

Australian Federal Parliament

Senate Committee Inquiry

Effective approaches to prevention, diagnosis and support for Fetal Alcohol Spectrum Disorders

A Submission from the
National Drug Research Institute

Dr Nyanda McBride and Naomi Ward
October 2019

Contact Details

Dr Nyanda McBride
National Drug Research Institute
Curtin University

Suggested Citation

McBride, N. and Ward, N. (2019). National Drug Research Institute's submission to the Australian Federal Parliament Senate Committee Inquiry into effective approaches to prevention, diagnosis and support for Fetal Alcohol Spectrum Disorders. National Drug Research Institute, Curtin University; Perth.



*The National Drug Research Institute appreciates the opportunity to provide a submission on this critical inquiry. In this submission, we focus on Strategies to Prevent FASD, which is most relevant to our research. **This written submission address issues associated with terms of references a. b. c and p.***

For more information on the National Drug Research Institute and the research it has completed, and continues to undertake, on FASD, visit <http://ndri.curtin.edu.au/> and, in particular, the [Enhancing Primary Prevention and Early Intervention](#) Research Priority Area.

Inquiry

Given that the FASD research field is developing, and that new research-generated knowledge is still emerging, it is recommended that any strategies/actions developed as part of this Inquiry be reviewed and modified regularly to incorporate new research findings.

Strategies to Prevent FASD

Prevention of FASD is still relatively new in Australia, particularly prevention that has proof of behavioural impact. To create prevention programs and policies that have the greatest likelihood of behavioural effect, development should include: relevant systematic reviews; relevant theories; input from experts with knowledge of the scientific/grey literature and/or expertise delivering programs to women/families; input from women and other intervention target groups; pilot testing with target groups and setting implementers; and efficacy testing using rigorous research design [1].

There is still a lot of work that needs to be done across sectors to embed prevention within families and communities. To ensure prevention approaches are comprehensive, the strategy should: 1) conduct action aligned with community prevention models such as The Prevention Framework (see Appendix 1); and 2) ensure individual interventions and policies within 1) have high level proof of behavioural impact (see Appendix 2).

Another consideration for FASD prevention is the prevention paradox. The prevention paradox comes into play when more harm may be prevented by targeting a larger though lower consuming proportion of the population [2]. A review of several FASD prevalence studies reports that a higher proportion of the population is affected by less severe FASD outcomes than those affected by FAS. If this pattern also proves to be in play in Australia then it has implications for policy and funding recommendations as it introduces the issue of the prevention paradox. The interplay between this and future research on the impact of low and moderate use of alcohol during pregnancy is an issue that will need clarification for Australian policy.

Recent Australian birth figures report that the majority of births in Australia were to women aged between 24 and 37 years [3]. The 2016 National Drug Strategy Household Survey reported an increase in the proportion of women in this same age group, 25-39 years, who drink to risky levels at least monthly (defined as four or more standard drinks per occasion) from 2013 (20.95%) to 2016 (24.05%) [4]. This information, along with earlier studies of the relatively high proportion of Australian pregnant women who consume alcohol [5, 6] over recommended levels [7], suggests the need for more nuanced preventative formative research with women/families in this category to ensure that policy and programs are behaviourally effective [8] (see Appendix 3).

A rapid review of the scientific literature indicates that Australian women who continue to drink alcohol during pregnancy:

- are older;
- have higher income;

have higher education;
 have higher socio-economic status;
 drink prior to pregnancy;
 drink during previous pregnancy;
 smoke and use other drugs;
 live in a rural and remote area.

[5, 8-12] .

These factors may provide important foci for future prevention. Additional factors from research with pregnant women (see Appendix 3) [8] indicate other possible prevention strategies by drinking group. In this study, risk level is defined by the Australian Guidelines to reduce risk from drinking alcohol (8). Introduced in March 2009, Guideline 4, which pertains to pregnant and breastfeeding women, states that:

Pregnant and breastfeeding women should note that not drinking is the safest option for the developing fetus and young babies who are breastfed. However, the level of risk is likely to be low if a woman has consumed only small amounts of alcohol (such as one or two drinks per week) before she knew she was pregnant or during pregnancy [7].

Therefore, risky consumption was defined as more than two drinks per week, low risk consumption was defined as one or two drinks per week; and no current risk was defined at discontinued consumption once pregnancy was recognised. The proportion of women from the study who were defined as having no current risk (now non-drinkers) was (33.1%), low risk (45.8%) and risky (21.1%).

Women who drink to *high risk* levels during pregnancy

Characteristics	Potential Intervention Strategies
Government health care card	Prevention programs combining alcohol and other drugs. Intensive individually targeted programs. Prevention programs combining alcohol and effective use of contraception. Complex mix of interventions. Intervention throughout childbearing years. Provision of up to date and detailed information about alcohol and FASD – including lifelong cognitive and behavioural impact on child, confounding factors, social and economic costs.
Asked by health professional about drinking level during prenatal visits	
Single	
Negative comment about their drinking from their partner	
Use of other drugs – tobacco and cannabis	
Have an unsupportive partner	
Have a planned pregnancy	
Work fulltime	Research
Consumed alcohol in previous pregnancy	
Consumed alcohol during preconception	

Believe that low level alcohol consumption acceptable during pregnancy	Qualitative formative intervention research to identify intervention delivery methods, components, strategies and content that resonate with this group of women. Replication of formative intervention study in other jurisdictions and with other groups of women.
Believe no harm to earlier children with alcohol use during pregnancy, and unlikely this time	

*Women who drink to **low risk** levels during pregnancy*

Characteristics	Potential Intervention Strategies
More likely to consume wine	Promote alternative to alcohol use in social situations.
Consumed alcohol in previous pregnancy	
Consumed alcohol during preconception	Intensive individually targeted programs.
Believe that low level alcohol consumption acceptable during pregnancy	Specific point of sale, warning labels or taxation strategies.
Believe no harm to earlier children with alcohol use during pregnancy, and unlikely this time	Social support programs. Target partners, family and friends to extend social support for reduced use.
Identified benefits of drinking during pregnancy particularly socialising	Provision of up to date and detailed information about alcohol and FASD – including lifelong cognitive and behavioural impact on child, confounding factors, social and economic costs.
Higher level of education	
	Research
	Qualitative formative intervention research to identify intervention strategies that would resonate with this group of women. Replication of formative intervention study in other jurisdictions and with other groups of women.

*Women who **cease alcohol consumption** on confirmation of pregnancy*

Characteristics	Potential Intervention Strategies
Full time home duties	Potentially open to preconception alcohol interventions. Specific point of sale, warning labels or taxation strategies (child bearing age, contemplation stage). Social support programs. Target partners, family and friends to extend social support for reduced use.
Less risky behaviours	
	Research

	Qualitative formative intervention research to identify issues and traits pertinent to this group with possible use in wider prevention activity.
	Replication of formative intervention study in other jurisdictions and with other groups of women.

Stigma and FASD

Maternal guilt and fear associated with FASD are necessary considerations for policy and practice. This issue largely stems from the “blame” approach that takes women’s alcohol use out of the cultural and social context in which it occurs and may result in historical guilt of mothers who have at some time in the past had an alcohol-exposed pregnancy, whether inside or outside past policy guidelines, which affected their child [13], or possible terminations by women who have drunk alcohol during early pregnancy when the pregnancy was not yet recognised. Additionally, consideration needs to be given to the possible stigmatisation of mothers, particularly as the name of the syndrome is directly related to the actions of the mother. Campaigns that raise awareness of risks of alcohol consumption during pregnancy also need to consider the creation of unnecessary anxiety or the “worried well,” particularly given the current dearth of information about low level use during pregnancy.

It is interesting to note that an international conference on FAS held a plenary session with mothers of children born with FAS. The presenters unanimously spoke of the need for strong messages for women not to use alcohol while pregnant, that the stigma and shame fall to the background during a life time of supporting a child with FAS [14]. These women were from a range of countries and noted the need for early and ongoing intervention to reduce the occurrence and impact of alcohol use during pregnancy. Early formative work with Australian women also indicated that contemporary women want a clear understanding of current research to guide their decisions about alcohol during pregnancy (see Appendix 3), and that “scare tactic” can be effective. Women also overwhelmingly want their health professional to inform them about drinking during pregnancy and FASD, however, research suggests that Australian General Practitioners (GPs) in particular are hesitant to do so [15] due to the perceived sensitivity of the issue. This reluctance among the health profession to provide appropriate advice [15] and information indicates the need for effective training so the needs of women and their families are met.

Possible actions to reduce stigma

- Remove any possibility of future legal impact.
- Identify that current and past policy supports various levels of alcohol use during pregnancy (community issue). Note that current policy still allows for low risk of two drinks per week during pregnancy.
- Identify and include biological fathers and live in partner in policy (family issue).
- Train health professionals to provide brief interventions, which includes discussions about

possible future impacts around stigma. Also identify that some health professionals do not discuss or advocate alcohol cessation during pregnancy [15].

- Identify and address Australia's high rate of alcohol use. This has an impact on community acceptance of alcohol use during preconception and pregnancy, and social facilitation of pregnant women's alcohol use by family and friends.
- Conduct formative research with women and their partners to incorporate their opinions and experiences in policy and interventions to reduce stigma.
- Introduce concept and reduction strategies in school-based alcohol education programs (for example, as done in the School Health and Alcohol Harm Reduction Project, see <http://ndri.curtin.edu.au/research/shahrp/index.cfm>) [16].

Psychosocial Factors Linked to Alcohol Exposed Pregnancies

A recent systematic literature review by NDRI (in final preparation) has identified psycho-social factors which may increase the risk of alcohol consumption during pregnancy for women and therefore, the risk of FASD. This systematic review provided replicated findings that anxiety in pregnancy is associated with a higher risk of alcohol consumption. Two studies reported an increase risk of alcohol consumption with general anxiety [17] and anxiety associated with concerns of having a child with a disability [18]. The role that anxiety plays as a risk factor for continued alcohol consumption during pregnancy and therefore FASD is consistent with the findings of other studies that have explored the relationships between alcohol use and anxiety in the context of other health outcomes for the child [19-21]. Research in this area would be enhanced by consistent use of diagnostic systems and psychometrics.

Depression was associated with alcohol consumption during pregnancy. Continued alcohol use in pregnancy was strongly associated with high ratings of depression symptoms [22], as was self-rating of sadness by women [23] and high scores on the Edinburgh postnatal Depression scale [17]. This is consistent with other studies [24]. As with the area of anxiety research in this area would be further supported by clear definitions and comparable measures of depression.

There is strong evidence that abuse during pregnancy is associated with continued or increased alcohol use during pregnancy, with three studies in this review contributing to this finding. In particular, increased alcohol use during pregnancy was associated with abuse during pregnancy [25]; physical abuse; intimate partner violence; and physical abuse in the past year [22]. One study reported that a prior history of abuse, definition unknown, was predictive of binge drinking during pregnancy [26]. Future studies in the area of abuse and alcohol use would benefit by distinguishing between abuse type and occurrence (prior to or during pregnancy). Studies tended into aggregate abuse category which did not lend itself for greater interpretation. While less clear about the role of historical abuse, domestic violence is emerging as a predictive factor for alcohol consumption in pregnancy [27].

The research studies in this review were consistent around the role of drinking behaviours of others in a woman's social network. Several studies demonstrated that women were at greater risk of continued and/or binge drinking where drinking alcohol problems in the family were reported [28]; partners or friends drinking or using drugs [29]; problematic drinking by the father [30]; problematic drinking by the brother [30]; and problematic drinking by the mother's

father [31]. These repeated findings provide strong evidence that psycho-education on the risks of alcohol consumption during pregnancy is as important for partners and family as it is for women.

Using the psycho-social risk factors identified in this review, it should be possible to profile women at high-risk of alcohol consumption. Health professionals can use these factors to identify and support vulnerable women in pregnancy. Further targeted intervention programs to address stressors and mental health factors is essential as a way helping women to reduce or cease alcohol consumption in pregnancy.

Fathers Role in Alcohol Exposed Pregnancies

A recent systematic review of the role of fathers in alcohol exposed pregnancies [32] (see Appendix 4) concluded that it is important to recognise decisions about alcohol use during preconception and pregnancy are not the sole responsibility of women but occur within the context of the home and the broader social environment, and therefore require more complex policy to assist in reducing alcohol-exposed pregnancies and increasing the potential for healthy fetal and infant outcomes.

The overarching findings from this review concluded that paternal alcohol use by a live-in male partner is associated with maternal alcohol consumption during pregnancy (a study among pregnant Australian women reported that more than 75% of women who drank during pregnancy usually drank with their partner, and that 40% of drinking occasions were initiated by their male partner, see Appendix 3) and that preconception alcohol use by the biological father can impact sperm, fetal, and infant health. It is therefore important to recognise, conceptualise and verbalise, at all levels, that decisions about alcohol use during preconception and pregnancy are not the sole responsibility of women but occur within the context of the home and the broader social environment, and thus require more complex policy and programs to assist in reducing alcohol-exposed pregnancies and increasing the potential for healthy fetal and infant outcomes.

The review found that this area of research is largely underdeveloped and could benefit from a comprehensive range of studies to develop the field. Similarly, the review found that the research that has been done to date has not been translated into policy or practice in any standardised or meaningful way.

References

1. McBride N. School drug education: intervention development and research. Springer: Singapore. 2016.
2. Hawks D. Is it possible to recommend safe drinking levels without increasing per capita consumption? Another aspect of the prevention paradox. *British Journal of Addiction*. 1989;84:371 - 5.
3. Australian Bureau of Statistics. Births, by nuptiality, by age of mother. <http://stat.data.abs.gov.au/Index.aspx?QueryId=498> accessed 17/08/2017. Commonwealth of Australia. 2016.
4. Australian Institute of Health and Welfare. National Drug Strategy Household Survey (NDSHS) 2016 key findings. retrieved from <http://www.aihw.gov.au/alcohol-and-other-drugs/data-sources/ndshs-2016/alcohol/>. 2017: 26/07/2017.
5. Callinan S, Room R. Alcohol consumption during pregnancy: Results from the 2010 National Drug Strategy Household Survey. Canberra: Centre for Alcohol Policy Research. 2012.
6. Cameron C, Davey T, Kendall E, Wilson A, R M. Changes in alcohol consumption in pregnant Australian women between 2007 and 2011. *Medical Journal of Australia*. 2013;199(5):355-7.
7. National Health and Medical Research Council. Australian Guidelines to reduce health risk from drinking alcohol. National Health and Medical Research Council: Canberra. 2009.
8. McBride N, Carruthers S, Hutchinson D. Reducing alcohol use during pregnancy: Listening to women who drink as an intervention starting point. A formative intervention research study. *Global Health Promotion*. 2012;2(6):6-18.
9. L B, Black E, Powers J, Loxton D, Elliott E, Shakeshaft A, et al. Geographic and Maternal Characteristics Associated with Alcohol Use in Pregnancy. *Alcoholism: Clinical and Experimental Research*. 2011;35:1230-7.
10. Rimmer C, De Costa C. A retrospective review of self-reported alcohol intake among women attending for antenatal care in Far North Queensland. *Aust N Z J Obstet Gynaecol*. 2006;46:229-33.
11. Chang G, McNamara T, Orav E, Wilkins-Haug L. Alcohol use by pregnant women: partners, knowledge, and other predictors. 67. 2006:245-51.
12. Peadon E, Payne J, Henley N, D'Antoine H, Bartu A, O'Leary C, et al. Attitudes and behaviour predict women's intention to drink alcohol during pregnancy: the challenge for health professionals. *BioMedical Central*. 2011;11(1):584.
13. Parker T, Maviglia M, Lewis P, Gossage J, May P. Psychological distress among Plains Indian mothers with children referred to screening for Fetal Alcohol Spectrum Disorders. *Substance Abuse Treatment, Prevention & Policy*. 2010;5(22):UI 20819208.
14. Russell E. The power of knowledge: Reflections from the experiences of birth mothers. Reflections of a birth mother. In: 4th International Conference on Fetal Alcohol Disorder Syllabus. The University of British Columbia: Vancouver. 2011. 2011.
15. France K, Henley N, Payne J, D'Antoine H, Bartu A, O'Leary C, et al. Health professionals addressing alcohol use with pregnant women in Western Australia - barriers and strategies for communication. *Substance Use and Misuse*. 2010;10:1474-90.
16. McBride N, Farrington F, Midford R, Meuleners L, Philip M. Harm Minimisation in School Drug Education. Final Results of the School Health and Alcohol Harm Reduction Project (SHAHRP). *Addiction*. 2004;99:278-91.
17. Leis J, Heron J, Stuart E, Mendelson T. Depressive and Anxious Symptoms and Prenatal Alcohol Use. *Maternal and Child Health Journal*. 2012;16(6):1304-11.
18. Arch J. Pregnancy-specific anxiety: which women are highest and what are the alcohol-

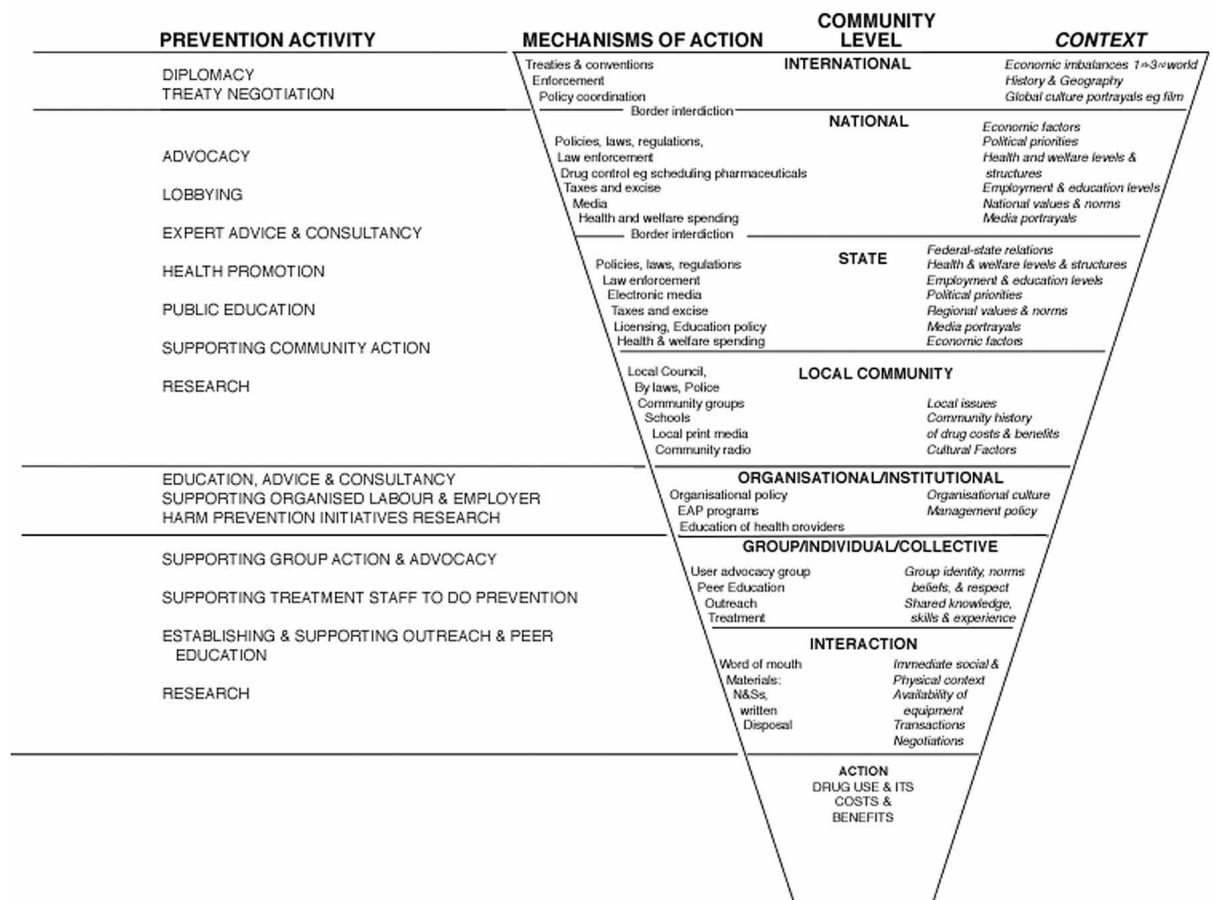
related risks? *Comprehensive Psychiatry*. 2013;54(3):217-28.

19. Parker T, Maviglia MA, Lewis PT, Gossage JP, May PA. Psychological distress among Plains Indian mothers with children referred to screening for fetal alcohol spectrum disorders. *Substance Abuse Treatment, Prevention, and Policy*. 2010;5.
20. Ding X-X, Wu Y-L, Xu S-J, Zhu R-P, Jia X-M, Zhang S-F, et al. Maternal anxiety during pregnancy and adverse birth outcomes: A systematic review and meta-analysis of prospective cohort studies. *Journal of Affective Disorders*. 2014;159(0):103-10.
21. Field T, Diego M, Hernandez-Reif M, Schanberg S, Kuhn C, Yando R, et al. Pregnancy anxiety and comorbid depression and anger: effects on the fetus and neonate. *Depression and Anxiety*. 2003;17(3):140-51.
22. Harrison M, Weinstangel H, Dalziel N, Moreau K. A collaborative outreach clinic for pregnant youth and adolescent mothers: Description of a pilot clinic and its patients/Une clinique d'approche collaborative à l'intention des adolescentes enceintes ou mères : la description d'une clinique pilote et de ses patientes. *Paediatrics & Child Health*. 2014;19(5):247-50.
23. Leonardson G, Loudenburg R. Risk factors for alcohol use during pregnancy in a multistate area. *Neurotoxicology and teratology*. 2003;25(6):651-8.
24. Pajulo M, Savonlahti E, Sourander A, Helenius H, Piha J. Antenatal depression, substance dependency and social support. *Journal of Affective Disorders*. 2001;65(1):9-17.
25. Kitsantas P, Gaffney K, Wu H, Kastello J. Determinants of alcohol cessation, reduction and no reduction during pregnancy. *Arch Gynecol Obstet*. 2014;289(4):771-9.
26. McDonald SW, Hicks M, Rasmussen C, Nagulesapillai T, Cook J, Tough SC. Characteristics of women who consume alcohol before and after pregnancy recognition in a Canadian sample: A prospective cohort study. *Alcoholism: Clinical and Experimental Research*. 2014;38(12):3008-16.
27. Naimi T, Lipscomb L, Brewer R, B G. Binge drinking in the preconception period and the risk of unintended pregnancy: implications for women and their children. *Pediatrics*. 2003;111(Suppl 1):1136-41.
28. Ceccanti M, Fiorention D, Coriale G, Kalberg W, Buckley D, Hoyme H, et al. Maternal risk factors for fetal alcohol spectrum disorders in a province in Italy. *Drug Alcohol Dependence*. 2014;145:201-8.
29. Leonardson GR, Loudenburg R. Risk factors for alcohol use during pregnancy in a multistate area. *Neurotoxicology and teratology*. 2003;25(6):651-8.
30. May PA, Gossage JP, White-Country M, Goodhart K, Decoteau S, Trujillo PM, et al. Alcohol consumption and other maternal risk factors for fetal alcohol syndrome among three distinct samples of women before, during, and after pregnancy: The risk is relative. *American Journal of Medical Genetics Part C: Seminars in Medical Genetics*. 2004;127C(1):10-20.
31. May P, Gossage J, Brooke L, Snell C, Marais a, Hendricks L, et al. Maternal Risk Factors for Fetal Alcohol Syndrome in the Western Cape Province of South Africa: A Population-Based Study. *American Journal of Public Health*. 2005;95(7):1190-9.
32. McBride N, Johnson S. Fathers' role in alcohol-exposed pregnancies. systematic review of human studies. *American Journal of Preventive Medicine*. 2016;51(2):240-8.
33. Lenton S. A framework for prevention. *Drug and Alcohol Review*. 2005;24(1):49-55.
34. McKay M, McBride N, Sumnall H, Cole J. Reducing the harm from adolescent alcohol consumption: results from an adapted version of SHAHRP in Northern Ireland. *Journal of*

Substance Use 2012;Early Online:. 2012:1-24.

Appendix 1: The Prevention Framework

The systematic development of individual behaviour-based interventions provides an important contribution to a whole-of-community approach to change. However, it is important to keep in mind that multifactorial, community-wide, evidence-based interventions are likely to be the most effective way to create comprehensive change within a complex society, while also enabling individual behaviour change. The Prevention Framework, initially proposed by North American community intervention researcher Harold Holder, provides one guide to planning, understanding and describing prevention activity and research across society by comprehensively identifying different community and social levels for intervention [33]. Although not theory or database driven, it provides one form of conceptualising possible comprehensive community prevention foci, activities, and mechanisms for action at various levels from international to local, and by doing so, identifies different stratas of intervention research and possible entry points for intervention research.



The Prevention Framework provides insight into the extensiveness and scope of activity that can optimise societal health change, and it acts as a reminder to researchers working in individual settings or with individual target groups that they are only one part of a bigger picture. If multiple interventions are aimed at, for example, reducing youth risky alcohol consumption, then significant shifts in societal behaviour is more likely to occur. However, this

will only be the case if all intervention researchers work towards developing interventions that have proven behavioural impact. When this level of research is reached and applied to policy and practice, then a whole-of-community approach is more likely to improve societal health and reduce societal health costs [1].

Appendix 2: Evidence and Proof of Impact

There are three levels of evidence that inform the behavioural effectiveness of a program.

These three levels of evidence are:

- 1) **Evidence-based programs** that have been developed and informed by past knowledge in the field (i.e. systematic literature reviews) and, when this is not available by current best practice, informed by practice, wisdom and experts. This approach does not provide any evidence of behavioural impact.
- 2) A program with **proof-of-impact** is one that has undergone rigorous longitudinal impact assessment and shown statistical significant behaviour change in the target population. This outcome provides a good level of evidence of behavioural impact.
- 3) A program has **well established proof-of-impact** when it has been replicated in another jurisdiction under the lead of another research team, with statistical significant behaviour change that supports the original study. This outcome provides a high level of evidence. [1]

If a program is solely evidence-based, there is no proof that behaviour change will result from implementation. However, if a program has well established proof-of-impact, then there is a general understanding that if it is delivered as intended, with the intended target group, by trained staff, then a level of behaviour change can likely be expected [16, 34].

Original Article

Reducing alcohol use during pregnancy: listening to women who drink as an intervention starting point

Nyanda McBride¹, Susan Carruthers¹ and Delyse Hutchinson¹

Abstract: Objectives. This study assesses factors that contribute to alcohol consumption during pregnancy and identifies potential intervention strategies to reduce consumption. **Methods.** The study sample includes 142 pregnant women who attended a public hospital for prenatal health care in Perth, Western Australia. All participants returned a self-completion survey. **Results.** Women who discontinued drinking during pregnancy were significantly more likely to be engaged in full time home duties and had completed less formal education. Women who continued to drink were more likely to have drunk in previous pregnancies and during the preconception period. Nearly 40% of high risk women reported a negative comment in response to their drinking. One-third of women in the risky group were advised by a health professional not to drink alcohol. Women were most likely to drink in their own home or at the home of a friend. **Conclusions.** Participatory research with women who drink while pregnant can assist in identifying potential intervention strategies that have resonance with this group and therefore more potential for creating behaviour change. **Implications.** The World Health Organization recognises, and has done for over 10 years, that alcohol use during pregnancy which results in Foetal Alcohol Spectrum Disorder is the leading cause of environmental-related birth defects and mental retardation in the Western world. (Global Health Promotion, 2012; 19(2):6-18)

Keywords: Health promotion, prevention, maternal, alcohol, foetal, pregnancy, programme development

Introduction

The effects of maternal alcohol consumption on the developing foetus have been documented since recorded history; however, it is only during the last four decades that scientific evidence has confirmed that alcohol is directly associated with physical and neurodevelopmental disorders (1). Concerns about alcohol use during pregnancy relate to Foetal Alcohol Spectrum Disorder (FASD), a disorder that describes a range of adverse effects which can have a high impact on quality of life (2-5). FASD incorporates Foetal Alcohol Syndrome (FAS), a serious condition associated with heavy alcohol use, particularly in early pregnancy. Infants born with

this condition display structural brain abnormalities, deficits in growth and neurological development resulting in a range of lifelong disabilities (2).

Interest in possible foetal health effects associated with lower level of alcohol use during pregnancy has resulted in policy changes in Australia and internationally. A review of international alcohol policies indicates that several countries have updated policies that relate to pregnant women within the last few years, including Australia (6-8). There is, however, a divergence of policy advice with some countries and organisations, including the World Health Organization (9), stating that pregnant women should not drink, while others state that not drinking is the safest option but that one or two

n.mcbride@curtin.edu.au

1. Correspondence to: Nyanda McBride, National Drug Research Institute, GPO Box 1987, Perth, Western Australia 6845, Australia. Email:

(This manuscript was submitted on August 12, 2010. Following blind peer review, it was accepted for publication on June 23, 2011)

drinks per week is considered low risk. The revised Australian guidelines adopt the second approach. This divergence in policy illustrates variation in interpretation of the limited number of studies providing information on the impact of low level use of alcohol during pregnancy (10).

As guidelines for the consumption of alcohol use during pregnancy become more supportive of low level and non-use, there is an increasing need for programmes to assist those women who may find it difficult to stop or reduce consumption. Evidence-based interventions need to include information from the target group in the early stages of development to ensure that strategies and methods are appropriate, useful and resonate with the target audience (11).

Objectives

This paper reports on an explorative, descriptive study designed to assess factors that contribute to alcohol consumption during pregnancy, and to identify potential intervention points, methods and strategies to reduce consumption. The paper discusses the differences between pregnant women who drink at risky levels, those who drink at low risk levels and those who discontinued drinking early in pregnancy.

Method

This study was approved by several ethics committees including: Curtin University of Technology Human Ethics Committee; King Edward Memorial Hospital for Women Ethics Committee (and associated Scientific Advisory Sub-Committee); Southern Metropolitan Area Health Service Human Research Ethics Committee; Northern Metropolitan Area Health Service Human Research Ethics Committee; and Joondalup Health Campus Human Research Ethics Committee. Over a 14 month period between October 2006 and December 2007, 144 anonymous self-completion surveys were returned to the researchers from pregnant women attending antenatal care in one of six public hospitals in Perth, in Western Australia. Two of these returned surveys were deleted from subsequent analysis as they did not meet inclusion criteria (inclusion criteria: consumed alcohol at some stage during their pregnancy; over 19 years of age; English primary language; non-indigenous; metropolitan antenatal attendance).

The study is based on the Social Learning Theory (cognitive) (12,13), which in addition to focusing on individual behaviour, and in particular the interplay between three individual-oriented concepts, observational learning, expectancies and self efficacy (14), also identifies the impact of environmental influences. Environmental influences include the physical environment and the situation of use, and the individual's perception of these. Based on this theory the survey was designed to assess: the demographics of women who consume alcohol during pregnancy (age, income, education, marital status, living arrangements, socio-economic factors, employment); individual factors including pregnancy history/ies (number of full term pregnancies, age of living children, alcohol consumption in past pregnancies); past and current alcohol consumption (alcohol quantity and frequency questions were based on those used in the Australian National Drug Household Survey (15) – see immediately below for more detail on these variables); benefits and detriments to alcohol consumption (both open ended questions); the use of other drugs; and environmental influences including setting and situation of alcohol consumption (where and with whom consumption takes place, motivation for consumption, impact of important others on consumption, health professional's advice on alcohol use while pregnant). An open ended question was also included to elicit any other issues that may impact on alcohol use during pregnancy. The survey underwent external expert review and was piloted with a group of pregnant women to assess face and content validity.

Alcohol consumption was defined using combined frequency and quantity variables for each alcohol beverage type. Frequency was defined by questions asking 'how often did you usually have a drink of (beer, wine, spirits, other)?' Response options included: 'every day or nearly every day', 'three or four times a week', 'once or twice a week', 'one to three times a month', 'seven to 11 times in the 12 month period', 'three to six times in the 12 month period', 'twice in the 12 month period', 'once in the 12 month period' or 'never in the 12 month period' for each beverage type. Quantity was defined by asking 'On those days that you drank (beer, wine, spirits, other) how many standard drinks did you usually have per day?' Respondents were asked to refer to a standard drinks diagram to answer these questions.

Recruitment of women was conducted by hospital-based staff who asked new clients about their current alcohol consumption as part of the admission process. New clients who responded that they consumed alcohol were invited to complete a survey. Surveys were also available in antenatal waiting rooms. Information and Facts Sheets were attached to surveys along with a reply-paid envelope. Participants were self-selected and were able to withdraw from involvement during any stage of the research. All participants who decided to withdraw from the study were offered information about alcohol use during pregnancy which included contacts for health practitioners, counsellors and other support services. This information was also attached to the end of each survey.

A liaison person from each hospital was identified to facilitate and coordinate the study. Half hour training sessions were held for antenatal staff with additional information provided in staff areas. The antenatal clinic from each participating hospital was offered \$250 as a reimbursement for staff time.

Statistical analysis

Sample size

Sample size calculation (provided by ABS online at <http://www.nss.gov.au/>) indicates that based on the overall population of 12,203 live births in Perth, Western Australia during 2004 (16) (this figure excludes teens, Aboriginal, non-English speaking and non-metropolitan births as per study entry criteria), a final sample of 118 respondents would be sufficient to meet accepted levels of statistical power (95% confidence level with confidence interval ± 0.09) (17).

Analysis

The Shapiro–Wilk W Test was used to test the normality of dependent variables for each risk group (18). Results showed that at least one risk group had a significant non-normal distribution for each dependent variable (except age). Normal distribution is a required assumption for the ANOVA test. As this assumption was not met, the non-parametric equivalent Kruskal–Wallis H Test was used to assess differences in the three risk groups. Descriptive data have been presented to illustrate the differences and similarities between groups.

Risk groups

Three risk groups were identified and formed the basis of comparison for the statistical analysis in this paper. All 142 pregnant women included in the study noted that they consumed alcohol at some stage during their pregnancy. The first risk level group, however, discontinued consumption (no risk – now non-drinker) once they realized they were pregnant, the second risk level group consumed at low risk levels and the third group consumed at risky levels. Risk level is defined by the Australian Guidelines to reduce risk from drinking alcohol (8). Introduced in March 2009, Guideline 4, which pertains to pregnant and breastfeeding women, states that:

pregnant and breastfeeding women should note that not drinking is the safest option for the developing foetus and young babies who are breastfed. However, the level of risk is likely to be low if a woman has consumed only small amounts of alcohol (such as one or two drinks per week) before she knew she was pregnant or during pregnancy (8).

Therefore, risky consumption is defined as more than two drinks per week, and low risk consumption is defined as one or two drinks per week. The proportion of women from the study who were defined as having no risk (now non-drinkers) was (33.1%), low risk (45.8%) and risky (21.1%).

Results

Demographics

Two demographic variables were significantly different between groups: level of education ($p = 0.022$) and current employment status ($p = 0.042$) (Table 1). Descriptive data (Table 2) indicate that women in the low risk group were more likely to have a higher education than women in the no current or risky groups. A third of the women in the low risk group (33.9%) had a university degree compared with 14.5% on the no current risk group and 20% in the risky group. A similar proportion of women in each group had completed education to TAFE level (no current risk: 19.1%; low risk: 21.5%; risky: 16.7%).

Table 1. Statistically significant variables by risk level group

	<i>Risk level group</i>	<i>N</i>	<i>Mean rank</i>	<i>Chi-square</i>	<i>Df</i>	<i>Asymp. sig.*</i>
Demographics						
Education	No current risk	47	58.46	7.601	2	0.022
	Low risk	65	79.34			
	High risk	30	74.95			
	Total	142				
Employ	No current risk	47	83.31	6.351	2	0.042
	Low risk	65	65.52			
	High risk	30	65.97			
	Total	142				
Pregnancy histories						
Drink during previous pregnancies	No current risk	46	71.88	6.237	2	0.044
	Low risk	63	74.82			
	High risk	29	54.17			
	Total	138				
Did you drink before pregnancy / pre-conception?	No current risk	45	75.70	12.870	2	0.002
	Low risk	64	66.50			
	High risk	29	66.50			
	Total	138				
Preferred type of alcohol						
Type most often drunk – beer	No current risk	37	82.61	13.437	2	0.001
	Low risk	64	60.20			
	High risk	30	57.88			
	Total	131				
Alcohol use in the 12 months prior to pregnancy						
Beer how often in 12 months prior to pregnancy	No current risk	36	76.53	15.015	2	0.001
	Low risk	56	53.13			
	High risk	25	46.92			
	Total	117				
Wine how often in 12 months prior to pregnancy	No current risk	38	80.76	16.387	2	0.000
	Low risk	60	51.64			
	High risk	25	58.34			
	Total	123				
Spirits how often in 12 months prior to pregnancy	No current risk	36	70.13	9.546	2	0.008
	Low risk	56	61.38			
	High risk	27	43.63			
	Total	119				
Situation of alcohol use						
Benefits and concerns						
Benefits	No current risk	34	72.09	15.088	2	0.001
	Low risk	62	58.50			
	High risk	28	59.71			
	Total	124				

Table 1. (Continued)

	<i>Risk level group</i>	<i>N</i>	<i>Mean rank</i>	<i>Chi-square</i>	<i>Df</i>	<i>Asymp. sig.*</i>
Anyone ever made negative comment/pressure?	No current risk	42	78.83	8.710	2	0.013
	Low risk	63	64.00			
	High risk	29	58.69			
	Total	134				
Health Professionals Advice						
Did doctor/health carer ask about alcohol use – current pregnancy?	No current risk	43	76.99	7.810	2	0.020
	Low risk	64	65.16			
	High risk	27	57.94			
	Total	134				
Other drug use						
Do you use any other drugs?	No current risk	44	72.36	8.289	2	0.016
	Low risk	64	70.06			
	High risk	27	56.00			
	Total	135				

*This is the level of statistical significance output from the Kruskal-Wallis H Test in SPSS. It is the significance level of the differences between groups.

Note: Skip questions were used before: Benefits and Concerns, and questions on alcohol use in the 12 months prior to pregnancy.

Descriptive data (Table 2) indicate that women in the no current risk group were more likely to be engaged in full time home duties (46.8%) compared with women in either the low or risky groups (30.8% and 23.3% respectively). A similar proportion of women in each group worked part time (no current risk: 31.9%; low risk: 27.7%; risky: 33.3%); however, women in both risky (33.3%) and low risk (33.8%) groups were more likely to work full time than women in the no current risk group (12.8%). A small proportion of women in the no current (4.2%) and low risk (4.6%) groups were studying.

Pregnancy histories

Two pregnancy history variables were significantly different between risk level groups: drinking during previous pregnancies ($p = 0.044$) and drinking before pregnancy (preconception) ($p = 0.002$) (Table 1). Under 15% of women in the no current risk group consumed alcohol during previous pregnancies; however, women in the low risk group were over twice as likely and women in the risky group were over four times as likely to have drunk alcohol in

previous pregnancies (Table 2). A high proportion of women in all study groups consumed alcohol during the preconception period; however, the no current risk group were significantly less likely to drink during this period (17%) than women in the low risk (1.5%) or risky (3.3%) groups (Table 2).

Over two-thirds of women in the no current and low risk groups had planned their pregnancy compared with just over half of the women in the risky group (Table 2). The majority of women had their pregnancy confirmed early with over 50% of each group gaining confirmation by week five (no current risk: 56.5%; low risk: 56.9%; risky: 53.3%) and over 90% by week nine (no current risk: 95.7%; low risk: 96.9%; risky: 93.3%).

Preferred type of alcohol

One preferred type of alcohol variable was significantly different between risk groups (Table 1). This was the type of alcohol most often drunk – beer ($p = 0.001$). Women in the no current risk group were significantly less likely to consume beer (14.9%) compared with women in the low (52.3%) and risky (56.7%) groups.

Table 2. Descriptive data by risk level group

<i>Variable</i>	<i>No current risk</i>	<i>Low risk</i>	<i>Risky</i>
DeMOgRAPHICS			
Age (mean)	28.64	29.56	29.96
Income (medium, mode)	\$52-68k, \$45-60k	\$60-75K, \$45-60k	\$60-75K, \$45-60k
Education (mean, mode)	2.6, 12 years	3.61, 16 years	3.43, 12 years
Marital status = married or defacto (%)	93.6	92.3	83.3
Living arrangement = with partner (%)	91.5	90.8	90
Centrelink healthcard (% yes)	19.1	16.9	30
Postcode = inner suburbs (%)	8.5	18.8	13.3
Employment (mode, alpha reported)	Homeduties	full time	full or part time
Country of Birth = Australia (%)	76.6	75.4	76.7
Aboriginality (% yes)	6.4	0	3.3
PRegNANCy HISTORIEs			
Number of full term pregnancies (mean, mode)	2.3, 2	2.15, 1	2.27, 1.2
Age of living children (mean, mode)	6.11, 2	5.44, 2	4.86, 2
Number of weeks pregnant (mean)	21.65	23.76	22.55
Was the pregnancy planned? (% yes)	68.1	67.7	53.3
Week pregnancy was confirmed (mean)	5.19	6.29	5.86
Did you drink in previous pregnancies (% yes)	14.9	35.4	60
Did you drink prior to pregnancy preconception (% yes)	83	98.5	96.7
PRefeRReD TyPe Of AlCOHOL			
Type of alcohol usually consumed*			
- beer (%)	10.6	15.4	23.3
- wine (%)	34	63.1	40
- spirits (%)	31.9	13.8	26.7
Type most often drunk			
- beer (%yes)	14.9	52.3	56.7
- wine (% yes)	53.2	73.8	51.1
- spirits (%yes)	51.1	46.2	50
- other (% yes)	4.3	6.2	6.7
AlCOHOL uSe IN 12 MONTHS PRIOR TO PRegNANCy			
Beer			
How often in 12 months prior to pregnancy (% 1-2 /week or more, mode)	12.7, never	32.4, 1-2 time/month	40, 1-2 time/month
How many SD per occasion (mean, mode)	2, 1	2.3, 1	2.7, 3
Wine			
How often in 12 months prior to pregnancy (% 1-2/ week or more, mode)	23.4, 1-2 time/month,	61.6, 1-2 times/month	43.3, 3-4 times/week
How many SD per occasion (mean, mode)	never, 2.7, 2	2.6, 2	2.7, 2
Spirits			
How often in 12 months prior to pregnancy (mean, mode)	12.7, Never	16.9, 1-3 times/month	36.6, 1-3 times/month
How many SD per occasion (mean, mode)	2.8, 2	2.8, 2	3, (2,3)
AlCOHOL uSe SItUATIOn			
Where do you usually drink?			
- home (% yes)	72.3	87.7	93.3
- pub/bar (% yes)	19.1	21.5	33.3
- friends house (% yes)	53.2	70.8	70
- restaurant (% yes)	29.8	53.8	40

Table 2. (Continued)

<i>Variable</i>	<i>No current risk</i>	<i>Low risk</i>	<i>Risky</i>
Where do you most regularly drink? (select one venue)*			
- home (%)	57.4	60	73.3
- pub/bar (%)	8.5	3.1	10
- friends house (%)	8.5	18.5	13.3
- restaurant (%)	8.5	10.8	0
- other (%)	2.1	1.5	0
Who do you usually drink with?			
- partner (% yes)	63.8	81.5	73.3
- friend/s (% yes)	68.1	86.2	76.7
- alone (% yes)	6.4	15.4	13.3
Who do you most regularly drink with?*			
- partner (%)	51.1	55.4	50
- friend/s (%)	29.8	27.7	30
- alone (%)	2.1	6.2	10
- other (%)	2.1	1.5	3.3
Who usually suggest you drink?			
- you (% yes)	78.7	83.1	83.3
- partner (% yes)	36.2	38.5	40
- friend (% yes)	38.3	29.2	40
Who most regularly make suggestion?*			
- you (%)	63.8	66.2	70
- partner (%)	8.5	12.3	6.7
- friend (%)	12.8	16.9	13.3
- other (%)	0	1.5	0
BeNefITS AND CONCERNs			
Are there benefits of drinking? (% yes)	55.3	93.8	90
- taste (% yes)*	14.9	46.2	40
- relax (% yes)*	31.9	52.3	63.3
- socialising (% yes)*	25.5	21.5	33.3
Do you have concerns about drinking? (% yes)	17	33.8	50
- FAS (% yes)*	6.4	26.2	30
- liver (% yes)*	4.3	1.5	0
- newguid (% yes)*	2.1	3.1	6.7
Has anyone ever made negative comment/pressure? (% yes)	12.8	32.3	40
- Mother*	0	7.7	3.3
- Partner*	0	4.6	13.3
- Doctor*	0	0	6.7
- other friends/family*	8.5	12.3	10
HeALTH PROfESSIONAIS ADvICE			
Did doctor or health carer ask about alcohol use in previous pregnancies? (% yes)	36.2	50.8	46.7
Did doctor or health carer ask about alcohol use in current pregnancy? (% yes)	55.3	76.9	80
Has doctor or health carer provided advise on alcohol during current pregnancy? (% yes)	38.3	60	56.7
What was their advice? (% don't drink, occasional drink OK)	21.3, 0	33.8, 7.7	33.3, 3
OTHeR DRug uSe			
Do you use any other drugs? (% yes)	8.5	12.3	30
- Tobacco (% yes)	4.3	6.2	16.7
- Cannabis (% yes)	2.1	10.8	13.3
- Other (% yes)	4.3	4.6	3.3

(Continued)

Table 2. (Continued)

<i>Variable</i>	<i>No current risk</i>	<i>Low risk</i>	<i>Risky</i>
OTHeR CoMMeNTS*			
Do you have any other comments about alcohol use during pregnancy? (% yes)	21.3	33.8	43.3
- Confusing because of conflicting advice	20	18.2	0
- Did not know I was pregnant	20	4.5	7.7
- Moderate consumption is acceptable	10	63.6	61.5
- Should not drink while pregnant	50	9	7.7
- More/accurate information required	0	4.5	15.4
- Other	0	0	7.7

Significant differences bolded

Means all fall within 95% Confidence Interval upper and lower boundaries

Some variables have multiple modes (all listed in parentheses)

Variable values: **education:** 0-primary, 1-to year 10, 2-year 11 or 12, 3-Tafe certificate, 4-Associate Diploma, 5-Undergraduate Diploma, 6-Bachelor Degree, 7-Masters/Post Grad. Diploma, 8-Doctorate. **How often in 12 months prior to pregnancy:** 0-everyday, 1-3 to 4 times per week, 2-1 to 2 times a month, 3-1 to 3 times a month, 4-7 to 11 times in 12 months, 5-3 to 6 times in 12 months, 6-twice in 12 months, 7- once in 12 months, 8-never in 12 months.

* some missing responses

Alcohol use in the 12 months prior to pregnancy

Three variables measuring quantity and frequency of alcohol consumption in the 12 months prior to pregnancy were statistically significant between drinking level groups (Table 1). These included: how often beer was consumed in the 12 months prior to pregnancy ($p = 0.001$); how often wine was consumed in the 12 months prior to pregnancy ($p < 0.000$); and how often spirits were consumed per occasion in the 12 months prior to pregnancy ($p = 0.008$).

Women in the no current risk group were two and a half to three times less likely to consume beer once or twice a week, or more often, in the 12 months prior to pregnancy than women in either the low risk or the risky groups. Women in the no current risk group were nearly two to two and a half times less likely to consume wine one or twice a week, or more often, in the 12 months prior to pregnancy than women in either the low or the risky groups. Women in the no current risk and low risk groups were two to three times less likely to consume spirits once or twice a week, or more often, in the 12 months prior to pregnancy than women in the risky group.

Situation of alcohol use

There was no significant difference in any of the alcohol use situational variables between risk level

groups. When asked to select one venue where they were most likely to drink, the majority of study women selected their home, with a smaller proportion of women selecting a friend's house, or a pub or bar (Table 2). A small proportion of no current and low risk women also selected a restaurant (Table 2). However, women generally drank in a range of settings as indicated in open option questions. Women in each risk level group were most likely to drink in their own home or at the home of a friend, and at times in a restaurant or a pub or bar (Table 2).

Benefits and concerns about alcohol use

Two benefit and concern variables were significantly different between the three drinking level groups (Table 1). These included: recognised benefits of drinking alcohol (while pregnant) ($p = 0.001$) and receiving a negative comment about drinking (while pregnant) ($p = 0.013$). All the women in the low and risky groups continued to drink alcohol during pregnancy and the majority of these women recognise that there were benefits to drinking compared with a smaller proportion of women in the no current risk groups who had discontinued drinking. The most noted benefit reported by women in all study groups who answered this question was that of relaxation (Table 2). The low and risky groups were more likely to enjoy the

taste of alcohol, and each group had a proportion of women who gained social benefits from drinking (while pregnant) (Table 2).

Nearly one-third of women in the low risk group and a higher proportion of women in the risky group reported a negative comment in response to their drinking (Table 2). Family and friends (other than mother and partner) were most likely to make a negative comment about drinking in the no current and low risk groups, with partners most likely to make a negative comment about drinking for women in the risky group (Table 2).

A proportion of women in each group had concerns about drinking during pregnancy (Table 2). The most common concern noted by women who responded to this question was the potential risk of FAS to their unborn child with approximately one-third of women who continued to drink during pregnancy reporting this concern.

Health professional advice

One health professional variable was significantly different between risk level groups: did a doctor or health professional ask about alcohol use during your current pregnancy? ($p = 0.020$). Descriptive data (Table 2) indicate that although over half of the women in the no current risk group were asked about their current alcohol use, they were less likely to be asked about their current alcohol use than women in either the low or risky groups.

Other drug use

There was a significant difference in the proportion of women from each study group who reported use of other drugs ($p = 0.016$) (Table 1). A higher proportion of women in the risky drinking group reported other drug use compared with women in the no current and low risk groups (Table 2). Women in the risky group were most likely to use tobacco and cannabis in addition to alcohol, while women in the low risk group were more likely to use cannabis in preference to tobacco.

Other comments

There was no significant difference in the number of women from each study group who chose to make an additional comment about alcohol use during pregnancy (Table 2).

Women in the no current risk group were over five times more likely to comment that women should abstain while pregnant compared with other study women (Table 2). Women in the low and risky groups were most likely to comment that moderate consumption during pregnancy is acceptable (Table 2). Some of these comments were related to prior pregnancy outcomes.

Although all professional advice is that abstinence is best, out of my friends and associates most women who have children have taken alcohol whilst pregnant with no obvious harm to their children, making the decision to consume it myself on occasions much easier. (Low risk woman)

Everything in moderation I feel is acceptable – food and alcohol although I watch what I eat. I am more concerned about smoking for which I have tried everything to give up and can't although I still try this every morning. (Risky woman)

Approximately one-fifth of women in both the no current and low risk groups made comment about the conflicting advice they received from health professionals (Table 2). Women in the low and risky groups asked that more accurate research information be available (Table 2).

There is a lot of contrasting literature. One booklet I received contradicted the midwives advice. If the health profession wishes to pursue a zero tolerance line towards alcohol consumption during pregnancy they need to provide details and the reports and statistics which have led to this stance. I personally find it a difficult notion that all alcohol consumption is excessive. (Low risk woman)

I know I shouldn't drink or smoke but sometimes it's a small relief from life's stress and situations. Also midwives and people can make you feel very guilty without perhaps encouraging and supporting you in quitting. (Risky woman)

Discussion

This descriptive study focuses on the experiences, situations and context of some Australian women who drink alcohol while pregnant, in order to gather

information that may assist in the development of intervention research planning and strategies. Based on Australian Guidelines, three risk level groups were identified: women who ceased drinking during pregnancy (risk exposure during the non-recognised phase of pregnancy), women who continued to drink to low risk levels (one to two standard drinks per week) and women who continued to drink to risky levels (greater than two standard drinks per week). As noted in the Australian Guidelines, risk refers to the impact of alcohol use on the health of the developing foetus rather than any possible health impact on women. Although there was a significant difference between risk level groups for some variables, those variables where no statistical significant was reported are of practical significance for they help to define intervention foci for alcohol consuming pregnant women generally, rather than for specific risk level groups.

There were several features unique to **women in the risky group**. They were **more likely to have a Government Health Care Card**; **be single**; **experience a negative comment about their drinking from their partner**; **use other drugs, in particular tobacco and cannabis**. Previous studies report that partners play a significant role in modifying prenatal behaviours and therefore may be an important target for interventions (19,20). However, the risky women in this study were **less likely to have a partner** and were **more likely to have a less supportive partner**, suggesting that alternative forms of social support interventions are necessary. Some risky women stated that they were **concerned about drinking during pregnancy, but less so than about their use of other drugs, particularly tobacco**. **Combined prevention efforts** may therefore be an important consideration, as will be **intensive individually targeted programmes** to assist in quitting multiple substances. This is particularly important as recent research confirms the synergistic effects of alcohol and tobacco use during pregnancy on preterm labour, birth weight and growth restriction (21). Risky women were **less likely to have a planned pregnancy**. Research suggests that unplanned pregnancies can result from **ineffective contraception use** often associated with the use of alcohol (22). The **combination of drinking and ineffective contraception suggests that interventions with combined messages** for women who drink to risky levels may be an important form of intervention.

Effective programmes focusing on these two issues will possibly reduce the number of alcohol exposed pregnancies. The **social determinates that have given rise to women's risky use of alcohol (and other drugs) during pregnancy are likely to be complex and will therefore require a complex mix of intervention, the focus of which can perhaps best be identified during focus groups or in-depth interviews** and will require cross sectional planning, implementation and spending.

There were **similarities between women from the low and risky groups** which may prove useful in identifying intervention foci. Women in these groups: were **more likely to work fulltime, were up to four times more likely to have consumed alcohol in previous pregnancies and were more likely to consume alcohol during preconception**. These findings highlight the importance of targeting women **prior to and in the early stages of pregnancy**. Prevention programmes that **target women during childbearing years** will also be important as research findings from this study and others show that **pre-pregnancy drinking levels predict drinking levels during pregnancy (19,23); that alcohol use 10 years earlier can predict alcohol consumption during pregnancy (23,24); and that preconception health and lifestyle issues can play a significant role in postnatal outcomes (25,26)**. Programmes that target women of childbearing age are an important feature of policy and programmes in the USA, a country which is considerably more advanced than Australia in dealing with prevention of harmful outcomes for infants associated with alcohol use during pregnancy (27). The importance of intervention programmes focusing on women of childbearing age is further reinforced by the 'no current risk' women in this study who gave up drinking once pregnancy was confirmed, but who had not reduced consumption in the non-recognised phase of pregnancy. These women may be more attuned to cease consumption if there is a possibility of pregnancy, particularly if information and programmes are available during the preconception phase.

Women in the low and risky drinking groups were most likely to be asked by a health professional about their current alcohol use and to be advised to stop (most commonly) or reduce use. That this **advice was not adopted (particularly by risky women) suggests the need for more intensive intervention**. Chang *et al.* (20) have noted that Brief

Interventions (approximately 25 minutes' duration) can be effective in modifying drinking behaviour of pregnant women in a clinical setting. Women in the low and risky groups were most likely to make comment that moderate consumption during pregnancy is acceptable. These comments were often based on the observation that no harm had occurred to infants from previous pregnancies and therefore was unlikely to have an impact on future pregnancies. However, a proportion of women from both groups were concerned about the potential for FAS and asked that more accurate research information be available. This request reinforces the need to provide up-to-date and more detailed information about FAS/FASD to women of childbearing age, women who are planning to become or who currently are pregnant. Information could include the potential of lifelong learning and behavioural problems that may result in affected children (and the associated social and economic costs) and detailed information about current understandings of confounding factors that impact on the likelihood of the presentation of FAS or FASD. Information may also include the lack of available research into the effects of low level use during pregnancy and how this relates to Australian Guidelines for women, and the current dearth of effective tools for adequately diagnosing FAS or FASD in Australia and resultant under reporting and under diagnosing of these conditions. There is an immediate need to make up-to-date information widely available and to conduct further research in areas where information is limited.

Nearly half of the study women continued to drink alcohol to low risk levels during pregnancy and these women were more likely to have a higher level of education than women in either the no risk or risky groups and were more likely to consume wine as their preferred alcohol of choice. These findings are common among other research into predictors of alcohol use during pregnancy (19,28). That women in the low risk group were more likely to select wine as their alcohol of choice indicates the potential for specific point of sale, warning label or taxation strategies. Furthermore women who drank to low risk levels were likely to identify the benefits of drinking during pregnancy, particularly the benefit of socialising, suggesting the potential intervention targets of partners, family and friends to extend social support for reduced use and the

need for strategies that promote alternatives to alcohol use in social situations.

There are some variables that are unique to women who chose to cease alcohol consumption on confirmation of pregnancy that may be pertinent to prevention efforts. Women in this group were most likely to be engaged in full time home duties, however, there are issues inherent to this group that predisposes them to drink less during preconception and to stop drinking during pregnancy that were not uncovered in this study. This group tended to display fewer risky behaviours generally, indicated by a smaller proportion of women in this group reporting use of other legal and illegal drugs. They were also less likely to identify benefits of drinking and were over five times more likely to make additional comment that women should abstain from alcohol while pregnant. To assist in intervention planning there is a need to conduct focus groups or in-depth interviews to help clarify some of the issues and traits that are pertinent to this group of women. These factors may be subsequently introduced into prevention activity to assist in reducing alcohol use during pregnancy in women who do drink or are considering drinking during pregnancy.

All study participants noted that they were most likely to drink at home, suggesting the potential for point of sale intervention, labelling regulations and social support programmes. All study women had their pregnancy confirmed early in their pregnancy with over 50% of each group gaining confirmation by week five and over 90% by week nine. This highlights the opportunity women have for reducing or ceasing alcohol consumption during early pregnancy and a clear opportunity to conduct intervention activity during early pregnancy. However, over 50% of the women in the study continued to drink after confirmation of pregnancy, which reinforces the appropriateness of prevention programmes and campaigns that target women of childbearing age generally, and women in the preconception phase specifically.

There are several study limitations. The study recruits were self-selected, were required to meet the selection criteria and were drawn from public hospitals in the Perth area. A higher number of surveys were issued to hospitals than were returned to researchers. This discrepancy may be partially explained by factors inherent to the study including: women who were issued surveys subsequently

noting that they were not eligible; and a change of interest in completing a self-completion survey without any external motivation. The survey involved a controversial issue that had gained increased media exposure during the period of the study, and this may also have impacted on motivation to be involved. Additionally, there were some hospital related issues that appeared to have impacted on returns, including: withdrawal from the study; change of staff with different levels of interest/motivation to promote the study and discuss the surveys with potential respondents in line with the training provided by study staff. Although face and content validity included input from the target group, there is also the possibility that the study variable did not encompass all issues relating to alcohol consumption during pregnancy. **Focus groups with women who consume alcohol during pregnancy would add to our understanding of the depth of issues that impact and influence women who consume alcohol during pregnancy.**

Exposure to alcohol during the prenatal period is the leading cause of preventable birth defects and developmental problems in the USA, where diagnosis and notification are rigorous (27). In Australia, where diagnosis and notification of FAS/D are limited, there is a higher level of alcohol use among women of childbearing age and pregnant women (27,29), therefore Australia is likely to have a higher unrecorded level of FAS/D (26,29). To ensure optimal outcomes for infants and children in the future, **multiple levels of intervention** are likely to be required, focusing on programmes, laws and regulations that are based on evidence of impact (30). However, **the minutiae of intervention must also involve information gained directly from the target group, as programmes that resonate with the target audience and meet their needs will be most effective in creating change** (31). This formative descriptive study of pregnant women's alcohol related experiences and situation of use, although not generalisable to a broader population, can assist in identifying target group informed strategies and components for testing in future intervention research. The formative intervention research undertaken in this study is particularly important in the early stages of intervention development (11) as is the case in Australia, or when the behavioural impact of evidence based programmes has limited scope, as noted in recent systematic literature

reviews of interventions to reduce alcohol use during pregnancy (32,33). **Replication of this type of formative intervention study among other groups and in other jurisdictions will be important in helping to identify and shape potential intervention research.**

References

1. Jones K, Smith D. Pattern of malformation in offspring of chronic alcoholic mothers. *Lancet*. 1973; 1: 1267–1271.
2. Stratton K, Howe C, Frederick B (eds). *Fetal Alcohol Syndrome: Diagnosis, epidemiology, prevention, and treatment*. Washington DC, USA: Institute of Medicine Division of Biobehavioral Sciences and Mental Disorders, National Academy Press; 1996.
3. Bertrand J, Floyd R, Weber M et al. *Fetal Alcohol Syndrome: Guidelines for referral and diagnosis*. Atlanta, GA, USA: Centers for Disease Control and Prevention; 2004.
4. Streissguth A, Bookstein F, Barr H, Sampson P, O'Malley K, Young J. Risk factors for adverse life outcomes for fetal alcohol syndrome and fetal alcohol effects. *J Dev Behav Pediatr*. 2004; 25: 228–238.
5. Burden M, Jacobson S, Jacobson J. Relation of prenatal alcohol exposure to cognitive processing speed and efficiency in childhood. *Alcohol Clin Exp Res*. 2005; 29: 1473–1483.
6. UK Department of Health. Alcohol and pregnancy. http://www.dh.gov.uk/en/PublicHealth/Alcoholmisuse/DH_125368. 3 April 2012.
7. Alcohol Advisory Council of New Zealand. Low risk drinking guidelines. <http://www.alcohol.org.nz/LowRiskDrinking.aspx> July 2007.
8. National Health and Medical Research Council. *Australian guidelines to reduce health risk from drinking alcohol*. ISBN 1864963743. Canberra, Australia: NHMRC; 2009.
9. World Health Organization. *Framework for alcohol policy in the WHO European region*. Copenhagen, Denmark: WHO; 2006: 15.
10. O'Leary C. Fetal alcohol syndrome: Diagnosis, epidemiology, and developmental outcomes. *J Paediatr Child Health*. 2004; 40: 2–7.
11. Holman D. The value of intervention research in health promotion. Presented at the Western Australian Health Promotion Foundation *Enriching and improving health promotion research* seminar. 16 October 1996, in Perth, in Western Australia.
12. Bandura A. *Social foundations of thought and action: A social cognitive theory*. Englewood Cliffs, NJ: Prentice Hall; 1986.
13. Glanz K, Lewis F, Rimmer B (eds). *Health behaviour and health education: Theory, research and practice*. San Francisco, CA, USA: Jossey-Bass Inc; 1990.
14. Nutbeam D, Harris E. *Theory in a Nutshell. A practitioner's guide to commonly used theories and models in health promotion*. Sydney, Australia: National Centre for Health Promotion, University of Sydney; 1998.

15. Australian Institute of Health and Welfare. 2007 National Drug Strategy Household Survey: Detailed findings. Drug statistics series no. 22. Cat. no. PHE 107. Canberra, Australia: AIHW; 2007.
16. Gee V, Hu QM, Ernstzen A. Perinatal statistics in Western Australia, 2005. Twenty-third annual report of the Western Australian Midwives' Notification System. Perth, Western Australia: Department of Health; 2006.
17. Neuman WL. Social research methods: Qualitative and quantitative approaches (6th ed). Boston: Pearson; 2006.
18. Shapiro S, Wilk M, Chen H. A comparative study of various tests for normality. *J Am Stat Assoc.* 1968; 63: 1343–1372.
19. Chang G, McNamara T, Orav E et al. Brief intervention for prenatal alcohol use: A randomized trial. *Obstet Gynecol.* 2005; 105: 991–998.
20. Colman M, Colman N, Murray J. Mutual support groups to reduce alcohol consumption. *Health Mark Quart.* 1990; 7: 47–63.
21. Odendaal H, Steyn D, Elliott A, Burd L. Combined effects of cigarette smoking and alcohol on perinatal outcomes. *Gynecol Obstet Invest.* 2009; 67: 1-8.
22. Ingersoll KS. Reducing alcohol-exposed pregnancy risk in college women: Initial outcomes of a clinical trial of a motivational intervention. *J Subst Abuse Treat.* 2005; 29: 173–180.
23. Russell M, Martier S, Sokol R et al. Screening for pregnancy risk-drinking. *Alcohol Clin Exp Res.* 1994; 18: 1156–1161.
24. O'Neill S, Parra G, Sher K et al. Clinical relevance of heavy drinking during the college years. Cross-sectional and prospective perspectives. *Psychol Addict Behav.* 2001; 29: 311–321.
25. US Centers for Disease Control and Prevention, Department of Health and Human Services. Why is preconception care a public health concern? <http://www.cdc.gov/ncbddd/preconception/whypreconception.htm>. 12 April 2008. Content source: National Center on Birth Defects and Developmental Disabilities.
26. Freda M, Moos M, Curtis M. The history of preconception care: Evolving guidelines and standards. *Matern Child Health J.* 2006; 10: S43–S52.
27. Kyskan C, Moore T. Global perspectives on Fetal Alcohol Syndrome: Assessing practices, policies and campaigns in four English-speaking countries. *Can Psychol.* 2005; 46: 153–165.
28. Ebrahim S, Luman E, Floyd R, Murphy C, Bennett E, Boyle C. Alcohol consumption by pregnant women in the United States during 1988-1995. *Obstet Gynecol.* 1998; 92: 187-192.
29. Elliott E, Bower C, Payne J et al. Fetal alcohol syndrome in Australia. *Alcohol Clin Exp Res.* 2006; 30: 174A–174A.
30. Lenton S. A framework for prevention. *Drug Alcohol Rev* 2005; 24: 49–55.
31. Williams C, Perry C, Farbaksh K, Veblen-Mortenson S. Project Northlands: Comprehensive alcohol use prevention for young adolescents, their parents, school, peers and community. *J Studies Alcohol.* 1999; 13: 112–124.
32. Stade BC, Dailey C, Dzendoletas D, Sgro M, Dowswell T, Bennett D. Psychological and/or educational interventions for reducing alcohol consumption in pregnant women and women planning pregnancy. *Cochrane Database Syst Rev.* 2009; 2: CD004228. DOI: 1002/14651858.CD004228.PUB2.
33. Lui S, Terplan M, Smith EJ. Psychosocial interventions for women enrolled in alcohol treatment during pregnancy. *Cochrane Database Syst Rev.* 2008; 3: CD006753. DOI: 10.1002/14651858.CD006753.PUB2.

Appendix 4

Fathers' Role in Alcohol-Exposed Pregnancies



Systematic Review of Human Studies

Nyanda McBride, PhD,¹ Sophia Johnson, PhD²

Context: The role of paternal alcohol consumption on fetal and infant health outcomes, and on social facilitation of maternal alcohol consumption during pregnancy, has not been well established. This review identifies the range of impacts of paternal preconception alcohol consumption and alcohol consumption during partner's pregnancy, on maternal consumption, and fetal and infant health outcomes.

Evidence acquisition: The review accessed articles from the following databases: Scopus, Science Direct, Wiley Online, MEDLINE, ProQuest Central, PsycINFO, and Web of Science. The review included medium- and large-scale studies that provided separate paternal alcohol results, had a non-respondent rate $\leq 20\%$, an attrition rate $\leq 10\%$ per year of data collection up to 30%, and were published between 1990 and 2014. The review included both randomly and non-randomly selected studies, and both case-control and non-case-control studies with notation on risk of bias.

Evidence synthesis: Independent extraction and assessment of articles by two authors was conducted using predefined data fields, including study quality indicators, during 2015. Studies included in the review (11 studies, N=41,062) provide evidence that paternal alcohol consumption during preconception or during pregnancy has an impact on maternal health and alcohol consumption during pregnancy, fetal outcomes, and infant health outcomes.

Conclusions: Attention to paternal preconception health care related to alcohol consumption is an important future focus in policies dealing with reproductive, prenatal, fetal, and infant health.

(Am J Prev Med 2016;51(2):240–248) Crown Copyright & 2016 Published by Elsevier Inc. on behalf of American Journal of Preventive Medicine. All rights reserved.

Introduction

Pregnancy and fetal health have traditionally been considered the province of women. This responsibility has extended to the issue of alcohol exposure during pregnancy, with many current international alcohol policy guidelines recommending reduction or non-use of alcohol by women.^{1–5} Concerns surrounding alcohol-exposed pregnancies often relate to Fetal

Alcohol Spectrum Disorders (FASD), a range of conditions associated with alcohol-caused structural damage

behavioral, and social capacity.⁷ This systematic review focuses on paternal contribution to alcohol exposure prior to and during pregnancy. Research reports that men may play a role in social facilitation of maternal alcohol use during preconception and pregnancy, with a

U.S. study reporting that pregnant women who drink heavily are more likely to have a partner who is a heavy

drinker.⁸ A recent study among pregnant Australian

er. to the fetal brain⁶ leading to reduced intellectual,

From the ¹National Drug Research Institute, Faculty of Health Sciences, Curtin University, Perth, Western Australia, Australia; and ²National Drug Research Institute, Curtin University, Perth, Western Australia, Australia Address correspondence to: Nyanda McBride, PhD, National Drug Research Institute, Faculty of Health Sciences, Curtin University, GPO Box U1987, Perth WA 6845 Australia. E-mail: n.mcbride@curtin.edu.au. 0749-3797/\$36.00
<http://dx.doi.org/10.1016/j.amepre.2016.02.009>

women reported that more than 75% of women who drank during pregnancy usually drank with their partner, and that 40% of drinking occasions were initiated by their male partner.⁹ Social determinants research also links paternal and maternal drinking, recent maternal drug use,¹⁰ high life stress,^{11,12} maternal psychopathology,¹³ custodial changes, current drug use in the home, and exposure to violence.¹⁴ Several of these findings have a level of implicit partner involvement. Animal studies contribute to the picture of biological fathers having a role in alcohol-exposed pregnancies with reports of an

association between alcohol and poor sperm development,^{15,16} alcohol and fetal vulnerability to low body weight,¹⁷ as well as on physical and mental development of offspring, even in the absence of maternal alcohol exposure.^{18,19}

Methods

Objective

The objective of this study was to identify well-conducted primary studies with human populations, across several domains that report findings on paternal contribution to alcohol-exposed pregnancies and its association with maternal alcohol consumption, and fetal and infant outcomes.

Parameters

This review accessed primary studies published in peer-reviewed journals between 1990 and 2014. Several databases were used to detect studies. These included Scopus, Science Direct, Wiley Online, MEDLINE, ProQuest Central, PsycINFO, and Web of Science. A variety of key words were used to search for primary studies. The following combinations were most effective in finding relevant articles: *fetal alcohol spectrum disorder* (♢father, ♢sperm, ♢paternal, ♢father, paternal alcohol consumption), *paternal alcohol effect* (♢embryo, ♢fetus), *preconception* (♢fetal alcohol, ♢paternal alcohol), and *fetal alcohol* (♢sperm, ♢father).

The selection criteria included published peer-reviewed journal article; good-quality research design; reported on paternal effect separate from maternal effect; reported on preconception, prenatal, fetal, and infant outcomes prior to primary school age (6 years); and published between 1990 and 2014. Good-quality research design was determined by the inclusion of case/control;

random allocation to case/control (Table 1); sample size deter-

mined by power calculations; a low non-respondent rate (to reduce selection bias); a low attrition rate (to reduce attrition bias); representativeness; scale (a combination of sample size and extensiveness of study jurisdiction); time period; and source or report. Study design criteria required a non-respondent rate <20% (unless differences between respondents and non-respondents were assessed and no statistically significant difference was reported, or sample size was based on power analysis and random selection applied) and an attrition rate <10% per year of data collection up to 30%. When selection criteria were not provided, earlier reports or author contact occurred to gain required detail. Two researchers

These are identified when results are premised by the term *adjusted*. Periphery suppositions made by study authors and secondary un hypothesized findings are not included in this review.

Results

The initial database search identified 150 potentially relevant publications. After deleting duplicates, and on assessment of the whole article, 11 primary studies were accepted into the review (Figure 1).

Summary of Included Studies

Table 1 provides an overview of the studies accepted into the review. In summary, of the 11 studies accepted into the review, the majority were conducted in the U.S. (n/45). Three studies were conducted in the last 5 years. Four studies were large population studies, five were prospective studies, and five studies included case-control designs. Eight studies used paternal reports on paternal alcohol consumption. A total of 35,080 cases (41,062 with controls) were included in this review (two studies drawing from the same parent study counted once [noted with subscript]). Given the range of review criteria, some studies within the review have been identified as having lower risk of bias (n/46) and others as having a higher risk of bias (n/45) in the context of this review (italicized in Table 1). Risk of bias was determined by a series of additional criteria: random selection, case/control, and population base.

Table 2 provides a summary of the epidemiologic tenants of causality related to the findings of this review.

These tenants are based on Hill's summation. However,

independently ranked each study for acceptance during 2015.

Method of Analysis

No data transformation was undertaken during the analysis stage. Results were combined under six themes. Three themes are reported in this review: (1) paternal social facilitation of maternal drinking, and relationship quality; (2) effects of alcohol on sperm health; and (3) impacts on fetal/infant health. The strength of findings is based on the number of studies contributing to a finding while taking into account studies with less risk of bias and studies with potentially greater risk of

bias (noted in italics, Table 1). Several studies controlled for confounding factors/moderators during analysis.

it should be noted that the epidemiologic tenants of causality list is not intended to be a checklist or definitive criteria for causality.^{31,32}

Paternal Social Facilitation of Maternal Drinking and Relationship Quality

Three studies reported on paternal alcohol consumption and its effects on maternal consumption, social facilitation of maternal consumption, and the quality of relationship on maternal consumption. One study was a large-scale study,²¹ one a medium-scale study,²³ and the other a small-scale study.²⁰ Two studies highlighted that women who drank during pregnancy were more likely to have a live-in male partner who consumed alcohol.^{20,23} Bakhireva and colleagues²⁰ in their Ukraine study further reported that 51.2% of pregnant women drank if their male partner was a heavy or frequent drinker (adjusted $p < 0.001$); that pregnant women who consumed alcohol in the most recent 2 weeks of pregnancy were more likely to have a partner who was a risky drinker or had signs of an alcohol problem (adjusted $p < 0.001$); and that risky paternal drinking was significantly associated with continued maternal drinking (AOR/434.1).

Table 1. Accepted Studies: Citation, Country, Perspective, Study Design/Potential Bias

Citation of primary study	Country	Perspective	Study design
<i>Bakhireva et al. (2011)</i> ²⁰	Ukraine	Impact of paternal drinking on maternal drinking and relationship by maternal drinking risk level Maternal report (18–19 weeks' gestation) Paternal age: not provided	Cross-sectional baseline cohort from larger study Small scale: two prenatal clinics n ¹ /4166 (78% of eligible cases—demographics of non-respondents not significantly different from study cohort) No random selection No case-control Time period: one data collection point
<i>Czeizel et al. (2013)</i> ²¹	Hungary	Paternal preconception care Paternal report / biomedical data Paternal age: mean 29.5–35.9 years in 1984–1989 and 1998–2010, respectively	Prospective study Large scale: population, country wide N ¹ /420,603 (81.4% of eligible cases) No case control (but compared to national data) Time period: multiple data and medical collection points
<i>Frey et al. (2012)</i> ²²	U.S.	Paternal preconception care Paternal report Paternal age: mean 34 years	Quantitative study Small scale: two primary care practices N ¹ /4132 (99% of eligible cases) No random selection Case-control—n/a Time period: one data collection point
<i>Klonoff-Cohen et al. (2003)</i> ^{23,a}	U.S.	Impact of paternal consumption on IVF and GIFT Paternal report Paternal age: 38.3 years	Prospective study (past and current exposure) Medium scale: six fertility centers N ¹ /4221 couples (91% of eligible cases) No random selection No case-control Time period: data collected in the first 2 weeks of treatment; outcome measured as it occurred (within a 6-month period) ^a
<i>Milne et al. (2013)</i> ²⁴	Australia	Impact of paternal alcohol consumption on offspring—early childhood (acute lymphoblastic leukemia) Paternal/maternal reports High non-respondent rate for brain tumor therefore not included Paternal age: case; 0–25 years 6.4%, 25–34 years 61.7%, 35+ years 17%	Retrospective study Medium scale: 10 pediatric oncology centers N ¹ /4416 cases (80% eligible cases), n ¹ /4750 paternal data control (matched, 60% of eligible controls) Controls randomly selected Case-control Time period: one data collection point; outcome measured from medical records
<i>Passaro et al. (1998)</i> ²⁵	England	Impact of paternal alcohol consumption on offspring—preconception Paternal age: 0–20 years 1.1%, 20–29 years 45.2%, 30–39 years 47.1%, 40–49 years 6.1%, 50+ years 0.5% Paternal/maternal report	Longitudinal study Large scale: one county N ¹ /47,756 (90% of all eligible women, 81% of all eligible men) No random selection No case-control Time period: 18 weeks' gestation, outcome post birth record ^a
<i>Roeleveld et al. (1992)</i> ²⁶	Netherlands	Impact of paternal alcohol consumption on offspring—early childhood Paternal/maternal report Paternal age: 30.3 years (at birth of child)	Retrospective study Medium scale: medical files one region N ¹ /4340 cases (90% of eligible cases), N ¹ /4362 children control (not matched) 89% of eligible controls) No random selection Case-control Time period: medical records (0–15-year-olds), one data collection parental interview

(continued on next page)

Table 1. Accepted Studies: Citation, Country, Perspective, Study Design/Potential Bias (*continued*)

Citation of primary study	Country	Perspective	Study design
Steinberger et al. (2002) ²⁷	U.S.	Impact of paternal alcohol consumption on offspring—infant Medical and parental report Paternal age: 11–20 years 6.25%, 21–30 years 60.4%, 31–40 years 31.25%, 41–63 years 2.1%	Retrospective study Large scale: three-state population study (partial in two) N¼ Of 4,390 cases in original study, 55 had this condition (all eligible cases). N¼3,572 control (95% of eligible cases from first or second selection) Random selection (control) Case-control Time period: medical record (0–1-year-olds), one data collection parental interview
<i>Henriksen et al. (2004)²⁸</i>	Denmark	Impact of paternal alcohol consumption on fetus Paternal/maternal reports Paternal age: r29–29%, Z30–30%	Prospective study Large scale: nationwide recruitment N¼430 cases (100% of eligible cases) No random selection No case-control Low N due to low population prevalence Time period: 0, monthly for up to 6 months or until pregnant, then at time of spontaneous abortion
Windham et al. (1995) ^{29,a,b}	U.S.	Impact of paternal alcohol consumption on offspring—infant Maternal report Paternal age: not provided ^a	Prospective study Medium scale: 11 hospital laboratories N=Cases 1,233 (97% of eligible cases), N=Control 1,300 (matched) (88% of eligible cases) Random selection (control) Case-control Time period: medical records; one data collection interview
Windham et al. (1992) ^{30,a,b}	U.S.	Impact of paternal alcohol consumption on fetus Maternal report Paternal age: not provided ^a	Prospective study Medium scale: 11 hospital laboratories N=Cases 626 (81% of eligible cases), N=Control 1,300 (matched) (88% of eligible cases) Random selection (control) Case-control Time period: medical records; one data collection interview

Note: Italicized, higher risk of bias in the context of this paper.

^aAuthor contacted.

^bDrawn from same study.

GIFT, gamete intrafallopian transfer; IVF, in vitro fertilization.

Although risky paternal drinking was associated with continued maternal drinking during pregnancy, risky paternal drinking was also associated with risky maternal drinking but mothers quitting on knowledge of pregnancy (AOR¼27.1). However, the strength of association was greatest between risky paternal drinking and continued maternal drinking during pregnancy.

The quality of the couple’s relationship also had an impact on maternal drinking. Bakhireva et al.²⁰ found that women who reported significantly less satisfaction with their relationship (adjusted *p*¼0.001) and who reported less ability to discuss relationship problems (adjusted *p*¼0.032) were more likely to continue drinking during pregnancy (AOR¼34.1).

In a large-scale study reporting on a preconception health clinic in Hungary,²¹ the social influence of male

partners was also reported. If male partners were actively supportive of involvement, then women were nearly 20% more likely to actively follow the preconception health-care protocol provided at the clinic, including reducing alcohol consumption.

Effects of Alcohol on Sperm Health

One large-scale²¹ and one medium-scale study²³ provided information about the effects of alcohol on sperm health. The medium-scale study conducted in the U.S.²³ reported that low-level use of alcohol by men on in vitro fertilization (IVF) or gamete intrafallopian transfer (GIFT) did not have a significant effect on sperm count, motility, morphology, the number of fertilized oocytes, the number of transferred embryos, achievement of pregnancy, development of multiple births, or infant

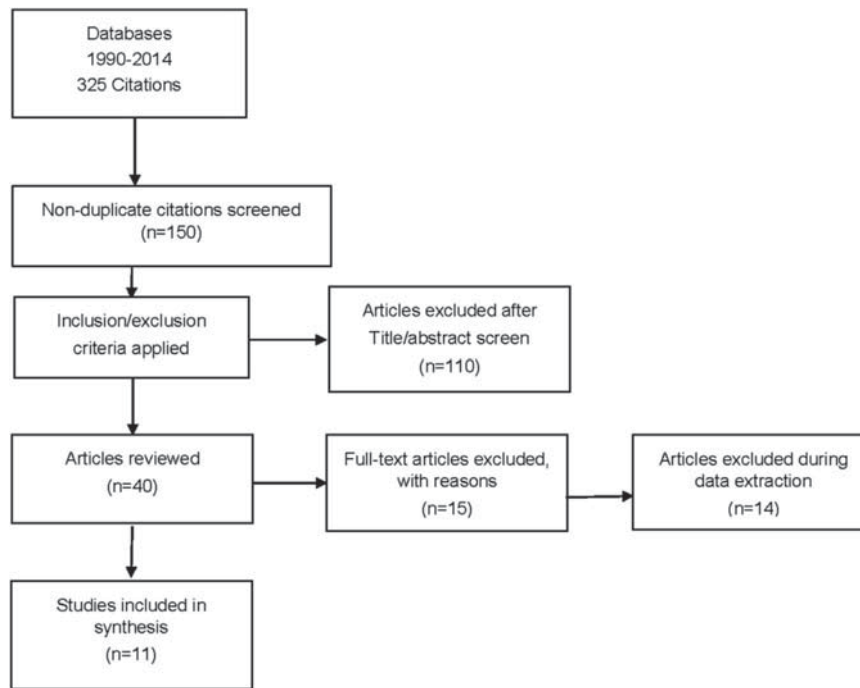


Figure 1. PRISMA flow chart.

gestational age. However, drinking by men in the period prior to undergoing IVF or GIFT was highly associated with failure to achieve a live birth and spontaneous

miscarriage (described further in the next section). This

association was evident in the week before sperm collection with an increase in one can of beer (AOR¹/45.64, *p*¹/0.02) and in the week before sperm collection with an increase of 12 g of alcohol per day (AOR¹/38.04, *p*¹/0.01), respectively.²³

Secondary findings from a large-scale study in Hungary²¹ noted that in a voluntary sperm sample from 76.1% (N¹/15,680) of men involved in the study, there was a decline in the mean number of spermatozoa, compared with the Hungarian average, with a substantial reduction between 1984 and 1993. There was also a significant increase in underdeveloped spermatozoa (11%–31%) between 1984 and 1993 but no further decrease after this date.

Impacts on Fetal/Infant Health

Seven studies contributed information about the impacts of paternal alcohol consumption on fetal and infant health. Three of these studies were large-scale studies, and the remainder were medium-scale studies (two medium-scale studies were drawn from the same parent study and are denoted by subscript indicators *a*, *a1*, and *a2* hereafter). All seven studies focused on preconception paternal consumption, with four studies_a also reporting on paternal alcohol consumption during pregnancy and

one of these including post-pregnancy data. Three studies reported on spontaneous abortion,^{23,28,30}_{a1} two on birth weight,^{25,29}_{a2} and single studies reported on live birth,²³ gestational mental retardation,²⁶_a age,²⁹ single

heart ventricle,²⁷ and acute lymphoblastic leukemia.²⁴

Klonoff-Cohen and colleagues²³ reported in their study of the effects of paternal preconception alcohol consumption on spontaneous abortion and live birth that paternal consumption 1 month (AOR¹/42.28, *p*¹/0.03) and 1 week before IVF or GIFT (AOR¹/2.43, *p*¹/0.04), and paternal consumption during Week 1 of IVF or GIFT (AOR¹/3.14, *p*¹/0.02), and 1 week before sperm collection (AOR¹/8.32, *p*¹/0.01) significantly decreased chances of live birth when several confounders were controlled. This result was more pronounced when the male partner drank more alcohol per day (Z12 g vs 012

g) in all time periods except 1 year before Day 1 of IVF or GIFT. When this same level of alcohol was considered for miscarriages, there was an increase in miscarriages

1 week before IVF or GIFT attempt (AOR¹/3.99, *p*¹/0.04), Week 1 of IVF or GIFT (AOR¹/5.97, *p*¹/0.02), and during the week of sperm collection (AOR¹/38.04, *p*¹/0.01). Additionally, an increase in one can of beer 1 month before IVF or GIFT (AOR¹/2.70, *p*¹/0.04), during Week 1 of IVF or GIFT (AOR¹/8.24, *p*¹/0.03), or during the week of sperm collection (AOR¹/45.64, *p*¹/0.02) resulted in more risk to live birth outcome. Hendrickson et al.²⁸ also found that male alcohol intake was associated with increased risk of spontaneous abortion. In this

Table 2. Review Findings Related to Epidemiologic Tenants of Causality

	Strength	Consistency	Specificity	Temporality	Biological gradient	Plausibility	Coherence	Experimental	Analogy
Paternal social facilitation of maternal drinking, and relationship quality	High	High	High	Present	Present	High	Present	Yes	Limited
Effects of alcohol on sperm health	Moderate	Needs replication	High	Present	Present	Moderate	Present	No human studies	Limited
Impacts on fetal/infant health									
Spontaneous abortion	High	High	High	Present	Present	Theoretical	Present	No human studies	Limited
Acute lymphoblastic leukemia	Moderate	Needs replication	Moderate	Present	Present	Theoretical	Unknown	No human studies	Limited
Ventricle malformation	Moderate	Needs replication	Moderate	Present	Present	Theoretical	Unknown	No human studies	Limited
Live birth	Moderate	Needs replication	Moderate	Present	Present	Theoretical	Unknown	No human studies	Limited
Low birth weight	Low	Low	Low	Present	Present	Theoretical	Unknown	No human studies	Limited

McBride and Johnson / Am J Prev Med 2016;51(2):240-248

Note: Caveat: The Epidemiologic Tenants of Causality list is not intended to be a checklist or definitive criteria for causality.^{31,32}

Strength (effect size): A small association does not mean that there is not a causal effect, though the larger the association, the more likely that it is causal. Consistency (reproducibility): Consistent findings observed by different persons in different places with different samples strengthens the likelihood of an effect.

Specificity: Causation is likely if there is a very specific population at a specific site and disease with no other likely explanation. The more specific an association between a factor and an effect is, the bigger the probability of a causal relationship.

Temporality: The effect has to occur after the cause (and if there is an expected delay between the cause and expected effect, then the effect must occur after that delay).

Biological gradient: Greater exposure should generally lead to greater incidence of the effect. However, in some cases, the mere presence of the factor can trigger the effect. In other cases, an inverse proportion is observed: greater exposure leads to lower incidence.

Plausibility: A plausible mechanism between cause and effect is helpful (knowledge of the mechanism is limited by current knowledge).

Coherence: Coherence between epidemiologic and laboratory findings increases the likelihood of an effect (lack of such [laboratory] evidence cannot nullify the epidemiologic effect on associations).

Experiment: Occasionally it is possible to request to experimental evidence.

Analogy: The effect of similar factors may be considered.

study, men who consumed ten or more drinks per week during preconception had two to five times increased risk of spontaneous abortion than men who did not drink during preconception when several confounders were taken into account (adjusted relative risk, 4.4; 95% CI/4.5, 12.6, $p < 0.05$). In their earlier study, Windham

and colleagues³⁰ also found paternal preconception

consumption at Z14 drinks per week (AOR/4.12, 95% CI/0.84, 1.7), and between one and six drinks per week (AOR/4.12, 95% CI/0.95, 1.6) resulted in higher risk of spontaneous abortion (OR/4.12).

The two studies that reported on the association between paternal preconception alcohol consumption and birth weight had contrasting findings. The 1998 large-scale study by Passaro et al.²⁵ found no association between drinking and non-drinking male partners and birth weight; however, it was noted that the low number of high-level drinking fathers is likely to have impacted

on the results. Windham and colleagues²⁹ noted an

increased risk of low birth weight and gestational age when more alcohol per week was consumed: one to 13 drinks per week (AOR/4.12, 95% CI/0.7, 1.9); 14–20 drinks per week (AOR/4.13, 95% CI/0.5, 2.9); and Z21 drinks per week (AOR/4.14, 95% CI/0.7, 2.6).

Of the three studies reporting on single health effects of paternal prenatal alcohol consumption, one reported a nil effect and two an association. Roeleveld et al.²⁶ found that there was no association with paternal preconception (to 6 months postnatal) consumption of alcohol with mental retardation of offspring. Milne and colleagues²⁴ reported a U-shaped relationship with the amount of paternal alcohol consumption in the 12 months prior to pregnancy and risk of acute lymphoblastic leukemia, and no risk with maternal alcohol consumption. The paternal association is reported to have been highest with beer intake between Z21 to 28 beers per week (AOR/2.07, 95% CI/0.96, 4.45, $p < 0.03$) and at any alcohol intake and beer at Z28 days per week (AOR/4.120, 95% CI/0.79, 1.83, $p < 0.005$, and

AOR/4.123, 95% CI/0.73, 2.05, $p < 0.03$, respectively). Steinberger et al.²⁷ reported that all cases of ventricle malformation were associated with daily preconception paternal alcohol consumption (median unbiased OR/42.0, 95% CI/4.1, 3.9, $p < 0.019$) and that cases of abnormal situs were also associated with paternal preconception alcohol use (median unbiased OR/43.0, 95% CI/4.1, 11.1, $p < 0.04$).

Discussion

The overarching findings from this review conclude that paternal alcohol use by a live-in male partner is associated

with maternal alcohol consumption during pregnancy, and that preconception alcohol use by the biological father can impact sperm, fetal, and infant health.

The following summary of evidence is based on well-conducted studies, with all studies meeting the inclusion criteria of the review. Therefore, notation of “higher risk

of bias” is relevant to this inclusion and in comparison to

“low risk of bias” studies in this review only, rather than to studies that were rejected as part of this review’s criteria and process.

The effects of paternal alcohol consumption on sperm health, impacts on fetal/infant health, and maternal drinking and relationship quality during pregnancy are noted in two, seven, and three studies, respectively, indicating a moderate to high level of replication and evidence of association. One of the two studies contributing information about sperm health was particularly useful in helping to define level of preconception use on

pregnancy, birth, and infant outcomes, noting that spon-

aneous abortion and failure of live birth was significantly associated with paternal preconception alcohol use during Week 1 of IVF/GIFT, and even more so at 1 week before sperm collection, and that this result was higher when male partners drank more alcohol per day. In particular, men who drank ten or more drinks per week during preconception had a two to five times increased risk of spontaneous abortion than men who did not during this period. The findings from this study indicated that the most critical period for paternal alcohol consumption and negative outcome was 1 week before sperm collection. Various studies in the review make some suggestions as to why this association might occur such as DNA damage to sperm; however, they provide limited direct evidence. A recent systematic review and meta-analysis reported that alcohol has a direct impact on sperm volume, with uncertain findings on sperm density, count, progressive motility, and morphology.³³ Together, these findings indicate that alcohol is a modifiable risk factor for sperm quality and pregnancy outcome. Further replication is required to strengthen evidence of paternal alcohol consumption, sperm health, and impacts on fetal and infant health. However, given the indicative nature of the findings in this area, policies recommending biological fathers to reduce or abstain from alcohol during the preconception phase, particularly during the period of sperm development prior to conception, have value.

Other impacts of fetal/infant health are reported in seven studies, five of which have a low risk of bias, and three reporting single health effects. Results provide evidence of association between paternal preconception alcohol consumption and impact on several measured fetal/infant health indicators, particularly with replicated evidence on spontaneous abortion at both low and

moderate levels of paternal preconception alcohol use (two higher risk of bias studies, one low risk of bias study). Single study findings provide some evidence that paternal preconception alcohol use is associated with acute lymphoblastic leukemia at high-level use (without maternal use); ventricle malformation with daily use; and live birth, low birth weight, and low gestational age with low and moderate paternal preconception alcohol use. However, the results focusing on low birth weight need to be considered in light of another study on low birth weight that found no association. These findings have research and translation implications, with single study and conflicting study results requiring further research clarification and conservative application to policy, but with replicated findings providing important evidence of appropriate translation to policy, particularly that focused on paternal preconception (i.e., during sperm development period and period of conception attempt) with low and moderate use of alcohol. Prospective preconception cohorts, which measure quantity, frequency, and timing of paternal (and maternal) alcohol consumption at regular stages during preconception and pregnancy, would provide valuable information on impacts to fetal and infant health that go beyond single health issue studies.

The impact of paternal alcohol consumption on social facilitation of maternal drinking and quality of relationship were reported in three studies, two of which reported that women were more likely to drink during pregnancy if their male partner drank, with maternal prevalence of drinking increasing if their partner was a frequent of heavy drinker. Four studies included in this review reported on prevalence of paternal alcohol consumption, suggesting that between 77% and 96% of men drank during their partner's pregnancy. These replicated findings on paternal/male partner social facilitation of maternal drinking during pregnancy have important translational impact, particularly to policies related to reducing maternal alcohol consumption during maternal preconception care (not replicated) and pregnancy (replicated) and for their association with FASD prevention.

Limitations

This review has several limitations associated with the review selection criteria, in particular bias related to the non-selection of unpublished data and non-English language articles. Furthermore, the review's selection criteria purposefully selected high-quality studies that were not limited to RCTs or clinical controlled trials. Attempts were made to keep selection bias to a minimum with criteria requiring $\geq 20\%$ or non-respondent rate with comparison between non-respondent and respondents, or to the general population, and by requiring $\leq 10\%$ attrition in a 1-year period. Potential limitations

related to the individual studies include possible survey bias when validity and reliability of survey items were not included in the publication. In addition, studies on paternal contribution to alcohol-exposed pregnancies have not, to date, included confounding factors associated with tri-generational exposure (neither maternal nor paternal). Finally, most of the studies in this review did not control for other parental drug use during preconception or prenatally.

Although there are a range of findings from well-conducted studies that met the criteria for inclusion in this review, the date of publication and origin of cohorts suggest that future research on more-contemporary populations from a range of nations would be beneficial. In particular, future studies would benefit from a range of international studies on paternal prevalence and pattern of alcohol use during preconception, pregnancy, and postpartum and their impact on sperm health; women's level of preconception, pregnancy, and postpartum (during breastfeeding) alcohol use; and fetal and infant health. In addition to other study design issues that contribute to quality, future studies should ensure a low non-respondent rate; random selection of cohorts (and where appropriate random allocation to case and control); the inclusion of case and matched control; and attrition $\leq 10\%$ each year. That only five of 11 studies in this review are considered as having a low risk of bias, and that 17 additional studies that had the potential for inclusion were rejected because of methodologic limitations, suggest that attention to focusing funding on well-designed studies is essential to forward this field of research.

Conclusions

The focus of this review provided the scope to overview several domains that contributed to understanding about prenatal alcohol use and its impact on maternal alcohol consumption and fetal and infant health. The results indicate that paternal preconception and prenatal alcohol use has various impacts on maternal prenatal health behaviors, fetal health outcomes, and infant health. It is therefore important to recognize that decisions about alcohol use during preconception and pregnancy are not the sole responsibility of women but occur within the context of the home and the broader social environment, and thus require more complex policy to assist in reducing alcohol-exposed pregnancies and increasing the potential for healthy fetal and infant outcomes.

The review found that this area of research is largely underdeveloped and could benefit from a comprehensive range of studies to develop the field. Similarly, the review found that the research that has been done to date has

August 2016

not been translated into policy or practice in any standardized or meaningful way.⁵

No financial disclosures were reported by the authors of this paper.

References

1. National Health and Medical Research Council. *Australian Guidelines to Reduce Health Risk From Drinking Alcohol*. Canberra: National Health and Medical Research Council, 2009.
2. UK House of Commons Science and Technology Committee. *Alcohol Guidelines*. London: The Stationery Office Limited by the authority of the House of Commons, 2012.
3. U.S. Department of Agriculture, U.S. DHHS. *Dietary Guidelines for Americans*. Washington, 2010. 7th ed. Washington, DC: U.S. Government Printing office, 2010.
4. Butt P, Beimes D, Gilksman L, Paradis C, Stockwell T. *Alcohol and Health in Canada: A Summary of Evidence and Guidelines for Low Risk Drinking*. Ottawa: Canadian Centre on Substance Abuse, 2011.
5. International Alliance for Responsible Drinking. *International Guidelines on Drinking and Pregnancy*. www.iard.org/Policy. Published 2015. Accessed June 15, 2015.
6. Streissguth A, Barr H, Kogan J, Bookstein F. *Understanding the Occurrence of Secondary Disabilities in Clients With Fetal Alcohol Syndrome (FAS) and Fetal Alcohol Effects (FAE): Final Report to the Centers for Disease Control and Prevention on Grant No. R04/CCR008515 (Tech. Report no. 96-06)*. Seattle, WA: University of Washington, Fetal Alcohol and Drug Unit, 1996.
7. Streissguth A, Bookstein F, Barr H, Sampson P, O'Malley K, Young J. Risk factors for adverse life outcomes for fetal alcohol syndrome and fetal alcohol effects. *J Dev Behav Pediatr*. 2004;25(4):228–238. <http://dx.doi.org/10.1097/00004703-200408000-00002>.
8. McLeod J. Spouse concordance for alcohol dependence and heavy drinking: evidence from a community sample. *Alcohol Clin Exp Res*. 1993; 17:11346–11355. <http://dx.doi.org/10.1111/j.1530-0277.1993.tb05220.x>.
9. McBride N, Carruthers S, Hutchinson D. Reducing alcohol use during pregnancy: listening to women who drink as an intervention starting point. *Glob Health Promot*. 2012;19(2):6–18. <http://dx.doi.org/10.1177/1757975912441225>.
10. Accornero V, Morrow C, Bandstra E, Johnson A, Anthony J. Behavioral outcome of preschoolers exposed prenatally to cocaine: role of maternal behavioural health. *J Psychiatr Psychol*. 2002;27(3):259–269. <http://dx.doi.org/10.1093/jpepsy/27.3.259>.
11. Lewis PT, Shipman VC, May PA. Socioeconomic status, psychological distress, and other maternal risk factors for fetal alcohol spectrum disorders among American Indians of the northern plains. *Am Indian Alsk Native Ment Health Res*. 2011;17(2):1–21. <http://dx.doi.org/10.5820/aian.1702.2011.1>.
12. May PA, Gossage JP. Maternal risk factors for fetal alcohol spectrum disorders: not as simple as it might seem. *Alcohol Res Health*. 2011;34 (1):15–26.
13. Sood B, Delaney-Black V, Covington C, et al. Prenatal alcohol exposure and childhood behaviour at age 6 to 7 years: I. dose-response effect. *Pediatrics*. 2001;108:e34. <http://dx.doi.org/10.1542/peds.108.2.e34>.
14. Delaney-Black V, Covington CY, Templin T, et al. Teacher-assessed behaviour of children prenatally exposed to cocaine. *Pediatrics*. 2000;106(4):782–791. <http://dx.doi.org/10.1542/peds.106.4.782>.
15. Tanaka H, Suzuki N, Arima M. Experimental studies on the influence of male alcoholism on foetal development. *Brain Dev*. 1982;4:1–6. [http://dx.doi.org/10.1016/S0387-7604\(82\)80094-6](http://dx.doi.org/10.1016/S0387-7604(82)80094-6).

16. Jamerson P, Wulser M, Kimler B. Neurobehavioural effects in rat pups whose sires were exposed to alcohol. *Brain Res Dev Brain Res.* 2004;149:103–111. <http://dx.doi.org/10.1016/j.devbrainres.2003.12.010>.
17. Sittig LJ, Redei EE. Paternal genetic contribution influences fetal vulnerability to maternal alcohol consumption in a rat model of fetal alcohol spectrum disorder. *PLoS One.* 2010;5(4):e10058. <http://dx.doi.org/10.1371/journal.pone.0010058>.
18. Haycock P. Fetal alcohol spectrum disorders: the epigenetic perspective. *Biol Reprod.* 2009;81(4):607–617. <http://dx.doi.org/10.1095/biolreprod.108.074690>.
19. Ouko LA, Shantikumar K, Knezovich J, Haycock P, Schnugh DJ, le Ramsay M. Effect of alcohol consumption on CpG methylation in the differentially methylated regions of H19 and IG-DMR in male gametes—implications for fetal alcohol spectrum disorders. *Alcohol Clin Exp Res.* 2009;33(9):1615–1627. <http://dx.doi.org/10.1111/j.1530-0277.2009.00993.x>.
20. Bakhireva L, Wilsnack S, Kristjanson A, et al. Paternal drinking, intimate relationship quality, and alcohol consumption in pregnant Ukrainian women. *J Stud Alcohol Drugs.* 2011;72(4):536–544. <http://dx.doi.org/10.15288/jsad.2011.72.536>.
21. Czeizel A, Czeizel B, Vereszkey A. The participation of prospective fathers in preconception care. *Clin Med Insights Reprod Health.* 2013;7:1–9. <http://dx.doi.org/10.4137/CMRH.S10930>.
22. Frey KA, Engle R, Noble B. Preconception healthcare: what do men know and believe? *J Mens Health.* 2012;9(1):25–35.
23. Klonoff-Cohen H, Lam-Kruglick P, Conzalez C. Effects of maternal and paternal alcohol consumption on the success rates of in vitro fertilization and gamete intrafallopian transfer. *Fertil Steril.* 2003;79(2):330–339. [http://dx.doi.org/10.1016/S0015-0282\(02\)04582-X](http://dx.doi.org/10.1016/S0015-0282(02)04582-X).
24. Milne E, Creenop K, Scott R, et al. Parental alcohol consumption and risk of childhood acute lymphoblastic leukaemia and brain tumours. *Cancer Causes Control.* 2013;24(2):391–402. <http://dx.doi.org/10.1007/s10552-012-0125-5>.
25. Passaro K, Little R, Savitz D, Noss J. Effect of paternal alcohol consumption before conception on infant birth weight. *Teratology.* 1998;57(6):294–301. [http://dx.doi.org/10.1002/\(SICI\)1096-9926\(199806\)57:6<294::AID-TERA243.0.CO;2-X](http://dx.doi.org/10.1002/(SICI)1096-9926(199806)57:6<294::AID-TERA243.0.CO;2-X).
26. Roeleveld N, Vingerhoets E, Zielhuis G, Gabreels F. Mental retardation associated with parental smoking and alcohol consumption before, during, and after pregnancy. *Prev Med.* 1992;21(1):110–119. [http://dx.doi.org/10.1016/0091-7435\(92\)90010-F](http://dx.doi.org/10.1016/0091-7435(92)90010-F).
27. Steinberger E, Ferencz C, Loffredo C. Infants with single ventricle: a population-based epidemiological study. *Teratology.* 2002;65(3):106–115. <http://dx.doi.org/10.1002/tera.10017>.
28. Henriksen T, Hjollund N, Jensen T, et al. Alcohol consumption at the time of conception and spontaneous abortion. *Am J Epidemiol.* 2004;160(7):661–667. <http://dx.doi.org/10.1093/aje/kwh259>.
29. Windham G, Fenster L, Hopkins B, Swan S. The association of moderate maternal and paternal alcohol consumption with birth-weight and gestational age. *Epidemiology.* 1995;6(6):591–597. <http://dx.doi.org/10.1097/00001648-199511000-00005>.
30. Windham G, Fenster L, Swan S. Moderate maternal and paternal alcohol consumption and the risk of spontaneous abortion. *Epidemiology.* 1992;3(4):364–370. <http://dx.doi.org/10.1097/00001648-199207000-00012>.
31. Hill AB. The environment and disease: association or causation. *Proc R Soc Med.* 1965;58(5):295–300.
32. Kundi M. Causality and the interpretation of epidemiological evidence. *Environ Health Perspect.* 2006;114(7):969–974. <http://dx.doi.org/10.1289/ehp.8297>.
33. Ying L, Hui L, Yafei L, Jia C. Association between socio-psychological factors and male semen quality: systematic review and meta-analyses. *Fertil Steril.* 2011;95(1):116–123. <http://dx.doi.org/10.1016/j.fertnstert.2010.06.031>.