consumption and in the future risk developing more serious problems (9). Since women are more sensitive to alcohol than men and can be harmed earlier by less amounts (128;129) a threshold of 6 is recommended for women (9).

Timeline Followback (TLFB)

When a patient screens positive with any of the instruments discussed above, this is only the first step in a process that can lead to a diagnosis or no diagnosis. More importantly for the purpose of the line of studies in this thesis, screening positive or not does not provide information on how much alcohol the fetus has actually been exposed to. A more thorough history, or better yet a structured quantitative instrument is needed for this. Similar to what has been suggested by others (103), we have found Timeline Followback to be a method useful in assessing fetus' exposure to alcohol.

After the first study, it became apparent that we had identified a group of women that had consumed alcohol during pregnancy. It was also clear that we lacked data regarding how much alcohol the fetus had been exposed to. In order to screen for the actual exposure of the fetus/child, we used Timeline Followback (TLFB) in two studies.

The alcohol TLFB is a drinking assessment method that obtains estimates of daily drinking. Using a calendar, people provide retrospective estimates of their daily drinking over a specified period. The TLFB method not only has a high level of reliability and validity in the measurement of alcohol consumption in general populations (130;131), but also includes a method for determining the amount and timing of alcohol use. The TLFB provides information on separate dimensions of a person's drinking, such the number of drinking days, the maximum amount of alcoholic beverages consumed and temporal patterns such as weekend versus weekday drinking. From this information, alcohol exposure can be examined, based on dose for each exposure as well as when during fetal development the exposure occurred (103).

TLFB is a systematic interview method to obtain a day-by-day account of a person's actual alcohol consumption. It yields valid estimates of a person's drinking for up to 6-12 months (131). In the present studies, the period assessed by *TLFB* varied depending on the pregnancy week of admission (median 12, range 8-24). Throughout this period, daily consumption was reported in terms of standard glasses and categories of alcohol. These were converted to gram amounts of pure alcohol, yielding estimates of alcohol consumption. We set the threshold for positive screening on *TLFB* at either:

- Consumption of 70 g alcohol/week during two or more weeks
- Consumption of 60 g alcohol on the same occasion (binge), twice or more

When setting these criteria, we took into account two dimensions. Sustained average consumption above 10 g per day during pregnancy is clearly associated with a risk for adverse consequences (41;44;61;64). To avoid influence of occasional use, subjects were classified as *TLFB* screening positive if they reported consumption of 70 g or more for two or more weeks. In addition, binge drinking defined as consumption of approx. 5 standard drinks, or 60 g alcohol on a single occasion, is associated with a separate type of risk (75;78;79;132;133). Efforts have recently been made to develop specific simple methods to detect this type of risk (134), but as suggested recently (103), the day-by-day measures produced by *TLFB* are suitable also for directly addressing this aspect. Following the same conservative logic as above, two or more self-reported episodes of consumption above this level were required to classify a subject as positive.

The *TLFB* yields a great deal of information. We obtained information on how much alcohol the fetus had been exposed to during the weeks the pregnancy had been in progress, but also about the woman's pattern of alcohol intake during this period, both in terms of average weekly consumption, and periods of binge drinking.

Biochemical alcohol use markers (“Biomarkers”)

An obvious alternative or complement to *AUDIT*, *TLFB* or similar screening tools is to obtain blood samples for analysis of biomarkers indicating hazardous alcohol use. We therefore also evaluated the comparative performance of the most commonly employed biomarkers vs. the self-report tools.

Mean corpuscular volume (MCV) is increased by alcohol, but is unchanged or increases only modestly in the latter half of the pregnancy (135;136). It has previously been

reported that MCV might be a useful marker in detecting harmful alcohol consumption during pregnancy. In these studies, sensitivity varied between 11 - 40 % according to the drinking pattern and consumption levels, with the higher sensitivity found in subjects drinking 2-10 standard drinks daily (137-139).

Elevated gamma glutamyl transferase (GGT) can indicate alcohol effects on the liver, but GGT is also increased by numerous other factors. The sensitivity of GGT varies with consumption pattern. It is more likely to be elevated in regular than in episodic drinkers, and seems to be less sensitive in women (140;141). During a normal pregnancy GGT is unchanged or decreases (142), but studies on pregnant women have shown a sensitivity of 25% - 30 % in subjects drinking 1-3 drinks/day, with increasing sensitivity at higher consumption levels (137-139;143).

Serum transaminases (aspartate aminotransferase, AST, and alanine aminotransferase, ALT) are non-specific indicators of hepatic damage. During a normal pregnancy serum concentrations of AST and ALT are normal, although liver metabolic capacity may be reduced in late pregnancy, such as in eclampsia and intrahepatic cholestasis (142;144). In a study of pregnant women who drank 2- 10 standard drinks daily, the sensitivity for ALT and AST was only 19 and 15 % respectively (143).

Finally, transferrin, the organism's major iron transport protein, occurs in isoforms differing in their degree of glycosylation. Carbohydrate-deficient transferrin (CDT) isoforms are elevated by high alcohol intake (141;145). Although generally thought to possess a higher degree of specificity than other non-acute biomarkers for alcohol use, CDT has a moderate sensitivity in screening for alcohol problems in women. In a review of 16 studies Allen et al. reported that the median sensitivity was 51 % for all studies, with a wide range between moderate and heavy drinkers (145). During pregnancy, serum levels of CDT increase and are significantly higher in the third trimester than in the first. Female sex hormones appear to increase total transferrin but less so its carbohydrate-deficient isoforms. However, significant alcohol consumption will increase CDT to a larger extent (146;147). In a Finnish study of 44 pregnant women with alcohol abuse, CDT had a very low sensitivity, only 8 %, markedly lower than MCV and GGT (138).

In summary, few studies are available which assess the performance of laboratory markers when used in normal antenatal care to detect harmful drinking in pregnant women. A combination of MCV and GGT has been suggested to produce the highest sensitivity with an acceptable degree of specificity (138;139). The performance of this, or

other combinations of biomarkers compared with self-report based tools has to our knowledge not been evaluated previously.

Articles	Aims	Data collections/ Subjects	Method for analysis
<p>Title/ Paper I Beliefs and reality: detection and prevention of high alcohol consumption in Swedish Antenatal clinics. Acta Obstet Gynecol Scand. 2004 Sep;83(9):796-800.</p>	<p>Aimed to gain a better understanding of the actions, or lack thereof, of antenatal care (ANC) clinic midwives, when encountering women with substance and alcohol abuse related problems. Find out what ANC midwives perceive to be expected of them, what their perceptions of their own actions are, as well as the actions they take. Make an assessment of the ANC midwives' knowledge of resources available for dealing with substance abuse during pregnancy.</p>	<p>All antenatal clinics in Stockholm area (47 st), with 207 employed midwives 168 midwives participate from 46 antenatal clinics.</p>	<p>The collected data were coded and analysed using EPI INFO 6 (Center for Disease Control, Atlanta). Responses were tabulated in frequency tables and presented with descriptive statistics. Chi-square was used to test for possible differences between groups.</p>
<p>Title/ Paper II Fetus at risk: Prevalence of alcohol consumption during pregnancy estimated with a simple screening method in Swedish antenatal clinics Addiction. 2003 Nov;98(11):1513-20.</p>	<p>Examined the prevalence of hazardous or harmful alcohol consumption during pregnancy in a consecutive series of Swedish pregnant females.</p>	<p>Out of 1123 subjects who received AUDIT the 30 pregnancy week at a antenatal clinic in Stockholm, 1101 responded during the session.</p>	<p>Statistica 6.0 (StatSoft Inc., Tulsa, Oklahoma) was used for all analyses. AUDIT-scores were skewed, and were therefore compared using the non-parametric Wilcoxon U-test. Differences between observed frequencies were compared using two tailed Fischer Exact Test when possible, or else using χ^2-test with Yates' s correction.. Multiple logistic maximum-likelihood regression was carried out using the generalized linear-non (GMZ) module to examine the influence of pre-pregnancy AUDIT scores, age and education level for classifying</p>
<p>Title/ Paper III Unexpected prevalence of alcohol use among pregnant Swedish women: failed detection by antenatal care, and simple tools that improve detection Study of Alcoholism</p>	<p>Examined, in a randomised controlled manner, the feasibility of improving detection of hazardous alcohol consumption during pregnancies using easily available screening tools. Compare the performance of the following potential tools for this purpose: Laboratory markers (MCV, GGT, ASAT, ALAT, CDT), the Alcohol Use Disorder Identification Test (AUDIT) and Time-Line Follow-Back (TLFB).</p>	<p>The target population was women who came for the first visit to the antenatal care clinics between September 1st, 2001 and May 30th, 2002 (total number: 1106). Among these, 300 women were randomly selected for the RCT, by offering participation to all women admitted to the respective clinic on randomly alternating weekdays.</p>	<p>Statistica 6.0 (StatSoft Inc., Tulsa, Oklahoma) was used for all analyses. We compared the performance of AUDIT and TLFB delivered by regular antenatal care midwives, individually or in combination, to the control condition. AUDIT alone (23/139 vs 1/153; two tailed Fischer Exact.</p>
<p>Title/ Paper IV Identifying hazardous alcohol consumption during pregnancy: implementing a research-based model in real life.</p>	<p>Examined whether a screening strategy using the Alcohol Use Disorder Test (AUDIT) and Timeline Followback (TLFB) could be implemented under naturalistic conditions and with available resources; and whether it would improve detection to the extent previously shown in a research context.</p>	<p>10 midwives randomized to participate. All 153 subjects randomized to the control condition accepted participation, i.e. allowed access to their regular antenatal care records for extracting data. Among 162 subjects randomized to the intervention condition, 139 accepted.</p>	<p>Statistica 6.0 (StatSoft Inc., Tulsa, Oklahoma) was used for all analyses.</p>
<p>Title/ Paper IV Self-reported alcohol use habits among pregnant women: 2004 vs 1999.</p>	<p>Examined self-reported alcohol use habits among pregnant Swedish women: 2004 vs. 1999.</p>	<p>1248 pregnant women answered the questionnaire</p>	<p>Statistica 6.0 (StatSoft Inc., Tulsa, Oklahoma) was used for all analyses.</p>

Fig 2. Overview of the papers included in the thesis

AIMS OF THE STUDY AND RESEARCH QUESTIONS

This investigation was performed to study several aspects of alcohol use during pregnancy, including attitudes among ANC midwives which may influence their willingness and ability to identify women in need of intervention. In order to develop a clinically useful strategy, prevalence of alcohol use prior to and during pregnancy was examined, various screening instruments were evaluated for performance, and compared with regular antenatal care routines (“treatment-as-usual”, TAU). The feasibility of implementing them in regular ANC was also evaluated. Specifically, the studies examined:

- what midwives do if they identify women with problems related to alcohol
- how many pregnant women that have a hazardous alcohol consumption in the year prior to pregnancy
- whether a significant number of women continue to drink during pregnancy, and how use habits prior to pregnancy are related to the risk of continued consumption during pregnancy
- whether AUDIT and / or TLFB are better alternatives to use at the ANC in order to identify women who have a hazardous alcohol consumption than the questions posed by the midwives from the ANC medical records
- whether biomarkers are useful for the same purpose
- whether regular ANC midwives can implement AUDIT and TLFB methodology within existing resources and with a minimal training intervention
- whether prevalence of hazardous alcohol use among pregnant women has changed between 1999 and 2004

Since the 1980s, the standard operating procedure within ANC has been to ask the pregnant women about her alcohol consumption, and document the response in the maternal medical records (National Board of Health and Welfare, ANC medical record.). In Stockholm, Malmö and Gothenburg there is also a specialist team to treat pregnant women with serious substance abuse problems. Although alcohol consumption among women in Sweden was increasing, clinical experience indicated that very few pregnant women with alcohol use disorders were referred to the specialist resources. This led to the idea of studying what midwives in Stockholm do to identify women who have a harmful alcohol consumption, how they deal

with the problems and how many women admitted to the ANC that in fact have a harmful alcohol consumption.

Paper I

The first study aimed to examine whether ANC midwives identify women with problems related to alcohol, and if so how they deal with the problems. It also attempted to gain a better understanding of the actions, or lack thereof, of ANC midwives, when encountering women with substance and alcohol abuse related problems; to find out what ANC midwives perceive to be expected of them; what their perceptions of their own actions are; and what actual actions they take. It finally attempted to make an assessment of the ANC midwives' knowledge of resources available to them for dealing with substance abuse during pregnancy.

Paper II

A logical next step was to try and establish how many women among the pregnant women in Stockholm that in fact have a hazardous alcohol consumption (prevalence). In this study AUDIT was tested as a screening instrument on the pregnant women at the ANC (index group) as there was the opportunity for comparison with women in Sweden of the same age group (reference group). Thus, this study examined the prevalence of hazardous or harmful alcohol consumption prior to pregnancy in a consecutive series of Swedish pregnant females. It also obtained some crude measures of alcohol use during pregnancy, and examined the relation between use habits prior and use during pregnancy.

Paper III

The third study was a randomized controlled study to compare treatment as usual with an intensified screening strategy. In this study, women at the ANC were interviewed using AUDIT, TLFB and an extended psychosocial history in order to collect data on hazardous alcohol consumption prior to pregnancy, as well as measures of alcohol consumption during pregnancy. The number of positive findings was compared with the number of positive findings obtained by the ANC midwives following regular antenatal care routine. In the intensified screening group, the performance of the respective methods was compared.

Paper IV

The fourth study examined whether a screening strategy using the AUDIT and TLFB could be implemented under naturalistic conditions and within available resources; and whether it

would improve detection to the extent previously shown in a research context. The midwives at the ANC were randomized into one group that used the screening instruments and another group that continued to give treatment as usual (TAU). The number of positive cases from each group was compared.

Paper V

In order to assess possible trends in women's alcohol use habits over the period during which this series of studies was carried out, the fifth study repeated the examination of self-reported alcohol use habits among pregnant Swedish women 2004 vs.1999.

MATERIAL AND METHODS

Overall procedure and information

This thesis is based on data from ANC midwives in Stockholm County, obtained from pregnant women typically in early pregnancy in conjunction with their first visit (admission) to the ANC clinic, and in some cases in pregnancy week 30. The author of this thesis provided both verbal and written information. The same information was given to the obstetricians in charge of antenatal care and all midwives involved in the studies. The relevant chiefs who gave their written consent to the studies provided access to the antenatal care clinics.

Participants

In **Study I** all of the 47 ANC clinics in Stockholm were approached and 46 agreed to participate in the study. One clinic declined to participate referring to lack of time and heavy workload. Out of 207 forms sent out, 165 were ultimately returned, yielding a response rate of 79%.

In **Study II** 1123 subjects received the questionnaires, 1101 returned them, yielding a drop-out rate of only 2%. The group receiving the questionnaires was, however, a subset of the targeted population. Based on the entire population signing up for parental training (n=1327), drop-out was 15%. Since the survey was anonymous, no further analysis of drop-outs vs. participating subjects could be carried out.

In **Study III** all 156 subjects randomized to TAU accepted, i.e. allowed access to their antenatal care records for subsequent extraction of data. Among 150 subjects randomized to SCREEN, 147 accepted (drop-out: 2 %).

In **Study IV** all 153 subjects randomized to the control condition agreed to participate, i.e. allowed access to their antenatal care records for extracting data. Among 162 subjects randomized to the intervention condition, 139 accepted, yielding a drop-out rate of 14%.

In **Study V** 1258 subjects received the questionnaires, 1148 returned them, yielding a dropout rate of less than 1%.

Questionnaires and instruments

The questionnaire in **Study I** documented midwives' experience of women with problems related to alcohol abuse. A search of the literature did not identify any questionnaire developed for a similar purpose, and a semi-structured questionnaire consisting of 28 questions was therefore developed for this exploratory study. Subjects received a semi-structured questionnaire by regular mail, and were asked to respond anonymously. A stamped

and addressed envelope was included. A cover letter presented the purpose of the study and the questionnaire.

In **Studies II-V**, we used the AUDIT questionnaire to assess alcohol use among pregnant women in Stockholm, focusing on alcohol use prior to, as well as during, pregnancy, and asking whether the former would significantly predict the latter.

During the session of parental training routinely offered to every woman at the ANC-clinic the midwife gave oral information as approved by the ethics committee, and distributed the questionnaires. These were completed during a break and returned at the end of the session. Subjects gave their consent by anonymously returning the forms.

In **Studies III and IV** we used both AUDIT and TLFB. The latter is a systematic face-to-face interview method to obtain a day-by-day account of a person's actual alcohol consumption. It yields valid estimates of a persons drinking for up to 6-12 months. With the exception of a pilot study, TLFB has to our knowledge not previously been used on pregnant populations. The period assessed by TLFB varied depending on the pregnancy week of admission (median 12, range 8-24). Throughout this period, daily consumption was reported in standard glasses and categories of alcohol. All questionnaires were used face-to-face with the women after verbal and written information and were collected after the interview.

Data analysis

In **Study I** the collected data were coded and analysed using EPI INFO 6 (Center for Disease Control, Atlanta). Responses were tabulated in frequency tables and presented with descriptive statistics. Chi-square was used to test for possible differences between groups.

In **Study II** Statistica 6.0 (StatSoft Inc., Tulsa, Oklahoma) was used for all analyses. AUDIT-scores were skewed, and were therefore compared using the non-parametric Wilcoxon U-test. Differences between observed frequencies were compared using two tailed Fischer Exact Test when possible, or else using χ^2 -test with Yates's correction. Multiple logistic maximum-likelihood regression was carried out using the generalized linear-non (GMZ) module to examine the influence of pre-pregnancy AUDIT scores, age and education level for classifying pregnancies into low-risk (no alcohol consumption or consumption maximally once / month) or high-risk (alcohol consumption 2-4 times / month or more often).

In **Study III – V**, Statistica 6.0 (StatSoft Inc., Tulsa, Oklahoma) was used for all analyses. Frequencies were compared using χ^2 -test with Yates's correction.

Ethical considerations

All studies were approved by Stockholm South Human Subjects Ethics Committee, with the following registration numbers: **Study I** and **V** 178/03; **Study II** 288/00; **Study III** 199/00; **Study IV** 25/0.

In **Study I** and **II** and **V** we used anonymous questionnaires. Consent was implied by returning the questionnaire, and identity of individual respondents was not revealed. However, in **Study I** (the survey of midwives' attitudes) it was possible to identify the ANC from which the response had come. This could make it difficult to maintain anonymity if a particular ANC had very few midwives. In order to solve this problem, the origin of the questionnaires was masked as soon as the name of the ANC had been noted, and before the responses were evaluated. It was not noted again. In **Studies II** and **V**, which were anonymous AUDIT surveys among pregnant women, we were not able to establish in individual cases whether or not a women had answered the questionnaire, but did have control over how many questionnaires that were distributed and collected, respectively, so that drop-out rates still could be calculated.

In **Study III**, which was an interview study, the treating midwife acted only as an intermediary between the woman and the research midwife. The woman was informed by the research midwife and then randomized to the interview or control group. She was also informed that her treating midwife had not been told which group she had been randomized to, and was asked whether she was willing to participate in the study. This design meant that the women were never placed in a conflict of loyalty with their midwife thus feeling obliged to participate in the study.

In **Study IV** the midwives were randomized, also those giving information to the pregnant women. During the whole project the midwives showed themselves to be very willing and keen to participate. Written information was distributed to the pregnant women in which it was stated that they were in no way obliged to participate and that the care they were offered would not be affected if they declined to participate. This information was also given to the woman orally by the midwife. An initial concern was whether the women attending the ANC would feel a loyalty towards "their" midwife and towards the group to which she had been randomized, providing an undue influence to participate. This was evaluated in a pilot study, the conclusion of which was that the women did not feel pressured or otherwise reacted negatively; in fact, a few declined participation without problems.

SUMMARY OF FINDINGS

The results from **Study I** indicate that the ANC midwives found it difficult to identify women with hazardous alcohol consumption. They systematically question all women about their alcohol consumption during the past 3 months, on admission at the ANC, and during pregnancy week 32. Despite this the midwives reported definite difficulties in obtaining information, and expressed the desire for a clinically useful screening instrument in order to identify women in the risk zone as early as possible.

The study shows that the midwives need some form of help in order to better approach and handle alcohol related questions. They report meeting women who they think have problems related to substance abuse, but that they feel it is difficult to raise the issue and to start a dialogue with the patient about the nature of the problem and need for help. When they encounter a woman with problems they manage the woman's case themselves and try to help her as best they can, but this most often means no more than worrying throughout the course of the ANC followup. The midwives express the opinion that they should refer women with substance abuse problems to the specialist resource, in Stockholm "Familjesociala Mottagningen", ("Family Social Clinic"), which is open to all women in Stockholm with substance abuse-related problems. However, in 60% of cases, the midwives report actually managing the woman themselves at their own unit.

The results also show that, despite the lack of satisfactory tools, the midwives want to help the women with this type of problem and consider this to be part of their work.

In **Study II** the results indicate there are no difficulties in having pregnant women who attend ANC complete a screening questionnaire about their alcohol consumption. It takes very little time and the women show interest in the questions and are very willing to answer them. Alcohol consumption during pregnancy was shown to be considerably more common among the women in Stockholm than one had previously believed. It emerged that a simple screening instrument highlighted hazardous alcohol consumption in a way that had not previously been obtained at the ANC. The results of **Study II** also showed that that a simple screening instrument such as AUDIT can provide the midwives the help they need in identifying women in the risk zone regarding alcohol consumption. As many as 17 % of the women reported an alcohol consumption during the year before pregnancy at a level that could cause physical or mental problems if they were to continue. Thirty per cent of the women reported some continued alcohol consumption during pregnancy. Interestingly, pre-pregnancy alcohol use

habits and age significantly predicted continued alcohol use during pregnancy. The proportion of women reporting continued use during pregnancy is potentially worrying considering the teratogenic effects of alcohol on the fetus, but in order to interpret its significance, actual quantitative measures of consumption were clearly needed.

In **Study III** interviews were conducted with women admitted at the ANC for the first time because of pregnancy. The results show that despite the fact that the women were not anonymous when screened for alcohol consumption, screening and interviews did not pose any difficulties. Drop-out was low. Participating women expressed considerable interest in the questions and willingness to participate in the study. The results are in accord with those obtained in **Study II** regarding alcohol consumption prior to pregnancy, i.e. 17% hazardous alcohol use as defined by AUDIT scores of 6 or higher. In addition, a total of 26 % of the women reported that they at some time had tried illegal drugs, 7 % during the year prior to pregnancy, and 1% during pregnancy.

For continued consumption during pregnancy, biomarkers were of very little use, as women with pathologically elevated values turned out to be physically ill rather than high consumers of alcohol. Two women had a hazardous alcohol consumption and raised test results but were both identified by the screening questionnaire.

TLFB showed some self-reported alcohol consumption during the first trimester of pregnancy in 87% of the women, i.e. considerably more than the 30% found by cruder measures in Study II. In a vast majority of these cases, however, consumption was marginal. More importantly, the screening procedure identified a group of women (9%) who differed from the others in a worrying way. They screened positive both for hazardous use before pregnancy (AUDIT) and for continued consumption at levels documented to be harmful for the fetus during pregnancy (positive TFLB).

Other indicators support that the group identified in this manner is a high risk population. Thus, these women have a history of seeking contact with psychiatric services more often than others, and both smoke and have used illegal drugs at higher rates than the general pregnant population. Furthermore, they have significantly higher alcohol consumption with regard to number of occasions, amount and binge drinking.

In **Study IV** the screening strategy established through Study III, i.e. combined use of AUDIT and TLFB, was implemented amongst regular midwives at the ANC. Midwives at a large antenatal care clinic were randomized to receive brief training and then implement AUDIT

and TLFB (“intervention”); or to a waiting-list control group continuing to deliver care (“control”). In the intervention-condition, AUDIT was used to collect data about alcohol use during the year preceding pregnancy, and TLFB to assess actual consumption during the first trimester. Data were collected from new admissions over a period of 6 months.

The results show that there is no significant difference in the screening results between ANC midwives and the research midwife. The midwives in fact identified a higher proportion of women who had consumed alcohol up until new registration (95 % compared with 87%). With one day of training the midwives managed to use the screening instruments without difficulty and to identify women in the risk zone. The midwives reported neither problems with the technique nor resistance amongst the patients.

Study V is a repeat of **Study II** to analyse potential developments over the 5 year time span that separates them. The study showed a minimum of technical difficulties with a drop-out rate of less than 1%. Women’s risk drinking prior to pregnancy showed a tendency to increase, which is well in accord with other reports about the development of alcohol consumption in Sweden.

Similar to Study I, this study also showed that a group of the women continued to consume alcohol during pregnancy, but a gratifying result was that among the high consumers the year prior to pregnancy there is a reduction in alcohol consumption during pregnancy.

DISCUSSION OF METHODS, STRENGTHS AND WEAKNESSES

The questionnaire constructed for **Study I** used a mixture of qualitative and quantitative questions to provide insights about the midwives' intentions and actual way of working with women with alcohol related problems. There were no already tested questionnaires available that could provide a satisfactory answer to these questions. The ambition with the study was to generate hypotheses about how midwives work with and view alcohol related problems during pregnancy. No measures of what they actually do were obtained, and even less validated. This is a potential weakness of this study when viewed in isolation. However, its ability to generate hypotheses which have subsequently been possible to support using more stringent quantitative methods justifies in our opinion the methodology chosen.

Several factors influenced the choice when it came to the alcohol screening instruments. The most important of these was to find an instrument that focused not only or even primarily on dependency, but rather on identifying persons with hazardous alcohol consumption. This is important, since the amount of alcohol that can be harmful to the expected child is considerably lower than that which can harm an adult. The main reason for selecting AUDIT over several available instruments that are specifically tested for women was the availability of comparative data from the normal population, which we had access to with AUDIT. The choice of AUDIT over the specialized instruments is not likely to represent any major weakness, since a critical meta-analysis shows almost the same performance between these instruments (84).

One methodological problem present in practically all studies of alcohol and pregnancy is that the amount of alcohol to which the fetus is exposed during pregnancy is usually unspecified. With most screening instruments available, including AUDIT, the information is general, and a global measure is presented rather than amounts consumed on each occasion. The use of TLFB to obtain quantitative consumption data over time is a considerable strength of the present series of studies. Our experience of having used this instrument with pregnant women in regular antenatal care further shows that the TLFB is both feasible to use and very useful in this setting.

A related issue is at the core of properly translating these research findings into clinical practice. Thus, the biological significance of findings from this type of screening is often

questioned. As discussed elsewhere in this thesis, the hazards of low levels of alcohol consumption remain uncertain. Because of that, a prevalence of women screening positive with e.g. T-ACE, TWEAK or AUDIT is difficult to interpret, since their actual alcohol consumption levels remains unknown. The vast majority of women who continue some alcohol use during pregnancy do so at very low levels. However, the TLFB gives much more precise information, and showed that 15% of women consumed amounts of alcohol in early pregnancy which have been clearly shown to increase the risk for various adverse pregnancy outcomes. As disturbing as this result is, establishing this is a major strength of the present project. If conclusions in this matter are to be based on data rather than preconceived notions or emotions, this result alone should put to rest the discussion whether the problem of hazardous alcohol use during pregnancy is real or not.

Subjects for these studies were sampled through the use of consecutive series in regular antenatal care. Drop-out rates were low. The internal validity of the data is therefore likely to be very high. The issue that remains is whether sampling among relatively affluent women in the Stockholm area may yield data with lower external validity, i.e. generalizability for the rest of the country. However, preliminary studies across Sweden indicate that the sampling population on which the present thesis is based led to little if any bias in comparison with the rest of the country.

GENERAL DISCUSSION AND CONCLUSIONS

In this thesis we have found that most of the midwives in Stockholm encounter some women who they believe have alcohol related problems. The midwives worry about these women during their period of maternal care. This results in the contact between the midwife and the pregnant woman that does not fulfill the ambitions or achieve the quality that maternal care has. ANC midwives perceive that they lack tools and support to deal with substance use related problems, and a vast majority expresses that they would like a better method to work with. Knowledge about the harmful effects of alcohol and drugs during pregnancy is necessary but not sufficient in this effort. The major limitation appears to be inability to identify those expecting mothers who are in need of interventions.

Tried and tested screening instruments are available that can be used within primary care and which do not take too much of the staff's time. We hypothesized, and provide data supporting that it may be easier for the staff to have a questionnaire as a point of reference in order to routinely raise these issues with their patients in a natural manner.

Screening among pregnant women and asking them to anonymously report their alcohol consumption before and during pregnancy met with no problems, and the amount of time demanded was very little. The women completed the AUDIT questionnaires easily without assistance.

The extent of the problem was relatively unknown prior to the study. The reasons for this are twofold. First, the information that midwives routinely collect concerning alcohol consumption is not reported to the National Board of Health and Welfare's central registry. Secondly, our results show that even if they were, the measures obtained through the regular ANC routine are simply not valid, and vastly underestimate the use of alcohol both prior and during pregnancy. The present results show that there is a great need for implementing better screening instruments that can actually identify women's drinking habits.

Thus, as many as 17% of pregnant women in Stockholm have a harmful alcohol consumption in the year prior to pregnancy. Furthermore, there were many women who continue to drink alcohol during pregnancy. All women substantially reduced the amount they drank, but most continued some level of consumption during early pregnancy. This result alone came as a shock for many midwives in Stockholm, as they believed that practically all women chose total abstinence during pregnancy because of the information the women received about pregnancy and alcohol.

When results of **Study II** were presented, a common interpretation and response was that it was possible to conduct a study about alcohol habits at the ANC without any great problems only because responses were anonymous. The midwives were considerably more doubtful about whether this type of results might be obtained in a study involving face-to-face contact. It was clear that demonstrating a similar performance of AUDIT and / or other potentially useful instruments under non-anonymous conditions was necessary before any such instrument could be recommended for routine use at the ANC instead of the currently used method.

It is therefore an important result that no problems were experienced in getting the pregnant women to participate in the non-anonymous study of lifestyle and alcohol consumption at the ANC. On the contrary, the women showed great interest in these questions and readily wanted to talk about their own alcohol consumption. Questions often came up that also concerned their husbands' alcohol habits. The finding that as many as 87 - 95% of the women had drunk alcohol to some degree up until pregnancy week 6 was not what we or anyone had expected. We, along with the midwives at the ANC, were convinced that most women were completely abstinent during pregnancy. It is important to bear in mind that a vast majority of these women reported only marginal alcohol consumption. However, a significant minority consumed amounts which have been well established to increase the risk of adverse pregnancy outcomes.

A commonly expressed concern is that screening for alcohol use during pregnancy in itself may lead to worry which in most cases will be unjustified. In this context, it is an important observation that none of the women answered that they were upset or disturbed about accurately reporting how much they had drunk during their pregnancy. On the contrary, they were well aware whether they had drunk alcohol during early pregnancy, and this was what they were worried about. Most reported feeling relieved, partly by being able to tell someone about the amount of alcohol to which they had exposed their child, and partly by having the opportunity to discuss the possible negative consequences for the pregnancy. Despite the fact that the majority of the women had exposed their child to some alcohol during the first six weeks, none of them said that they were more worried after the interview than before.

The concern about inducing unwarranted worry was also common among the midwives at the ANC. They feared that in cases where significant alcohol consumption was reported, this may lead to the women raising the possibility of terminating the pregnancy. This concern turned out to be without foundation. No woman in the study raised this issue, despite many questions about what amount of alcohol that could harm the fetus. These

questions were for the most part left unanswered, but led to a discussion about what can happen when drinking during pregnancy. The women reported that they knew that alcohol was potentially harmful for the child and that they intended to be completely abstinent for the rest of the pregnancy.

Most women in the studies comprising this thesis reported that they substantially reduced the amount of alcohol they usually drank first on receiving a positive result to the pregnancy test, despite the fact that most pregnancies were planned and welcomed. The women were not prepared to take the "risk" of being abstinent needlessly while waiting for menstruation, if it did come. Most were also a little surprised when their pregnancy was confirmed, despite the fact that they had stopped using contraception and had had unprotected sex.

Psychologically, pregnancy seems to begin on admission to ANC. All women reported intending to be totally abstinent after admission, as they regarded this as a true confirmation of their pregnancy. This phenomenon has led us to advocate earliest possible admission at the ANC; perhaps immediately following positive pregnancy test, which for most women coincides with pregnancy week six. This would mean the woman would have the opportunity to receive information as early as possible about the negative effects of alcohol during pregnancy, contributing to many growing children being exposed to lesser amounts of alcohol. Early admission would also give those women who have a spontaneous abortion early during the pregnancy the opportunity to meet a midwife to whom she could naturally turn.

The results discussed so far emerged in studies conducted by a specialist midwife with experience and high motivation to raise these issues. The next question was obviously whether it would be possible to transfer the operating procedures developed in those studies to the everyday work of the ANC. A group of regular ANC midwives were therefore randomized to learn the screening methods. The intervention was minimal: one day, with a minimum of resources. They were instructed in the use of AUDIT and TLFB and also received information about the consequences of alcohol for pregnancy. The remainder of the midwives in the group continued to work according to the usual admission routines, awaiting the same training intervention in the future. All women coming to the ANC for the first time participated in the project, either as an intensified screening group or as the treatment-as-usual comparison group. The participation rate was very high and only a few women declined to participate.

Neither midwives nor patients reported any difficulties with the new way of working. Those women who screened positive were offered a follow-up visit to a psychiatrist, an offer which was received very positively. The women agreed to the follow-up in most cases and they considered that this improved the quality of the maternal care.

When the results were compiled at the end of the project, the midwives had almost identical results to those previously obtained by the specialist midwife. The only reasonable interpretation is that no specialized staff is required to administer the screening, and that these well-established methods work well if used in a clinical setting. An important indicator of the degree of success in implementing the research based strategy in regular ANC work was that when the project was completed and all the screening questionnaires for the research studies had been collected, the midwives that had been randomized to the intensified screening group continued to use the questionnaires in their work. They reported that it had become much easier to raise the issues of alcohol use with the help of the screening instrument, and that their contact with the pregnant women "flowed" in a much more natural way.

The final study of this thesis indicated that the proportion of women with hazardous alcohol consumption the year before pregnancy follows the general trend in Sweden, and is thus increasing. Despite this increase, a pronounced reduction was noted of high consumers during pregnancy. Possible explanations of this phenomenon can be that during the past two years in Sweden there has been an intensive debate about the damaging effects of alcohol on pregnancy and the growing fetus, in part caused by the attention attracted by the present project. There have also been massive campaigns in the daily and weekly press, as well as cinema advertising. There are no studies examining how much these campaigns have influenced the women, but a possible explanation is that pregnant women are sensitive and receptive to information and advice about the expected child's health. However the results of the final study need to be interpreted with caution. Another, much less attractive possibility is that with increased information, it is presently impossible to be pregnant in Sweden and not be aware that alcohol is generally considered to be incompatible with pregnancy. It is possible that some women therefore choose to conceal or underreport their alcohol consumption from the ANC.

SUMMARY IN SWEDISH (svensk sammanfattning)

Alkoholkonsumtion under graviditet : Hur skiljer vi myt från verklighet?

Bakgrund

I Sverige har vi sedan 1930-talet glädjande nog kunnat redovisa sjunkande siffror när det gäller morbiditet och mortalitet för mödrar och barn i samband med graviditet och förlossning. Till stor del får vi tillskriva dessa positiva resultat en allt mer professionell mödravård, som med sin inriktning på kontroll av den normala graviditeten sällar ut graviditeter som avviker medicinskt. När det gäller identifieringen och handläggningen av psykosocial problematik har barnmorskorna på MVC dock särskilda svårigheter då dessa problem sällan är specifika för graviditeten eller föräldrskapet.

I ett historiskt perspektiv har kvinnor haft en restriktiv hållning till alkohol. Kvinnors konsumtion och dryckesmönster har dock ändrats och inte minst bland de unga kvinnorna har konsumtionen ökat. Unga kvinnor debuterar i alkoholkonsumtion runt ca 13 års ålder och väljer att föda sitt första barn när de är i genomsnitt 30 år vilket betyder att de flesta kvinnor har varit alkoholkonsumenter i ca 17 år innan de går in i sin första graviditet.

Att alkohol är fosterskadande är ingen ny kunskap, utan finns beskrivet redan sedan antiken. I början på 1970-talet beskrevs sambandet mellan tillväxthämning och alkoholexponering under graviditet och i en klassisk artikel från 1973 beskrevs av Jones och Smith skadeeffekterna av alkohol på fostret och termen fetalt alkoholsyndrom (FAS) myntades. Sedan dess har utvecklingen gått snabbt och idag finns det ett starkt vetenskapligt stöd för att alkohol stör den invecklade process som pågår under fosterutvecklingen, med risk för påverkan på graviditetsutfall, barnets kognitiva funktioner, beteende och organutveckling. I stort sett alla gravida kvinnor i Sverige kommer i kontakt med MVC som därför får en central roll när det gäller att förebygga eller lindra fosterskador på grund av alkoholbruk. Det är därför viktigt att barnmorskorna har en beredskap och kunskap för dessa frågor idag.

Övergripande syfte med avhandlingen

Syftet med studierna var att kartlägga vad barnmorskorna gör om/när de identifierar kvinnor med problem relaterat till alkohol, samt att med screeningsinstrument pröva möjligheten att tidigt identifiera kvinnor med en riskfylld alkoholkonsumtion och erbjuda preventiva åtgärder. Detta för att förhindra att det väntade barnet exponeras för alkohol. Ytterligare ett syfte var att

implementera en fördjupad screeningsmetodik som hjälp för barnmorskorna att fånga fler positiva fall än sedvanlig handläggning.

De specifika syftena med studierna var:

I att beskriva hur barnmorskorna på mödravården i Stockholm handlar när de tror att patienten missbrukar alkohol eller andra droger samt vilka kunskaper barnmorskan har om graviditet och missbruk och samhällets resurser för missbruk.

II att kartlägga förekomsten av riskfylld alkoholkonsumtion under graviditet hos gravida kvinnor i Stockholm.

III att i en randomiserad studie använda screeningsinstrument i samband med nyinskrivningen på MVC, för att om möjligt förbättra identifieringen av riskfylld alkoholkonsumtion.

IV att undersöka om screening med Alcohol Use Disorders Test (AUDIT) och Timeline Followback (TLFB) kan implementeras som ett arbetssätt bland barnmorskorna på MVC, för att förbättra identifiering av riskfylld alkoholkonsumtion på samma sätt som i studie III.

V att jämföra förekomsten av riskfylld alkoholkonsumtion under graviditet hos gravida kvinnor i Stockholm i studier från 1999 och 2003.

Metoder

För insamling av datamaterial till studie 1 konstruerades en enkät med tjugoåtta strukturerade och ostrukturerade frågor.

I de övriga fyra studierna användes Alcohol Use Disorders Identification Test (AUDIT), som är ett gallrings- och screeningsinstrument inom alkoholområdet, avsett för tidig identifiering av riskfylld eller skadlig alkoholkonsumtion (se appendix 2). I studie 3 och 4 användes dessutom en djupare intervjuteknik enligt "Timeline follow back" (TLFB) som är ett etablerat internationellt skattningsinstrument som mäter alkoholkonsumtionen de senaste tre månaderna, både vad gäller mängd och mönster (se appendix 3). I studie 3 togs blodprov som analyserades med rutinanalyser för leverenzymerna (GGT, ASAT, ALAT), den etablerade alkoholmarkören kolhydratfattigt transferrin (CDT), och röd-blodkroppsvolym (MCV).

Resultat

Studie 1 visar på att barnmorskorna har svårigheter att identifiera kvinnor med en riskfylld alkoholkonsumtion. **Studie 2** visar att det finns enkla screeningsinstrument som skulle kunna ge barnmorskorna den hjälp de behöver för att kunna identifiera kvinnor som är i riskzon när det gäller alkoholkonsumtion. Det finns en tendens till att kvinnor som screenar positiv före graviditet har en större benägenhet att exponera sina foster för alkohol under graviditeten. 17 % av kvinnorna rapporterar att de året före graviditeten har en sådan konsumtion att den skulle kunna orsaka fysiska eller psykiska besvär för dem själva. 30 % av kvinnorna rapporterar alkoholkonsumtion under graviditeten.

I **Studie 3** intervjuas kvinnor som kommer till MVC för nyinskrivning pga. graviditet. Resultatet visar samstämmiga siffror med studie 2 vad gäller alkoholkonsumtion före graviditet. Vad gäller konsumtionen under graviditet visar den att betydligt fler än 30 % (87 %) av kvinnorna hade konsumerat alkohol under den första trimestern. De blodprover som togs för att identifiera skadlig alkoholkonsumtion visade en mycket låg användbarhet, där kvinnor med förhöjda prover visade sig vara fysisk sjuka och inte högkonsumenter av alkohol.

I **studie 4** implementeras metoden bland barnmorskorna på MVC. Resultatet visar att det inte finns någon skillnad i sensitivitet mellan MVC barnmorskorna och forskningsbarnmorskan. Med en dags utbildning för barnmorskorna klarar de utan svårighet av att använda screeningsinstrumenten och identifiera kvinnor i riskzon. **Studie 5** är en upprepning av studie 1 där resultat från studie 1 bekräftas.

Sammanfattningsvis visar resultaten på att:

- nuvarande rutinmässiga screeningmetod vad gäller alkoholkonsumtion före och under graviditet, identifierar inga eller ytterst få kvinnor och barn i riskzon.
- väl etablerade screeningmetoder finns tillgängliga och visar sig detektera betydligt fler än gängse metoder.
- inga omfattande resurstillskott behövs för att genomföra screeningen på MVC.
- patienterna förefaller nöjda med den utökade informationen och screeningen.
- med ett ökat fokus på riskerna med alkohol under graviditet påverkas gravida kvinnor och särskilt högkonsumenter minskar sin konsumtion.

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I dedicate this thesis to all unborn children and their expectant mothers.
Take care of yourselves!

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APPENDIX

Appendix 1 ANC journal

Appendix 2 AUDIT

Appendix 3 TLFB