

Preconception Counseling in the Prevention of Fetal Alcohol Syndrome: A Unique Window of Opportunity.

B Venugopala Rao¹ and Joydeep D Chaudhuri^{2*}

¹Department of Anatomy, Faculty of Medicine, MAHSA University, Kuala Lumpur, Malaysia.

²Department of Medical Physics, Sunnybrook Hospital, 2075 Bayview Avenue, M4N 3M5, Toronto, Canada.

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*For Correspondence

Department of Medical Physics,
Sunnybrook Hospital, 2075 Bayview
Avenue, M4N 3M5, Toronto, Canada.

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ABSTRACT

The role of alcohol in the causation of Fetal Alcohol Syndrome (FAS) has been firmly established. In most cases events leading to its occurrence have been set into motion prior to conception. Alcohol consumption during pregnancy, the sole causative agent of FAS, can therefore be prevented even prior to conception by implementation of preconception counseling (PCC). This review examines issues involved in the implementation of PCC in the prevention of FAS.

INTRODUCTION

"All scientific work is liable to be upset or modified by advancing knowledge. That does not confer upon us a freedom to ignore the knowledge we already have, or to postpone the action it appears to demand at a given time."

Bradford Hill, 1965

While there are obvious advantages of preconception care in the promotion of maternal and fetal health at any gestational period, counseling after the period of organogenesis has significantly less potential of decreasing the incidence of congenital anomalies. This is particularly relevant in the case of Fetal Alcohol Syndrome (FAS), a condition occurring in some children of mothers who have consumed alcohol during pregnancy. As a safe threshold for alcohol consumption during pregnancy has not been demonstrated in human or animal studies, women with the possibility of becoming pregnant are strongly advised to avoid alcohol consumption. However, numerous misconceptions exist regarding alcohol consumption during pregnancy. Thus, preconception counseling (PCC) has a pivotal role to play in the prevention of FAS, though its advantages have yet to be fully utilized as evident by the increasing incidence of FAS. This article reviews the current situation regarding the role of PCC in the prevention of FAS, and suggests interventions to prevent detrimental pregnancy outcomes resulting from maternal alcohol consumption.

FETAL ALCOHOL SYNDROME

Fetal Alcohol Syndrome (FAS), the most common cause of preventable mental retardation in the United States, occurs due to maternal alcohol consumption during pregnancy [1]. FAS has been reported worldwide in all socio-economic and racial groups [2,3,4,5,6]. FAS is included in the broader term Fetal Alcohol Spectrum Disorder (FASD) which describes a wide variety of effects in children prenatally exposed to alcohol. These effects can include impaired postnatal growth, mental retardation, and characteristic craniofacial abnormalities such as a thin vermilion border, smooth philtrum, and short palpebral fissures [7]. They are often associated with neurobehavioral disorders that can lead to mental health problems, learning deficits and inappropriate sexual behavior [8]. These deficiencies often

manifest as social problems such as unemployment and criminal behavior ^[9]. The prevalence of FASD has been reported as 9.1 per 1000 live births in the United States and FAS prevalence as 1–3 per 1000 live births ^[10].

Besides being a medical and social problem, FAS also constitutes a tremendous burden on health care resources. A thorough review by Lupton et al., 2004 estimates that the total expenditure by the state on one person with FAS in the United States is \$2 million, which includes \$1.6 million spent for medical treatment, special education and residential care and \$0.4 million for lost productivity ^[11]. In Canada estimated life time costs for one person with FASD has been estimated at approximately & 0.8 million ^[12].

Rising incidence of female alcoholism and Fetal Alcohol Syndrome

There is a worldwide increase in female alcoholism ^[13,14,15]. However, despite recognition of adverse effects of drinking during pregnancy, the incidence of FAS is on the rise ^[16,17,18]. Studies in the US and Canada have shown that about 10%–25% pregnant women consume alcohol during pregnancy ^[12, 18], with conservative estimates across other countries being approximately 18%–20% ^[19, 20]. Health warnings to avoid alcohol consumption in sexually active women not using birth control measures are frequently disregarded ^[21].

Moreover, majority of women tend to reduce alcohol consumption only when they recognize that they are pregnant ^[22, 23], with the reported mean time for recognition of pregnancy being 31–35 days ^[12, 18, 24]. This is significant finding since pregnancy; including the time period that the woman is not aware that she is pregnant is the period of vigorous organogenesis as demonstrated in studies by Streissguth et al., 1980, who have found a stronger negative effect induced by drinking during early pregnancy as compared to drinking in the fifth month of pregnancy ^[8]. This, coupled with the overall increasing incidence of drinking by women in the childbearing period has been identified as the major cause of increased physical and mental deficits in FAS ^[25].

Drinking Patterns in Women

Various definitions of drinking patterns exist in literature and each has its own merits and demerits. For consistency, one standard drink is defined as 341 ml (12 oz) of beer, cooler or cider, 142 ml (5 oz) of table wine (12% alcohol) or 43 ml (1.5 oz) of spirits ^[12]. For this review, in females mild drinking is defined as the consumption of less than 1 drink per week and moderate drinking as 1–8 drinks per week ^[26]. Women are considered heavy drinkers when consuming on an average nine or more drinks per week or participating in binge drinking ^[27]. Binge drinking in accordance with the National Institute of Alcohol Abuse and Alcoholism (NIAAA) is defined as a pattern of drinking alcohol that increases the Blood Alcohol Concentration (BAC) to about 0.08 gram-percent or above. For the typical adult female this corresponds to consuming 4 or more drinks in females in a 2 hour period ^[28].

UNINTENDED PREGNANCIES AND FAS

Unintended pregnancies are a cause of concern in relation to both maternal and fetal well-being in general and FAS in particular. An unintended pregnancy is defined as a pregnancy that was sooner than desired or was not desired at all ^[29]. In the United States about 40–50% pregnancies on average are unintended ^[30] with the number rising to above 80% in lower socioeconomic groups ^[31]. Similar reports are also available from other countries ^[32].

Typically the greatest percentages of unintended pregnancies occur in women younger than 30 years, with the highest incidence in women between the ages of 15 and 19 years ^[33]. Unintended pregnancy has also been found to be particularly high in women in the lower socioeconomic group with minimal levels of education ^[34].

Further, studies have shown that women with unintended pregnancies constitute one of the highest risk groups for fetal harm due to alcohol and other illicit drug use during pregnancy ^[35], and have a greater occurrence of binge drinking and alcohol dependence ^[36]. Furthermore, mothers with unplanned pregnancy are less likely to receive preconception care and regular prenatal examinations ^[37, 38]. Moreover, binge drinking and heavy drinking is associated with a higher risk of unprotected sexual activity and therefore unplanned pregnancies ^[39, 40]. Thus, women with unplanned pregnancies constitute a high-risk group likely to use alcohol during pregnancy and give birth to children with FAS.

PRECONCEPTION CARE AND PRECONCEPTION COUNSELING

Preconception care has been defined as specialized pre-pregnancy care and examination of women in the child-bearing age that focuses on issues not typically addressed during a routine medical examination, and is specific to ensuring an optimal pregnancy outcome for both the mother and the child ^[41]. It involves the systematic identification of maternal conditions that can adversely affect reproductive health outcomes and maybe amenable to treatment ^[42].

Preconception care includes three main components namely risk assessment, education and health promotion, and medical and psychosocial intervention [43]. Risk assessment one of the very crucial aspects of preconception care involves the identification and quantification of the risk resulting from a specific use of a substance or the occurrence of an event, taking into account the possible harmful effects on maternal and fetal outcomes. It typically involves quantification of risk and requires the establishment of accurate dose-effect and dose-response relationships in likely target individuals. Thus, it involves a multidisciplinary approach to issues related to maternal and fetal wellbeing. Preconception counseling (PCC) is a critical component of preconception care and includes advice on appropriate medical care and behavior for women of childbearing age prior to conception to optimize pregnancy outcomes [41]. It offers health care providers an opportunity to advise patients on numerous behavioral and lifestyle changes ranging from exercise and weight control to the use of medications and avoidance of illicit drugs.

The effectiveness of PCC has been demonstrated in reports of successful reduction of congenital anomalies associated with gestational diabetes [44], in prevention of neural tube defects by folic acid supplementation [45], and avoidance of fetal damage associated with epilepsy medication [46]. However, preconception care has traditionally focused on women who have a chronic medical problem and a history of poor outcome in a previous pregnancy [47]. Despite recognition of the benefits of preconception health care in all women of reproductive age, total implementation of this form of preventive medicine is still currently lacking [48]. However, the importance of this concept of health care in the promotion of maternal and fetal health is being increasingly recognized and guidelines and recommendations are currently being developed [47].

IMPORTANCE OF PCC IN PREVENTION OF FAS:

Screening and subsequent counseling before conception about the harmful effects of drinking during pregnancy creates the opportunity to identify and reduce the occurrence of FAS. Numerous efforts worldwide and particularly in North America have been undertaken to inform women of the harmful effects of drinking during pregnancy. However, they have met with limited success as judged by the increasing incidence of FAS.

Women of child-bearing age visit their physician an average of three times per year and each visit presents opportunities to deliver preconception care [49], and to thus minimize and even eliminate fetal risk due to drinking during pregnancy. In a large Canadian study, Tough et al., 2006 report that prior to pregnancy recognition, 13.5% of women surveyed reported heavy drinking including binge drinking while 36.4% reported moderate drinking. Also most women contemplating pregnancy did not abstain from alcohol or reduce consumption while trying to conceive [12]. Further, though most women recognize that alcohol consumption during pregnancy is harmful to the developing fetus, many appear not to be fully and accurately informed about the detrimental effects of alcohol consumption prior to pregnancy recognition. It is also interesting that the attitudes of women towards and actions concerning alcohol consumption during pregnancy are independent of their knowledge about the subject [12, 22].

This is particularly important as the immediate post-conceptual period is a critical period for healthy development of the fetus and most congenital anomalies can be traced to this period of organogenesis. By the end of the eighth week after conception and by the end of the first trimester any major structural anomalies of the forming fetus have already developed [50]. Ethanol exposure to embryos in utero during early gestation has been demonstrated to result in craniofacial deformities and neural abnormalities [51, 52] in mice, and muscular abnormalities in chicks [53]. As the average time between conception and pregnancy recognition has been reported to be approximately 31–35 days [12, 18, 24], there is sufficient time for alcohol to potentially adversely affect fetal development. Further, many women have their first prenatal check-up only at eight weeks of pregnancy or later [54], when the opportunity for initiation for maximally effective measures for prevention of FAS are lost.

Further, since a large majority of family physicians discuss birth control measures with women in the child-bearing age, this represents a useful forum to address problems of drinking during pregnancy. Thus, with specific emphasis on the risks of alcohol use when planning a pregnancy, preconception counseling strategies in women provide an opportunity to reduce the risk of occurrence of FAS.

CURRENT SCENARIO OF PCC IN GENERAL AND FAS IN PARTICULAR

A healthy baby and a healthy mother are valued hopes and dreams of all families and cultural heritages [55]. Towards this goal, it must be emphasized that PCC is not a conceptual idea, but an achievable target to address the role of behavioral changes in women of child-bearing age since more than 50% of women aged 18–39 obtain preventive health services in general in any given year [50].

The benefits of preconception health care have long been established, and there is strong evidence to suggest that preconception care can modify behavioral, medical and other health risk factors known to negatively impact pregnancy outcomes. However, the manifold advantages of PCC are currently not being maximally utilized by health care providers.

Health care providers, however, recognize the importance of preconception care and its positive impact on pregnancy outcomes, but only less than a quarter agree that it has a high priority in their work schedule. The common reasons for inability to provide adequate PCC include a lack of time, absence of adequate reimbursement incentives ^[41] and a perceived lack of patient interest and awareness ^[56].

Recent estimates suggest that approximately one third of pregnant women are routinely assessed for alcohol use even during routine prenatal care ^[57]. Studies in the United States ^[58] and the United Kingdom ^[56] show that very few of family physicians actually counseled women about preconception care even though they were in a position to do so in a great majority of situations. In a Canadian study, less than half of family physicians actually discussed alcohol use with women of child-bearing age before conception ^[59], whereupon most physicians reported discussing birth control measures with their women patients, providing an opportunity to discuss ways in which alcohol consumption could adversely affect pregnancy and birth outcomes. However, it is significant that alcohol use was rarely discussed by a high proportion of obstetricians and by an even higher proportion of family practitioners ^[47].

The majority of doctors (88.5%) felt that enquiries about alcohol consumption were very important during preconception care ^[41]. Residents in an American inner-city public hospital reported that though they were favorable towards preconception counseling, they demonstrated lower levels of proficiency in knowledge and management decision skills regarding preconception care ^[60], and deficiencies in specific areas of addiction and substance abuse ^[56]. Moreover, even during discussions of alcohol use during preconception period, the recommendations were often inconsistent and often not current. Discrepancies also existed in the interpretation of mild and moderate alcohol consumption among health care providers and resulted in a lack of clarity and consistency in advice for patients both before and during pregnancy ^[61].

Moreover, women in the child-bearing age often do not often use services offered within the framework of preconception care. In fact, an American study showed that only 17.3% patients frequently present for preconception care, while a third (32.3%) rarely presented for preconception care and counseling ^[41].

In women attending precounseling, common barriers include patient denial of a drinking problem and also popular myths contradicting the harmful effects of drinking during pregnancy. Further, specific issues compounding the problems of management of FAS include an unclear definition of when pregnancy began. Thus, the accuracy of any overall measure of alcohol consumption during pregnancy is often dependent on the woman's interpretation of when pregnancy began and is also influenced by recall bias. In addition, accurate assessments of alcohol use are often hampered by the social stigma associated with alcohol consumption and different methods of assessment of alcohol intake. Hence, women often tend to underreport or deny their drinking habits ^[62]. Further complicating matters are the widespread prodrinking messages that women of reproductive age receive from the media and popular culture ^[63].

In summary, barriers to successful implementation of PCC in FAS are similar to the categorical reasons for inconsistency in preconception care delivery summarized by Moos, 2004 ^[50]. These include a lack of knowledge regarding the incidence of unintended pregnancy, inadequate provider education, lack of confidence that preconceptional health counseling is valuable, and the belief that women in the child-bearing period know how to seek medical care appropriate to their needs, and concerns over absence of reimbursement coverage for preconceptional visits.

DISCUSSION

The risk perception of future parents regarding alcohol consumption in early pregnancy is generally low. It is disappointing that there has been such a slow reaction to an effective means of preventing FAS, since the timing of PCC is crucial, and universal prevention efforts have only been moderately effective. Thus intervention as a part of PCC should be regarded by health care providers as an excellent opportunity to reach women before they conceive.

Alcohol freely crosses the placenta and the BAC of the fetus is consistent with maternal BAC ^[64]. Considering the link between unplanned pregnancy, unprotected sex and alcohol consumption, PCC is critical in ensuring a healthy mother and child. This is imperative given that even women who abstain from drinking until the third trimester significantly reduce the likelihood of an adverse birth outcome ^[65].

However, despite this available knowledge, prenatal care has met with limited success in improving pregnancy outcomes. The prime reason being that many of the pathophysiological processes leading to adverse birth outcomes may have had their onset during or just after conception. Hence, by the time prenatal care is initiated it may be too late to alter the course or outcome of the pregnancy. This has highlighted the importance of PCC as a tool towards the improvement of maternal and fetal well-being. A key factor in the success of PCC is the accurate assessment of preconceptional risks through examination of the woman's reproductive, family and medical history, review of the woman's social concerns, drug or alcohol abuse and discussion and enquiry about birth control measures. This requires

absolute trust between the woman and her health care provider, and entails exchange of meaningful information and clarification of misconceptions regarding alcohol use during pregnancy. Thus, obtaining an accurate history of alcohol consumption and tailoring recommendations based on that increases the likelihood of reduction in the incidence of FAS. In 2004, the US Preventive Services Task Force recommended screening and counseling intervention in primary care settings to reduce alcohol misuse in adults including pregnant women [66].

Further, current research strongly suggests that active involvement of health care staff and the design of effective management systems could reduce the burden of PCC. However, research is needed to determine the best way to integrate PCC as a component of family medicine to reduce alcohol exposed pregnancies and decrease the incidence of FAS. In the succeeding sections we aim to discuss barriers to the use of PCC and provide a broad framework for the increased use of effective PCC in the prevention of FAS.

Identification of high-risk groups

Maximal utilization of health care resources in the prevention of FAS involves identification of women in the high-risk group who might indulge in drinking during pregnancy and who require PCC. The commonly identified risk factors include history of smoking, alcohol and drug use, physical or sexual abuse, loss of children to adoptive care, major depressive or post traumatic disorders, heavy drinking by male partner or any family member [66]. Identification of these women before they conceive pregnancy will enable health care providers to initiate vigorous prevention measures such as counseling for drinking problems, referral to specialized care and measures to encourage prevention of pregnancy until problems of alcohol abuse are resolved.

A common complaint with health care providers in the effective implementation of PCC is a lack of adequate time for proper history taking and subsequent identification of high-risk behavior. A self-administered screening questionnaire addressing specific behavioral issues such as alcohol consumption could be an efficient tool to incorporate in health care settings to reduce time spent in history taking. This method of identification of high-risk behavior has been demonstrated in a recent study of close to 200 couples in The Netherlands [67]. A significant finding in this study was the fact that self-reported alcohol and tobacco use was accurate, as verified by subsequent questioning [67]. Such questionnaires reduce time during history taking and also require couples to reflect on their health and lifestyle. Further, these questionnaires enable the identification of relevant topics and create more opportunities to educate women on the perils of drinking during and after conception. Moreover, the incorporation of such questionnaires into patients medical history charts lead to improved documentation of preconception care [68]. However, it needs to be emphasized that the above screening tools for alcohol use do not replace systematic clinical interviewing, since they are not diagnostically accurate and merely indicate that a woman is at risk for alcohol related problems.

Assessment of alcohol consumption

The assessment of alcohol consumption in a woman is a critical step in deciding the nature of PCC required. The frequency of alcohol consumption can be assessed by the number of times per week the woman has an alcoholic drink, while the quantity of alcohol consumed can be assessed by the usual number of drinks consumed on one occasion.

During the past decades several simple questionnaires that identify problem drinkers with high sensitivity and specificity have been validated [69]. Enquiries about alcohol consumption should be followed up with specific questions about heavy and binge drinking. While physicians often use liver function tests such as gamma glutamyltransferase (GGT) and aspartate aminotransferase to obtain evidence of alcohol abuse they are less sensitive and specific than screening tools for identifying women at risk [70,71]. Screening tools such as TWEAK (Tolerance, Worry, Eye-opener, Amnesia, Cut down) and the T-ACE (Tolerance, Annoyance, Cutdown and Eye opener) are useful [66]. Screening tests are recommended since they focus on indirect effects of drinking and may reduce denial in women [72]. A particularly useful tool is the Alcohol Use Disorder Identification Test (AUDIT), which detects early stages of problem drinking and focuses on drinking patterns during the past year. Since in this test patients complete the scale on their own, it enables the physician to use the completed form to frame follow up questions [73]. Due to a desire for anonymity, some pregnant women, particularly heavy drinkers, are more likely to reliably report accurate alcohol use in a computerized or paper form rather than direct face-to-face interview [74].

One striking finding, however, is that the clinical documentation of perceived level of problem drinking is less than a 25% due to inconsistent definitions of problem drinking [75]. This suggests that future studies addressing clinician recognition and intervention should address accurate documentation of alcohol disorders in the medical record.

Further, screening for alcohol consumption in the child-bearing ages has certain advantages. Even assessment of alcohol consumption alone seems to reduce alcohol consumption. Women asked about their alcohol use at different time points within a year reduced consumption by about 20% [76]. Moreover, it has been shown that even screening for alcohol use maybe a factor related to reduction of drinking [77].

Further, because of concerns of underreporting of alcohol consumption, many investigators also interview collateral informants such as spouse or partner [78].

Model of preconception care for prevention of FAS

Considering the diversity of women and the varied settings that impact delivery of preconception care in the reproductive age a single effective classic model of preconception care for prevention of FAS seems highly unlikely. Preconception care should therefore be tailored to meet the needs of individual women, taking into consideration socioeconomic, cultural and linguistic issues. Further, PCC should be a dynamic process that spans across different life stages in the same woman. Such variations however place restrictions on how interventions can and should be carried out.

The model should address in an effective and comprehensive manner each individual participant's needs and objectives to plan for further monitoring, service coordination, anticipatory guidance, health education and advocacy [42]. Recent studies have recommended offering PCC opportunistically to incorporate the information offered relevant to preconception care into routine well-woman visits by embedding issues regarding alcohol use in the broader context of health counseling in PCC [50]. The ideal model for the delivery of PCC would be the "one-stop shopping" propagated by Tanney and Lowenstein, 1997, in which physicians, nurse managers, psychotherapists and social workers work as a part of multidisciplinary team when caring for women with problems with alcohol abuse [79]. A more recent approach to problem drinking is known as "stepped care" and applies ideas derived from other areas of health care to the management of problems related to alcohol abuse [80].

Intervention measures

Intervention measures have been shown to successfully reduce alcohol use among female drinkers. Identification of women with drinking problems requires subsequent coordination with other services for individualized care. They can be a single very brief five minute session to multiple brief sessions. The content of these sessions typically includes advice, feedback, goal setting and additional contacts as necessary [66]. Particularly useful is motivational interviewing (MI) a counseling model that has also been successful in reducing alcohol use. Motivational interviewing is a relatively new cognitive-behavioral technique "that aims to help patients identify and change behaviors that maybe be placing them at risk of developing health problems or preventing optimal management of a chronic condition" [81]. This is a supportive talk therapy to enable the patient to analyze her problems and implement corrective behavior. It is of great consequence s that even brief sessions of motivational interviewing and more than one encounter increases the likelihood of significant benefit [82]. This combination of psychosocial and coordination between the services, supplemented with written patient educational material, has also been shown to also been effective in increasing contraceptive use in female drinkers who could become pregnant [83].

Education and training of caregivers in the practice of PCC

Effective implementation of PCC depends on the efficient training of personnel involved in its implementation. Most medical schools and continuing medical education programs worldwide offer minimal training in alcohol counseling. A study carried out at The University of Toronto Medical School revealed that there is little education devoted to the prevention and management of female alcoholism in general, and FAS in particular resulting in many myths and misconceptions [84]. Hence residency programs particularly in the specialties that provide primary care, namely Internal Medicine, Family medicine and Obstetrics and Gynecology, should ensure that their training prepares them to provide comprehensive preventive care specialties that emphasize preconception care and PCC. Clinical training should include reminders that significant numbers of risky drinkers remain unscreened or escape detection via questionnaires since their sensitivity rarely exceeds 85% and clinicians must remain alert to clinical cues related to hazardous or problem drinking [75]. However, simple educational efforts, training and encouraging health care providers to provide PCC might not be enough to ensure integration of skills in clinical practice. Health care practitioners need specific training in practical strategies that will encourage abstinence and participation in alcohol treatment program when necessary. Thus, medical training should also focus on proficiencies in communication skills and preventive and psychosocial counseling.

Nurse educators play an equally important role in PCC and they are interested in learning about PCC. A review of nursing texts reveals no emphasis on preconceptional health promotion, and a federal report on nurse practitioner primary curriculum reveals no emphasis on woman prepregnancy health status and pregnancy outcomes. Hence, paucity of information in basic training programs should be supplemented through continuing education. Further, efforts must be aimed at providing more education about screening and prevention of alcohol abuse in pregnancy to nurses in a supportive and non judgmental manner. Thus, the goal for all nurses should be to increase awareness among their female child-bearing age patients about the importance of planning a pregnancy and preventing birth defects in their infants [85].

CONCLUSION

The increase of female alcohol consumption is reflected as a corresponding increase in the incidence of FAS. This is since women can negatively affect fetal development by consuming alcohol after conception before realizing that they are pregnant, as well as throughout the duration of pregnancy. Hence, women should be made aware that early pregnancy is a particularly critical period for fetal development^[86] and of the concepts and potential benefits of PCC to pregnancy outcomes. Further studies have shown that women who do not intend to get pregnant are less likely to go for PCC, highlighting the importance of changing the behavior of such women.

Preconception care is also an important stage for health care givers and policy makers for planning of fetal wellbeing. Towards the goal of preconception care, the June 2005 National Summit on Preconception Care recognized that an amalgamation of local, state and national resources would provide important information related to the ability of current public health systems to address preconception care needs, as well as allow for the description of innovative models for delivery of such services^[87]. Further, the Health and Human Services has established a Health People 2010 goal to increase the number of pregnant women who report abstinence from alcohol use during the past month from a baseline rate in 1996–1997 of 86% to 94% by 2010^[66].

However, considerable work is necessary to implement screening and intervention measures for alcohol abuse as part of routine health care for women in the child-bearing period, and further research is required on effective strategies and supports for adoption of these services by physicians and health care planners. While brief interventions may be easily incorporated into routine primary care, effective management of serious alcohol abuse problems depends on multiple contacts over time. Preconception health promotion, therefore, should focus on general awareness among the public regarding reproductive health and risks to childbearing. Consistent with the conceptual framework of 2005 Bangkok charter on health promotion preconception care should be seen as a program for the future, a development agenda aimed at overall health of the family^[88]. This requires the need to raise the awareness of PCC by consumers, health care providers, third party carriers and policy makers.

Thus, the window of opportunity offered by PCC needs to be widened to include the prepregnancy period as the starting point for maximum beneficial effects on reproductive outcomes^[50].

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