UNIVERSITY OF CALIFORNIA, SAN DIEGO

SAN DIEGO STATE UNIVERSITY

Fetal Alcohol Spectrum Disorder (FASD) Prevention among AI/AN Women in San Diego County

A dissertation in partial satisfaction of the requirements for the degree

Doctor of Philosophy

in

Public Health (Epidemiology)

by

Annika C. Montag

Committee in charge:

University of California, San Diego
- Professor Christina D. Chambers, Chair
- Professor Matthew A. Allison
- Professor Andrew D. Hull
- Professor Kenneth Lyons Jones

San Diego State University
- Professor John E. Alcaraz
- Professor Stephanie K. Brodine

2014

The Dissertation of Annika C. Montag is approved, and it is acceptable in quality and form for publication on microfilm and electronically:

_____

_____

_____

_____

_____

_____

Chair

University of California, San Diego

San Diego State University

2014

TABLE OF CONTENTS

LIST OF ABBREVIATIONS

AEP: Alcohol-Exposed pregnancy

AIAN or AI/AN: American Indian / Alaska Native

ARBD: Alcohol-Related Birth Defects

ARND: Alcohol-Related Neurodevelopmental Disorder

CDC: Centers for Disease Control and Prevention

CHOICES: Changing High-Risk AlcOhol Use and Increasing Contraception Effectiveness Study

FASD: Fetal Alcohol Spectrum Disorder

FAS: Fetal Alcohol Syndrome

NARCH: Native American Research Centers for Health

NIH: National Institutes of Health

NOFAS: National Organization for Fetal Alcohol Syndrome

PAE: Prenatal alcohol exposure

PFAS: Partial Fetal Alcohol Syndrome

PHQ-9: 9-item Patient Health Questionnaire

SBIRT: Screening, Brief Intervention, and Referral to Treatment

SCTHC: Southern California Tribal Health Clinics (pseudonym)

T-ACE: Tolerance, Annoyed, Cut down, Eye-opener

TRD: Treatment Recommendation for Depression

WIC: Women, Infants, and Children

LIST OF TABLES

LIST OF FIGURES

ACKNOWLEDGEMENTS

I would like to express my deep gratitude to Dr. Tina Chambers for her patient guidance, mentorship, and prompt replies to my many questions. Talented, knowledgeable, and undaunted by last minute panics, she is an exceptional role model. My love of perinatal epidemiology is entirely due to her nurturing.

I offer my sincere appreciation to Dr. Stephanie Brodine for introducing me to the Southern California Native community and to the wonderful world of global health including infectious disease epidemiology; to Dr. Kenneth Lyons Jones for sharing his vast expertise and enthusiasm; to Dr. John Alcaraz for his clear, valuable statistical suggestions and explanations; to my friend Dr. Gail Laughlin and Dr. Richard Shaffer for interesting discussions and for teaching me how hands-on epidemiology is done; and to Dr. Matthew Allison, Dr. Andrew Hull, and Dr. John Clapp for their support and valuable input.

I can't express enough thanks to the wonderful project research associates, Tribal community members, and Tribal IRB members whose insights, enthusiasm, and generous sharing of knowledge were much appreciated and vital to the success of the project.

My thanks to Florencia Davis, Hollie Ward, and Kristin Deveraux for getting me out of (administrative) trouble with some regularity.

To friends who kept me sane and convinced me this degree was a feasible endeavor: dig ugs!

Lastly, I acknowledge the unwavering love and encouragement I receive from my family with whom everything is a grand adventure.

Chapters from this dissertation have been or will be submitted for publication. The dissertation author was the primary investigator and author of these papers.

Chapter 2, in full, has been submitted for publication of the material as it may appear in Maternal and Child Health Journal, 2014, Montag, A, Brodine, S, Alcaraz, J, Clapp, J, Allison, M, Calac, D, Hull, A, Gorman, J, Jones, K, Chambers C. *Vulnerability to Alcohol-Exposed Pregnancy among a Population of AIAN Women.* The dissertation author was the primary investigator and author of this paper.

Chapter 3, in full, has been submitted for publication of the material as it may appear in Alcoholism: Clinical and Experimental Research, 2014, Montag, A, Brodine, S, Alcaraz, J, Clapp, J, Allison, M, Calac, D, Hull, A, Gorman, J, Jones, K, Chambers C. *Preventing Alcohol-Exposed Pregnancy among an AIAN Population: Effect of a SBIRT Intervention.* The dissertation author was the primary investigator and author of this paper.

Chapter 4 is currently being prepared for submission for publication of the material in American Journal of Public Health. Montag, A, Brodine, S, Alcaraz, J, Clapp, J, Allison, M, Calac, D, Hull, A, Gorman, J, Jones, K, Chambers C. *Influence of Depression on Vulnerability to Alcohol-Exposed Pregnancy and Response to*

Intervention. The dissertation author was the primary investigator and author of this paper.

VITA

Annika Montag received the degree of Bachelors of Arts in Biological Basis of Behavior from the University of Pennsylvania and studied pharmacology at Linköping University, School of Medicine and Stockholm University, Department of Biochemistry, in Sweden. Prior to joining the SDSU/UCSD Joint Doctoral Program, Annika conducted research in pharmacology within the biotech and pharmaceutical industries.

SELECTED PUBLICATIONS/ORAL PRESENTATIONS

Montag A, Brodine S, Alcaraz J, Clapp J, Allison M, Calac D, Hull A, Gorman J, Lyons Jones K, and Chambers C. (in preparation) 'Influence of Depression on Vulnerability to Alcohol-Exposed Pregnancy and Response to Intervention.

Montag A, A Montag, M Dusek, A Mazzetti, L Nelson, M Ortega, D Calac, C Nyquist, J Clapp, C Chambers. (2014) '*Preventing Fetal Alcohol Spectrum Disorders in a Native American Population.*' San Diego Epidemiology Research Exchange, San Diego, California, May 2nd, 2014.

Montag A, Brodine S, Alcaraz J, Clapp J, Allison M, Calac D, Hull A, Gorman J, Lyons Jones K, and Chambers C. (submitted) 'Preventing Alcohol-Exposed Pregnancy among an AIAN Population: Effect of a SBIRT Intervention' *Alcoholism: Clinical and Experimental Research*

Montag A, Brodine S, Alcaraz J, Clapp J, Allison M, Calac D, Hull A, Gorman J, Lyons Jones K, and Chambers C. (submitted) 'Vulnerability to Alcohol-Exposed Pregnancy among a Population of AIAN Women' *Maternal and Child Health Journal*,

Montag, A., Clapp, J. D., Calac, D., Gorman, J. and Chambers, C. (2012) 'A review of evidence-based approaches for reduction of alcohol consumption in native women who are pregnant or of reproductive age.' *The American Journal of Drug and Alcohol Abuse*, 38(5) pp. 436-443.

Montag, A. C., Clapp, J.D., Calac, D.J., Chambers, C.D. (2012) *Prevention of Risky Drinking Among American Indian/ Alaska Native Women of Childbearing Age - Healthy Women: Healthy Native Nation.* Native Research Network 2012 National Conference. Seattle, WA, July 16-19, 2012.

Montag, A., Sirlin, C, Calac, D. (2012) *'Fatty Liver Among Southern Californian Adolescent American Indian/ Alaska Natives – The Liverlicious Project.'* Native Research Network 2012 National Conference. Seattle, Washington, July 18th, 2012.

Lee, J. P., Calac, Daniel, **Montag, Annika**, Brodine, Stephanie, Luna, Juan A., Flores, Rosalie Y., Gilder, David A., and Moore, Roland S. (2011) 'American Indian student involvement in tribal community-based research: Underage drinking prevention among rural Native Californians.' *Journal of Rural Community Psychology, 14(2)*

A Montag, GA Laughlin, D Kritz-Silverstein, DL Wingard, J Bergstrom, E Barrett-Connor. (2010) *'Do Markers of Inflammation Predict Incident Diabetes?*' San Diego Epidemiology Research Exchange, San Diego, California, May 7th, 2010. (Presentation awarded student *Bud Benenson Research Award*)

SELECTED POSTERS

Annika Montag, Marlené Dusek, Alexandrea Camp-Mazzetti, Liana Nelson, Marina Ortega, Dan Calac, Corinna Nyquist, Christina Chambers. 'Effect of a Web-based SBIRT (Screening, Brief Intervention, and Referral to Treatment) Intervention on Risky Drinking and Vulnerability to Alcohol-Exposed Pregnancy.' 2014 Pediatric Faculty Research symposium, UCSD

Alexandrea Camp-Mazzetti, **Annika Montag**, Marlené Dusek, Liana Nelson, Marina Ortega, Dan Calac, John D Clapp, and Christina Chambers. '*Healthy Women: Healthy Native Nation* – Lessons Learned in an FASD Prevention Project.' SACNAS 2013

Annika Montag, John D. Clapp, Dan Calac, Jessica Gorman, Marlené Dusek, Alexandrea Camp-Mazzetti, Liana Nelson, Marina Ortega, Christina Chambers. 'Assessment / Prevention of Risky Drinking Among American Indian/ Alaska Native Women of Childbearing Age: Preliminary Data. ' 2013 Pediatric Faculty Research Symposium, UCSD

Alexandrea Camp-Mazzetti, **Annika Montag**, Marlené Dusek, Liana Nelson, Marina Ortega, Dan Calac, MD, John D Clapp, PhD, and Christina Chambers, PhD, MPH. 'Knowledge Regarding Alcohol Use in Pregnancy Among Native American/Alaska Native Women of Childbearing Age - *Healthy Women: Healthy Native Nation* Project' SACNAS 2012

Annika Montag, John D. Clapp, Dan Calac, Christina Chambers. 'Assessment / Prevention of Risky Drinking Among American Indian/ Alaska Native Women of Childbearing Age.' 2012 Pediatric Faculty Research Symposium, UCSD

Annika Montag, John D. Clapp, Dan Calac, Marlené Dusek, Alexandrea Camp-Mazzetti, Liana Nelson, Marina Ortega, Christina Chambers. 'Assessment / Prevention of Risky Drinking Among American Indian/ Alaska Native Women of Childbearing Age

- *Healthy Women: Healthy Native Nation*. ‘ 2011 Pediatric Translational Research Symposium, UCSD

Annika Montag, Dan Calac, Geneva Lofton-Fitzsimmons, Lucy Cunningham, Donna Riley, Stephanie Brodine. ‘CA-NARCH Student Development Program: Applying a network model for American Indian/Alaska Native (AI/AN) success in higher education in San Diego County.’ 2009 NARCH/NIH Meeting

S Fredrickson, S Brodine, **A Montag**, J Habertson, A Thomas, S Reed. ‘Surveillance and Diagnosis of Schistosomiasis and Strongyloidiasis in Sudanese Refugees, San Diego County.’ 2009 Student Research Symposium, SDSU

FIELDS OF STUDY

Major Fields: Epidemiology, Pharmacology

Reproductive and Perinatal Epidemiology: Dr. Christina Chambers, Dr. Kenneth Lyons Jones, Dr. Andrew Hull

Infectious Disease Epidemiology: Dr. Stephanie Brodine

Chronic Disease Epidemiology: Dr. Gail Laughlin, Dr. Elizabeth Barrett-Connor, Dr. Claude Sirlin

Health Disparities Research and Global Health: Dr. Stephanie Brodine

Biostatistics: Dr. John Alcaraz

ABSTRACT OF THE DISSERTATION

Fetal Alcohol Spectrum Disorder (FASD) Prevention among AIAN Women in San Diego County

by

Annika C. Montag

Doctor of Philosophy in Public Health (Epidemiology)

University of California, San Diego, 2014
San Diego State University, 2014

Professor Christina Chambers, Chair

Prenatal alcohol exposure results in a variety of diverse conditions known collectively as Fetal Alcohol Spectrum Disorders (FASD). FASDs range from mild to severe and present a burden to the affected individual themselves as well as to their family and community. In the present study, we explore risk factors for vulnerability to prenatal alcohol exposure among a sample of 263 AIAN women of childbearing age in Southern California. In addition we evaluate the outcome of a culturally tailored web-based Screening, Brief Intervention, and Referral to Treatment (SBIRT) intervention over a 6-month follow-up period. Our findings are that a subset of our participants, roughly a third, was vulnerable to alcohol-exposed pregnancy. Approximately half of participants reported not drinking alcohol but those who did drink tended to drink in a heavy episodic or "binge" pattern. A quarter of participants used no form of birth control (including abstinence) while less than a quarter used highly effective contraception. Risk/protective

factors included knowledge regarding the risks associated with alcohol consumption, religiosity, and the perception of cultural norms. Participation in assessment alone, without exposure to the intervention, was sufficient to result in significant positive behavioral change (decreased drinks per week, $p<0.001$; frequency of binge drinking episodes, $p=0.017$; risk of alcohol-exposed pregnancy, $p<0.001$). There was no difference between treatment groups. Depression was associated with risk factors for vulnerability to alcohol-exposed pregnancy. Depressed women received additional benefit from the intervention, experiencing greater reduction in risky behavior than women not identified as depressed. Study results support the incorporation into future FASD prevention interventions of information regarding FASD and the risks of alcohol consumption, efforts to support healthy and to shift away from unhealthy cultural norms, contraceptive counseling, screening for depression, and personalized interventions for women identified as depressed. Findings that assessment alone reduces risky drinking and vulnerability to alcohol-exposed pregnancy indicate a value to assessment even when logistic limitations prevent the provision of an individualized intervention.

CHAPTER 1 BACKGROUND AND SIGNIFICANCE

Fetal Alcohol Spectrum disorders (FASD) are a range of conditions resulting from prenatal alcohol exposure. First identified by Kenneth Lyons Jones and David Smith in 1973 [1, 2], FASD encompasses Fetal Alcohol Syndrome (FAS), Partial Fetal Alcohol Syndrome (PFAS), Alcohol-related Neurodevelopmental Disorder (ARND), and Alcohol-related Birth Defects (ARBD). FASDs are the leading cause of developmental disabilities and birth defects. They are irreversible and entail lifetime consequences for the individual, their family, and society. In FAS, the most severe form of FASD, fetal development is so affected as to result in neurobehavioral dysfunction, growth restriction, microcephaly, and characteristic facial features[3-6]. FASDs cannot be cured and result in persistent deficits in cognitive and motor functions including learning and memory, complex thought, attention, and motor control, as well as psychosocial behavior[7-12]. Less severe forms of FASD are more difficult to identify but far more prevalent. Using a variety of methods, including school studies, May et al. estimated that FASD affects 2-5% of young elementary school children in the U.S. and that FAS may affect 2-7 per 1,000 people[13]. This estimate is higher than previous estimates including an estimate by Sampson et al. that FASD affects approximately 1% of the population[14]. FASD prevalence varies considerably among different populations. This is due to variation in the prevalence and pattern of prenatal drinking and the factors that influence this drinking. There is also modification of risk by nutritional status, age, and genetics [15-18].

FASD Diagnosis

Diagnosing FASD can be difficult, in particular when characteristic dysmorphology is absent or the disorder is further from FAS on the FASD spectrum. Most characteristics symptomatic of this range of disorders are not specific to FASDs. Guidelines from the CDC (2004) for diagnosing FAS are attached as Appendix A. Briefly, the symptoms that must be present for diagnosis include growth deficiencies (height or weight at or below the 10^{th} percentile), the facial features associated with FAS (smooth philtrum, thin vermilion, and small palpebral fissures), and central nervous system abnormalities (structural, neurologic, or functional). Jones et al. argued in 2010 for expanding the range of defects contributing to diagnosis of alcohol exposure during pregnancy [19]. Five current FAS/D diagnostic guidelines were compared by Astley who suggested that consensus is needed on a single set of guidelines and that FASD diagnosis should ideally be made by an interdisciplinary team in view of the disparate outcomes of the exposure[20]. Interventions will be more effectively focused to both prevent FASDs and provide services to individuals and families affected by FASDs when accurate and specific diagnosis can be made.

Risk Factors for FASD

The pattern of prenatal alcohol consumption influences the risk of FASDs. The pattern of drinking associated with the greatest risk of FASDs is heavy episodic drinking or binge drinking [21, 22]. Binge drinking produces higher blood alcohol concentrations which are associated with greater injury to the fetus. A greater number of drinks over the period of a month or two weeks has also been linked to negative effects in exposed children [23]. In populations where a pattern of moderate daily drinking is more common than binge drinking, a higher ratio of PFAS to FAS cases might be expected.

For example, a recent study in Italy identified 4.5 cases of PFAS for each FAS case [24]. Women who do not consume alcohol during pregnancy are not at risk for giving birth to children with FASD. There is no safe level of alcohol consumption during pregnancy. A recent study evaluating prenatal alcohol exposure and a number of outcomes including growth parameters, facial dysmorphology characteristic of prenatal alcohol exposure, and minor structural malformations found a linear relationship and no evidence of a threshold [25]. A review of well controlled studies including six published studies examining the effect of low to moderate alcohol consumption on the cognitive, social, and emotional development of children, found that four of the six showed an association between prenatal alcohol exposure and negative outcome (hyperactivity, behavioral problems, emotional problems, peer relationship problems, and attention deficit disorder) in children from 3-16 years [26]. Despite current controversy [27], there is at best inconclusive evidence of a threshold and the preponderance of data supports that there is no safe dose of prenatal alcohol exposure. One reason for the controversy is the difficulty involved in teasing out neurobehavioral effects of a particular exposure given the myriad potential confounders (nutrition, genetics, etc.). In 2005, the Surgeon General of the United States issued an advisory for all women who are pregnant or might become pregnant to not consume alcohol [28].

Timing of drinking during pregnancy also influences the type of injury to the fetus; the particular injury is related to the developmental phase of the fetus at the time of exposure. A particularly sensitive time for the development of the brain and some of the characteristic dysmorphology associated with FAS occurs early in the first trimester [29-31]. This is particularly relevant as more than half of all pregnancies in the U.S. and in

California are unplanned [32-34] and many women are unaware they are pregnant 4-6 weeks post-conception [35]. Edwards [36] found that time to recognition of pregnancy did not significantly differ between drinkers and non-drinkers, but noted a trend that *regular* drinkers (≤7 drinks/week and <4 drinks/day), not heavy drinkers, were more likely than non-drinkers to experience late recognition of pregnancy. To prevent alcohol-exposed pregnancies, it is therefore important to include all women of childbearing age who may consume alcohol in prevention/intervention.

Risk factors associated with FASD in the general population, beyond the magnitude and pattern of alcohol consumption of the individual women, are older age, high parity, use of other drugs including tobacco and illegal substances, unemployment, mood disorders (including depression and anxiety), family history of alcohol abuse, alcohol abuse by partner, tenuous marital status (cohabitation without marriage, separated, divorced), and community tolerance of risky drinking [16-18, 37-41].

Alcohol Consumption among Women of Childbearing Age

Alcohol consumption by women of childbearing age varies among different populations. The most recent national data from the 2004 to 2008 SAMHSA National Surveys on Drug Use and Health (NSDUHs) for American Indian or Alaska Native (AIAN) women and all women in the U.S. is shown in **Table 1.1**.

Table 1.1: Past Month Substance Use among American Indian or Alaska Native Women Aged 18 or Older Compared with the National Average: 2004 to 2008 [42]

Substance Use	AI/AN	National Average
Alcohol Use	38.6%	48.5%
Binge Alcohol Use (≥5 drinks/occasion/30 days)	24.2%	15.9%
Illicit Drug Use	8.5%	5.7%

This national data differs only slightly from the Behavioral Risk Factor Surveillance System (BRFSS) data from 2006-2010 where 51.5% of non-pregnant women aged 18-44 years consume alcohol and 15% binge drink. In the BRFSS data, binge drinking is defined as consuming four or more drinks on one occasion in the past 30 days [43].

Alcohol consumption varies significantly among tribes [37, 44-48]. The NSDUH data regarding binge drinking supports previous work by May [17, 37, 49] among others where binge drinking is the primary pattern of drinking among many AI/AN populations and rates of abstention are relatively high. In a study among Navajos, risk factors for female problem drinking included exposure to abuse and serious psychiatric disorders, including schizophrenia and depression [50]. The influence of peer pressure was far less important among female as opposed to male problem drinkers. Alcohol disorders and posttraumatic stress disorders have been found to be more prevalent among some American Indian populations than in the general population [51] and similar to the general population in others [45]. Social norms relating to alcohol consumption and self-other discrepancies have been used in alcohol interventions among non-AI/AN

populations with mixed results [52-55]. Overestimation of other women's drinking may contribute to increased drinking [56] and increased perception of risks associated with drinking may reduce consumption [57]. People tend to perceive their own drinking as healthier than it may be; of the people identified as needing treatment for abusive alcohol consumption in the 2007 National Survey of Drug Use and Health, 95% were unaware that they needed it [42, 58]. Drinking norms are not stable but change and evolve. An impressive, deliberate shift in drinking norms occurred within the Alkali Lake Shuswap Native American community [59]to decrease tolerance of risky drinking. A previous study among AI/AN in Southern California found drinking participants, male and female, less likely to report drinking more than they had intended to drink and less likely to report feeling guilty about their drinking than a non-AI/AN national sample [60], indicating a permissive cultural view of prevalent drinking patterns. Drinking prior to pregnancy is strong predictor of alcohol-exposed pregnancy [61]. The most effective factors in making women stop drinking are pregnancy and childcare [62], yet for some problem binge drinkers, these reasons are not enough. It is more difficult for dependent drinkers than non-dependent drinkers to cut down or cease drinking. The factors that induced the women to turn to alcohol in the first place may remain, and may continue to thwart efforts to abstain. Binge drinkers have been found less likely to reduce their drinking during pregnancy than moderate drinkers[63]. Binge drinking is associated with an increased risk of unintended pregnancies, further amplifying the risk of an alcohol-exposed pregnancy [64]. Furthermore, women engaging in binge drinking were found to be more likely to also smoke and experience violence in the preconception period, and to be more likely to consume alcohol and smoke during pregnancy.

Alcohol Consumption in Pregnancy

While most women reduce or discontinue alcohol use upon awareness of pregnancy [65, 66]), subgroups of women remain vulnerable to continued use: women who are unmarried, unemployed, depressed, risky drinkers, exposed to violence, or simply confused by health warning messages and the amount of alcohol their drinks contain [67-75]. Drinking during pregnancy is heavily influenced by social norms and therefore varies widely among populations. For example, the percent of women who drink alcohol during pregnancy is 0% in Saudi Arabia, 6% in Sweden [76], 7.4% in the U.S. [43] (down from Ethen's estimate of 30.3% in 2008 and the NSDUH finding of 10% in 2010), 34% in New Zealand [77], 42.8% in Western Cape province of South Africa [78], and 58% in Denmark [79]. It is not surprising, therefore, that among the limited populations studied, drinking during pregnancy among the heterogeneous AI/AN populations of the U.S. differs significantly. May et al. [17] published data from a prenatal clinic among Northern Plains Indians indicating 16.2% of pregnant women consumed alcohol. Other AI/AN studies have reported 36% of urban and 14% of reservation pregnant women consuming alcohol [80] and 53.4% at one prenatal clinic in the Northern Plains [81]. In contrast to previous studies[82], a more recent study based on the National Survey of Drug Use and Health (2005-2009) found lower past month alcohol consumption rates among pregnant (and non-pregnant) AIAN women than among White women (8.7% vs. 12 %) [83]. The prevalence and pattern of drinking among the AI/AN populations addressed in this study are unknown.

Depression among Women of Childbearing Age

First onset of depression in women [84] and prevalence of depression [85] peak during childbearing years. In the U.S., more than 14% of women 18-44 years of age screened positive for depression using the 9-item Patient Health Questionnaire (PHQ-9) in 2006 [86] and the most recent National Health interview survey found 10.7% of adult women feel depressed [87]. As with alcohol consumption and prevalence of FASD, depression varies among the different AI/AN communities [88, 89]. These differences underscore the need to respect, recognize, and take into account the heterogeneity both among and within AI/AN communities. Beals et al. [90] found less depression in an AI/AN population than in the general population. O'Connell et al. [44] describes a prevalence of 16% for mood disorders among female drinkers in two AI/AN populations. Perhaps most relevant to our study, 20% of 2,289 adult Alaska Native women tested positive for depression using the PHQ-9 instrument [91]. Among some AI/AN populations, women are at increased risk for depression as a result of the living conditions they experience. For example, AI/AN women are at increased risk of violence including domestic violence, rape, stalking, and assault [92-98], less than optimal health (diabetes, heart disease), accidents, smoking, obesity, low high school and college graduation rates, and living in poverty [99, 100]. Some of these conditions are a legacy of the long history of oppression, marginalization, and systematic persecution experienced by AI/ANs. In addition to these factors, AI/AN women may be at greater risk of depression due to historical trauma, loss of culture, lingering discrimination issues, and conflicts between traditional and modern culture [101-104]. The relationship between depression and alcohol problems (including binge drinking) in women has long been recognized [69, 105-112]. The relationship is U- or J-shaped with both abstainers

and heavy drinkers at higher risk for depression and anxiety disorders [113-115]. In women, as opposed to men, depression appears to predate alcohol problems [69, 116].

Depression and alcohol consumption also appear to be associated in pregnancy [117-120]. Depressed pregnant women are more likely to drink alcohol, binge drink, and smoke than non-depressed pregnant women, and less likely to receive prenatal care [119, 121-124]. Additionally, antenatal depression is associated with poor obstetric and fetal outcomes [125, 126]. Due to the potentially catastrophic consequences of untreated depression in pregnancy, it is important to identify and treat maternal depression as early as possible [127-129]. Sadly, a 2003 study found that even among women who are screened and identified as being in need of treatment for depression, 86% did not receive treatment [130]. Depression may prove to be important to FASD interventions in several ways: 1) as a factor to tackle in order to reduce vulnerability to having an alcohol-exposed pregnancy and 2) as a factor used to facilitate identification of vulnerability to alcohol-exposed pregnancy. In this paper we propose a third: as a modifying factor of intervention response that may be used to determine which type of intervention might prove most effective. Integrated assessment and treatment of both alcohol consumption and depression may enhance the efficacy of both.

Knowledge Regarding FASD

Knowledge concerning FASDs and risks associated with prenatal alcohol consumption is imperfect and inconsistent among different populations [70, 131]. When designing interventions to prevent FASDs, understanding misconceptions regarding drinking alcohol during pregnancy is critical. The more targeted information is to a specific population, the more likely it is to change behavior. Knowledge of health risks

can be enhanced by specific education and counseling [132-135]. The benefit of increased knowledge and corrected misconceptions has the greatest impact when obtained prior to conception in that it then has the potential to affect the entire pregnancy [136].

Interventions to Reduce Prenatal Alcohol Consumption among AIAN populations

Few of the interventions implemented to reduce prenatal drinking among AIAN communities have been evaluated, leaving questions about best strategies. In addition, most have produced disappointing results. Appendix B is a modified table of published evaluated studies from a recently published review[137]. Limitations that impact formal evaluation of the reviewed approaches include small and/or non-randomized samples, lack of control groups, and low follow-up rates. Limitations that impact the effectiveness of the interventions include failure to culturally adapt methodologies to incorporate community involvement, values, beliefs, and strengths, as well as respect for unique challenges facing AIAN communities. Recent studies have been more likely to recognize heterogeneity among AIAN communities and to tailor interventions to specific communities. In acknowledging the failure of interventions imposed from outside and the understandable distrust that a history of injustice and abusive research experiences has engendered, there is hope for effective future interventions [101, 138-142]. Lessons learned from the studies cited in Appendix B support using community-based participatory research (CBPR): conduct culturally competent research, target the intervention, incorporate community members in all aspects of intervention design and implementation, and address logistic hurdles such as transportation. Ideally, cultural targeting of a FASD intervention will involve awareness of the specific risk and

protective factors of the community such as alcohol consumption patterns, contraceptive use, understanding of risks, treatment and support options, nutrition, comorbidities such as mood disorders, genetics, and prevailing cultural norms.

Screening, Brief Intervention, and Referral to Treatment (SBIRT)

Screening, Brief Intervention, and Referral to Treatment (SBIRT) is a prevention and early intervention approach that uses wide screening, education and feedback specific to the participant, and professional treatment for those identified by the screening as positive for alcohol abuse problems [143-145]. The latter component, the incorporation of specialized treatment as warranted, sets the approach apart from those offering only brief interventions which have demonstrated largely positive but mixed results [146, 147]. Some reasons for lack of proven benefit may be that assessment alone may have a mitigating effect on risky drinking (although this has been controlled for in some studies) or that extreme risky drinking may decrease over time due to "regression toward the mean". Valuable lessons learned from Brief Intervention studies include that protocols with multiple contacts are more likely to alter behavior than single contact protocols [148] and that effectiveness may be related to the severity of the underlying condition [149, 150]. SBIRT has been used to motivate a reduction in alcohol consumption in a number of populations including emergency room and other healthcare setting patients [151-158], college freshmen [159], and WIC participants [160].

Native American Research Centers for Health (NARCH)

Native American Research Centers for Health (NARCH) is a partnership between the National Institutes of Health (NIH) and the Indian Health Service (IHS) with the goal of reducing AIAN health disparities. Tribal-academic partnerships, where the Tribal

partner is the managing partner, are established through this funding initiative to pursue Tribal priorities. Primary goals of NARCH grants go beyond the specific aims of individual projects and are to reduce distrust of research by AIAN communities and to create a cadre of competitive AIAN scientists engaged in research.

Goals of Dissertation

In recognition of the lack of effective interventions among AIAN women of childbearing age to reduce risky drinking and prevent FASD, as well as the unknown nature of risk factors for FASD in our specific local population, it was the purpose of this dissertation to describe and evaluate risky drinking and vulnerability to an alcohol-exposed pregnancy among AIAN women in a specific setting, and to test the effectiveness of a web-based intervention.

Our research questions were:

- Is this population vulnerable to alcohol-exposed pregnancy?
- What are the associations with or predictors of vulnerability to AEP?
- Does reporting symptoms of depression consistent with a diagnosis of depression in this population correlate with risky alcohol use?
- Does reporting symptoms of depression consistent with a diagnosis of depression in this population correlate with vulnerability to AEP?
- What is the effect of a population targeted SBIRT intervention of risky drinking among this population of AIAN women of childbearing potential?
- What is the effect of a population targeted SBIRT intervention on vulnerability to AEP?

Intervention

Data for these analyses was collected from women recruited into a NARCH funded randomized study using a web-based SBIRT intervention as treatment and "treatment as usual" for the control group. To determine prevalence estimates and potential correlates of risky drinking and potential alcohol-exposed pregnancies, recruitment was not limited by risky drinking profile. As primary motivation for behavioral change presented by this intervention was the health of a potential future baby, recruitment was limited to women of childbearing potential. The SBIRT intervention included a web-based portion which screened participants for risky drinking and provided individualized advice regarding alcohol consumption. Information regarding FASD was also incorporated into the web-based portion.

The study was approved by the UCSD, SDSU, and SCTHC Institutional Review Boards.

CHAPTER 2 VULNERABILITY TO ALCOHOL-EXPOSED PREGNANCY AMONG A POPULATION OF AIAN WOMEN.

Annika C. Montag[1,3,6], Stephanie K. Brodine[1], John E. Alcaraz[1], John D. Clapp[2], Matthew A. Allison[3], Dan J. Calac[4], Andrew D. Hull[5], Jessica R. Gorman[6], Kenneth Lyons Jones[6], Christina D. Chambers[3,6]

[1]SDSU Graduate School of Public Health, [2]Ohio State University School of Social Work [3]UCSD Department of Family and Preventive Medicine, , [4]Southern California Tribal Health Clinic, [5]UCSD Department of Reproductive Medicine, [6]UCSD Department of Pediatrics

Abstract

Objective: Fetal Alcohol Spectrum Disorders (FASDs) are caused by alcohol-exposure during pregnancy and are the leading preventable cause of developmental disabilities in the U.S. Rates of FASD vary with different patterns of prenatal drinking which, in turn, vary by population. Interventions to reduce FASD may therefore have to address culturally specific factors influencing prenatal drinking to be successful. Our objective was to determine whether Southern California AIAN women are vulnerable to alcohol-exposed pregnancies (AEP) and, if they are, correlates of vulnerability. Methods: AIAN women of childbearing age were recruited from three AIAN community health clinics. All participants completed a paper and pencil-based survey and a subset completed an additional web-based survey. Results: More than a third of 263 participants were vulnerable to AEP. Approximately half reported not drinking alcohol but the participants who did drink tend to drink in a heavy episodic ("binge") pattern. A

quarter of participants used no form of contraception (including abstinence) while less than a quarter used highly effective birth control. Participants had a high level of knowledge about FASD but a lower level of knowledge about risks of alcohol consumption to women. Correlates of vulnerability included a lower level of knowledge regarding risks of alcohol consumption, having had fewer pregnancies, being less religious, and a perception that other women in their peer groups consumed a greater number of drinks per week. Conclusions: A subset of women in this community engaged in risky drinking while not using effective contraception and is therefore vulnerable to AEP. Correlates of vulnerability suggest interventions target knowledge of risks and perception of cultural norms.

Keywords: Fetal Alcohol Spectrum Disorders, AIAN women, Alcohol, Prevention, Risk assessment

Introduction

Fetal Alcohol Spectrum Disorders (FASD) is an umbrella term for a range of conditions resulting from prenatal alcohol exposure, the most severe of which is called Fetal Alcohol Syndrome (FAS). First identified in the United States by Kenneth Lyons Jones and David Smith in 1973[1, 2], FASDs are thought to be one of the leading causes of developmental disabilities and birth defects. Using a variety of methods, including school studies, May et al. estimated that FASD affects 2-5% of young elementary school children in the U.S. and that FAS may affect 2-7 per 1,000 people[161]. This estimate is higher than previous estimates including an estimate by Sampson et al. that FASD affects approximately 1% of the population[14]. FASD prevalence varies considerably among different populations. This is due in part to variation in the prevalence and pattern of

prenatal drinking and the factors that influence this drinking. There is also modification of risk by nutritional status, maternal age, and genetics [15-18]. The pattern of drinking associated with the greatest risk of FASDs is heavy episodic drinking or binge drinking [21, 22]. Binge drinking produces higher blood alcohol concentrations which are associated with greater injury to the fetus. A greater number of drinks over the period of a month or two weeks has also been linked to negative effects in exposed children [23].

Women who do not consume alcohol during pregnancy are not at risk for giving birth to children with FASD. There is no known safe level of alcohol consumption during pregnancy. In 2005, the Surgeon General of the United States issued an advisory for all women who are pregnant or might become pregnant to not consume alcohol [28].

Risk factors associated with FASD in the general population, beyond the magnitude and pattern of alcohol consumption of the individual women, are older age, high parity, use of other drugs (including tobacco and illegal substances), unemployment, mood disorders (including depression and anxiety), family history of alcohol abuse, alcohol abuse by partner, tenuous marital status (cohabitation without marriage, separated, divorced), and community tolerance of risky drinking [16-18, 37-41].

More than half of all pregnancies in the U.S. and in California are unplanned [32-34], and alcohol exposure may occur in the 4-6 weeks post conception that for many women is prior to pregnancy recognition [35]. Edwards [36] found that time to recognition of pregnancy did not significantly differ between drinkers and non-drinkers, but noted a trend that *regular* drinkers (≤7 drinks/week and <4 drinks/day), not heavy drinkers, were more likely than non-drinkers to experience late recognition of pregnancy.

To prevent alcohol-exposed pregnancies, it is therefore important to include all women of childbearing age in interventions.

Alcohol consumption by women of childbearing age varies among different populations. The most recent national data from the 2004-2008 SAMHSA National Surveys on Drug Use and Health (NSDUH) for American Indian or Alaska Native (AIAN) women, as well as all women in the U.S., is shown in **Table 2.1**.

Table 2.1: Past Month Substance Use among American Indian or Alaska Native Women Aged 18 or Older Compared with the National Average: 2004 to 2008 [42]

Substance Use	AIAN	National Average
Alcohol Use	38.6%	48.5%
Binge Alcohol Use (≥5 drinks/occasion/30 days)	24.2%	15.9%
Illicit Drug Use	8.5%	5.7%

This national average data differs only slightly from the Behavioral Risk Factor Surveillance System (BRFSS) data from 2006-2010 where 51.5% of non-pregnant women aged 18-44 years consume alcohol and 15% binge drink. However, it should be noted that in the BRFSS data, binge drinking is defined as consuming four or more drinks on one occasion in the past 30 days [43].

Alcohol consumption varies significantly among AIAN tribes [37, 44-47, 162]. The NSDUH data supports previous work by May [17, 37, 49] among others where binge drinking is the primary pattern of alcohol consumption among many AIAN populations. Overestimation of other women's drinking (i.e. perceived social norms) may contribute to increased consumption [56] and increased perception of risks associated with drinking

may reduce consumption [57]. People tend to perceive their own drinking as healthier than it may be; of the people identified as needing treatment for abusive alcohol consumption in the 2007 National Survey of Drug Use and Health, 95% were unaware that they needed assistance [42, 58]. Drinking norms are not stable but change and evolve. Deliberately shifting social norms and correcting harmful "self vs. other" discrepancies in perceived social norms relating to alcohol consumption have been used in alcohol interventions among non-AIAN populations with mixed results [52-55]. An impressive, deliberate shift in drinking norms occurred within the Alkali Lake Shuswap AIAN community [59] to decrease tolerance of risky drinking. A previous study among AIAN in Southern California found drinking participants, male and female, were less likely to report drinking more than they had intended to drink and less likely to report feeling guilty about their drinking than a non-AIAN national sample [60], indicating a permissive cultural view of prevalent drinking patterns.

Pre-pregnancy drinking is a strong predictor of an alcohol exposed pregnancy (AEP) [61]. The most powerful factors associated with women discontinuing drinking are pregnancy and childcare [62], yet for some problem binge drinkers, these reasons are not enough. Binge drinking is associated with an increased risk of unintended pregnancies, further increasing the risk of an AEP [64]. Naimi [64] also found that women who binge drank were more likely to smoke and experience violence in the preconception period, and to drink alcohol and smoke during pregnancy.

Knowledge about FASDs and risks associated with alcohol consumption in pregnancy varies greatly among different populations and is often limited [70, 131]. Understanding misconceptions regarding drinking alcohol during pregnancy is important

to take into account when designing interventions to prevent FASDs. The more targeted information is to a specific population, the more likely it is to change behavior. Knowledge of health risks can be improved following targeted education and counseling [132-135]. The effects of increased knowledge and corrected misconceptions are maximized, in that they have the potential to affect the entire pregnancy, when obtained prior to conception [136]. In addition, health messages designed to change misconceptions may contribute to prevention of FASDs not only by their immediate effect on the individual but through their ability to change social norms over time.

A number of different strategies for preventing FASDs have been implemented in AIAN populations. Evaluated approaches were recently reviewed [137]. (See **Appendix B** for a modified table of evaluated interventions). Despite a distinct lack of relevant studies, the evidence suggests that an effective intervention should strive to include local community members in all aspects of the program from design to implementation, culturally target the intervention, and address logistic barriers to participation. This would include local community leaders, women of childbearing age, and Tribal government, as well as a well-trained AIAN staff.

Culturally targeting an FASD prevention intervention involves taking into account the specific risk and protective factors within a local population such as drinking patterns, birth control practices, comorbidities such as mood disorders, nutrition, available treatment and support options, and relevant prevailing cultural norms. Working with an AIAN population requires addressing the pervasive, and historically well founded, distrust of research and interventions imposed from outside the community [101, 138-140].

To address these issues in preparation for designing and implementing an intervention trial among AI women of reproductive age in one Southern California setting, we first conducted a survey to determine the prevalence of risk of an AEP and the maternal factors associated with higher or lower risk for that event.

Methods

Sample source: The population sample consisted of AIAN women from 18 to 45 years of age, of childbearing potential, recruited from one of three AIAN health clinics located in Southern California between April 2011 and September 2012. The sample used for each analysis will vary and is described in association with the particular analysis.

Ethics: This protocol was approved by University of California at San Diego (UCSD), San Diego State University (SDSU), and Southern California Tribal Health Clinic (SCTHC) Institutional Review Boards. A Certificate of Confidentiality (CoC) was obtained from the National Institutes of Health (NIH) to further protect the confidentiality of participants' data. A CoC assures legal protection against disclosure in civil, criminal, or other proceedings at all levels of government. All staff members completed human research subject protections training.

Recruitment and study protocol: Potential participants were approached in waiting areas of health clinics and screened for eligibility. See **Figure 2.1** for study flowchart. Interested and eligible participants were brought to a private room where they were taken through the consenting procedure, assigned a unique identifier, and completed a self-administered paper and pencil survey. A randomly selected subset of the women who completed the paper-based survey was then asked to complete a web-based survey.

Participants had the opportunity to be referred for treatment to a professional substance abuse counselor following completion of the survey (s). Participants were provided incentives in the form of a $10 gift card and a choice of a project fan or t-shirt emblazoned with the project logo.

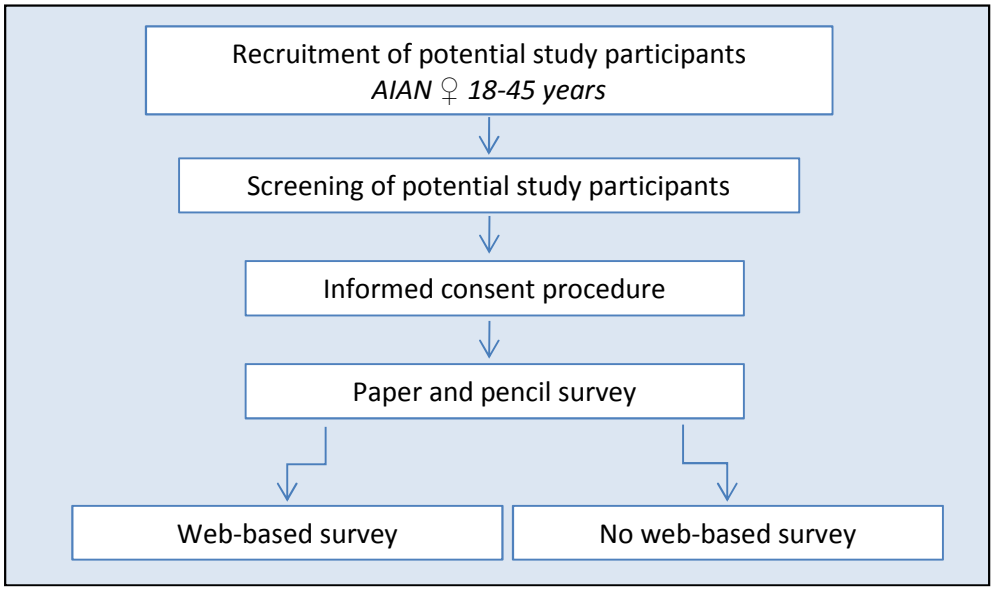


Figure 2.1: Study Flowchart

Data collection: Data was collected at recruitment from all participants and during the web-based survey from selected participants.

Paper and pencil questionnaire: The self-administered, paper-based questionnaire included questions regarding current relationship situation, employment, religiosity, income, gravidity, parity, birth control use and frequency of correct usage, current use of prescription and non-prescription medications, smoking, illegal drug use, awareness of FASD, and alcohol consumption including number of standard drinks consumed per week and per occasion, and

number of binge episodes in the past two weeks (binge defined in this setting as consuming ≥ 3 drinks/occasion).

Web-based questionnaire: Participants selected for the web-based survey self-reported information by computer regarding alcohol consumption over the past two weeks, pregnancy status, family history of alcohol problems, the age they began drinking alcohol, and contraceptive use. Illustrations of various alcoholic beverage containers were used to prompt recall (**Figure 2.2**). They were asked to complete a T-ACE questionnaire and a series of true or false knowledge questions about risks associated with alcohol consumption (**Appendix C**).

Figure 2.2: Preferred alcohol main choice alternatives. Each picture, when selected in the web-based intervention, leads to illustrations of different type glasses and amounts for each type alcohol.

Study Measures: The primary outcome variable was vulnerability to AEP. The "Vulnerability to Alcohol-Exposed Pregnancy" variable was defined in four categories: not at risk, at risk, not at high risk, and at high risk. Being "at risk" for an AEP was defined as 1) currently using alcohol and 2) using a less than highly effective contraceptive method. The NIAAA defines "risky drinking" for women as more than 3 drinks at one time or more than 7 drinks per week [163] For the purposes of this study,

we defined “binge” or “risky” drinking as 3 or more standard drinks per occasion and/or 8 or more drinks per week as this level of consumption has been predictive of risk of adverse pregnancy outcomes in other studies [17, 164-167]. Being “at high risk” for an AEP was defined as “at risk” plus either consuming 3 or more drinks per occasion or consuming 8 or more drinks per week. The categories of vulnerability to AEP were not mutually exclusive, i.e., all “at high risk” women were also included in the “at risk” category. In fact, only 15 women were classified differently between the two risk categories. The comparisons in the present paper are between “at high risk” and “not at high risk”.

Standard drinks were defined as in **Figure 2.3**.

Figure 2.3: Definition of a “Standard Drink”

Categorization of contraceptive effectiveness is shown in **Figure 2.4** [168].

Effectiveness Category	Contraceptives in Category
High → Less than one pregnancy/100 women per year	*Sterilization, IUD, Implant*
Medium High → 2-9 pregnancies/100 women per year	*Breastfeeding, Shot, Pill, Ring, Patch*
Medium Low → 15-24 pregnancy/100 women per year	*Diaphragm, Male /Female Condom, Withdraw, Sponge, Cervical Cap*
Low → ≥25 pregnancy/100 women per year	*Fertility-Awareness Based Methods*

Figure 2.4: Effectiveness categorization of contraceptives

Family risk of alcohol dependency was calculated based on the number of blood relatives the participant reported as having, or having had in the past, "problems with drinking alcohol (i.e. drink too much/alcoholic)". Two points were counted for each parent or sibling; one point for each grandparent, aunt, uncle, or cousin. The family risk score is interpreted as follows: 1 point = low risk, 2-3 points = medium risk, 4-6 points = high risk, and 7 or more points = very high risk[169].

T-ACE (Tolerance, Annoyed, Cut down, Eye-opener) is a validated screening instrument of four questions structured to identify risky drinking[170] found to be effective in an AIAN population [171]. The T-ACE questions and scoring were as follows: How many drinks does it take to make you feel tipsy/high? (≤2 = 0 points, >2 = 2 points); Have people annoyed you by criticizing your drinking? (No = 0 points, Yes =

1 point); Have you felt you ought to cut down on your drinking? (No = 0 points, Yes = 1 point); Have you ever had a drink first thing in the morning to steady your nerves or to get rid of a hangover? (No = 0 points, Yes = 1 point). A score of ≥2 was considered positive for risky drinking ("T-ACE positive" variable). Answering all questions negatively indicated a 1.5% probability of being a risky drinker ("T-ACE severity" variable). The likelihood of being a risky drinker increased to 62.7% when all questions were answered positively.

A few questions occurred, in slightly different formats, in both the paper and web-based questionnaires. Agreement was good between them with "drinks per week" being the most different but not significantly so (2-tailed p-value = 0.6292). Answers from the paper and pencil questionnaire were prioritized for use in analysis as these were available from all participants. Where a question was left blank in the paper questionnaire, the web-based answer was used.

Statistical Analyses: Comparisons of continuous, dichotomous, or categorical variables were conducted using t-tests (continuous), χ^2 (dichotomous), Fisher's exact test (dichotomous with small cell sizes), and nonparametric analyses (for data not normally distributed and not log-transformed). Normality in continuous variables was investigated through skewness and kurtosis. ANOVA was used to examine associations among population characteristics. Paired t-tests were used to explore whether participants believed other women drank more or less than they did. The vulnerability to AEP outcome variable was tested as dichotomous ("at high risk" vs. "not at high risk"). Logistic regression was used to test for predictors of vulnerability to AEP, i.e., defined as at high risk of an AEP vs. not at high risk. First, each predictor was tested in a logistic

regression model to determine whether there were significant independent associations with that one factor and vulnerability to AEP. Then, multiple logistic regression analysis was used examine all variables previously found to be significant. All two-way interactions among significant variables were tested. Two final models were constructed as the number of participants included in analysis varied depending upon which variables (from the paper and pencil or the web-based survey) were used. While everyone had the opportunity to answer questions on the paper and pencil survey, only approximately half of participants had the opportunity to fill out the web-based survey.

Statistical significance was defined as 2-sided, p-value of <0.05. Statistical analyses were carried out using SPSS (PASW 18, SPSS Inc., Chicago, IL).

Results

A total of 263 women were enrolled in the study. Of these, 29 were pregnant at recruitment. **Table 2.2** shows characteristics of the sample population by pregnancy status. There were significant differences between pregnant and non-pregnant participants in terms of cohabitation status, and alcohol and illegal drug use. Pregnant women were less likely to smoke (13.8% vs. 31.2%) although this was of borderline statistical significance ($p=0.052$). Pregnant participants were excluded from all further analyses.

Table 2.2: Characteristics of 263 women by pregnancy status

Variable	Total (Mean±SE or %) *n=263* [a]	Not Pregnant (Mean±SE or %) *n=234*	Pregnant (Mean±SE or %) *n=29*	p-value[e]
Demographic characteristics				
Age (years)	28.3 ± 0.5	28.5 ± 0.5	26.7 ± 1.2	0.228
Has had a child (%)	66.9	65.4	79.3	0.133
Children (number)	1.51 ± 0.09	1.50 ± 0.10	1.55 ± 0.26	0.867
Pregnancies	2.07 ± 0.13	2.00 ± 0.14	2.71 ± 0.32	0.081
Wants more children (%)	60.2	59.9	63.0	0.760
Cohabitating (%)	45.4	42.4	69.0	0.007
Employed (%)	40.5	41.7	31.0	0.272
Religious (%)	85.6	86.1	81.5	0.519
Smoker (%)	29.3	31.2	13.8	0.052
Illegal drugs (%)	12.5	14.0	0	0.031
Alcohol Consumption Variables				
Ever drank alcohol	95.0	95.2	93.1	0.666
Currently consume alcohol	47.5	52.3	7.1	<0.001
Age at first drink [b]	15.2 ± 0.2	15.1 ± 0.3	15.9 ± 0.7	0.331
Drinks per week [b]	3.24 ± 0.44	3.62 ± 0.49	0.26 ± 0.22	<0.001
Drinks per occasion [b]	2.00 ± 0.23	2.24 ± 0.25	0.07 ± 0.05	<0.001
Binge episodes / 2 weeks [b]	1.17 ± 0.20	1.31 ± 0.22	0.04 ± 0.04	<0.001
Current binge drinker (%)[b]	43.4	48.2	3.6	<0.001
Family alcohol dependency risk [c]	14.3 ± 1.7	13.5 ± 1.8	19.7 ± 5.5	0.224
T-ACE [c]	2.07 ± 0.13	2.07 ± 0.14	2.08 ± 0.40	0.987
T-ACE severity (%)[c]	11.6 ± 1.3	11.5 ± 1.4	12.5 ± 4.4	0.812
T-ACE positive [c]	73.5	74.0	69.2	0.714
Perception of other women's drinking				
Drinks per week [d]	7.38 ± 0.61	7.57 ± 0.66	5.37 ± 1.20	0.304
Drinks per occasion [d]	3.40 ± 0.21	3.43 ± 0.22	3.05 ± 0.50	0.591
FASD Awareness				
Heard of FASD (%)	71.5	72.2	65.5	0.645
Know someone affected by FASD (%)	31.7	32.2	27.6	0.749
Not sure if know someone affected (%)	9.2	9.4	6.9	

[a] Sample size varies due to inclusion of selected variables in the web-based survey and missing values.
[b] n = 248
[c] n = 112
[d] n = 234
[e] comparing non-pregnant to pregnant participants using ANOVA for continuous variables and chi-square test for categorical variables

Table 2.3 shows demographic characteristics of the non-pregnant participants by vulnerability to AEP. Comparisons are between 141 participants "not at high risk" and 88 participants "at high risk" for AEP as values are missing for five women. Participants at high risk of AEP had fewer children and fewer pregnancies but were not different in age (p = 0.826). They also tended to be less religious (p = 0.026).

Table 2.3: Demographic characteristics of 229 non-pregnant women by AEP risk status

Variable	Total (Mean±SE or %)	At High Risk (Mean±SE or %)	Not At High Risk (Mean±SE or %)	p-value [a]
Demographic characteristics	*n=229*	*n=88*	*n=141*	
Age (years)	28.7 ± 0.5	28.5 ± 0.8	28.8 ± 0.7	0.826
Has had a child (%)	66.4	59.1	70.9	0.065
Pregnancies (number)	2.03 ± 0.14	1.58 ± 0.19	2.31 ± 0.19	0.011
Children (number)	1.53 ± 0.10	1.28 ± 0.15	1.69 ± 0.13	0.046
Wants more children (%)	59.8	68.6	54.1	0.033
Cohabitating (%)	43.2	40.9	44.6	0.584
Employed (%)	42.2	43.5	41.3	0.744
Religious (%)				0.026
Not at all	14.2	18.1	11.9	
Somewhat	73.9	77.1	71.9	
Very	11.9	4.8	16.3	
Smoker (%)	31.9	34.1	30.5	0.570
Illegal drugs (%)	14.3	15.5	13.7	0.709

[a] Comparing At High Risk to Not At High Risk non-pregnant women using ANOVA for continuous variables and chi-square test for categorical variables; missing values for 5 women; sample size for selected variables varies due to missing values.

When looking at alcohol consumption variables there were, by definition, differences in the variables contributing to risk allocation for an AEP. Drinks consumed per occasion and per week, as well as binge episodes over a two week period, were significantly different between participants "at high risk" and those "not at high risk" for an AEP among the total population (**Table 2.4**). Among current drinkers, however, only

drinks consumed per week were significantly different. Age at first drink, drinks needed to feel tipsy, and family risk of alcohol dependency were not different by risk status. Whether "at high risk" or "not at high risk", the cultural norm in this sample appeared to be binge drinking when drinking. The T-ACE screening tool scores for risky drinking were significantly associated with vulnerability to AEP. Preferences for type alcohol did not differ by vulnerability to AEP.

The perception of how much other women drink did not differ between risk groups among current drinkers. Among those "at high risk" for an AEP, there was no significant difference between how much they estimated that other women drink per week or per occasion and how much they reported drinking themselves (paired analysis, not shown). On the other hand, current drinkers "not at high risk" for an AEP believed other women drink more per week than they do themselves (paired analysis, $p<0.001$). The mean difference between perceived consumption of alcohol by other women and personal consumption was greater for those "not at high risk" than for those "at high risk" but not significantly so (**Table2. 4**).

Table 2.4: Drinking pattern of 218 non-pregnant women by AEP risk status

Alcohol Consumption Variable	Total Population (Mean±SE or %)	At High Risk (Mean±SE or %)	Not At High Risk (Mean±SE or %)	p-value [a]
All Women	*N = 218*	*N = 86*	*N = 132*	
Drinks per week	4.24± 0.57	9.16 ± 1.25	1.11 ± 0.24	<0.001
Drinks per occasion	2.45 ± 0.27	4.77 ± 0.50	0.96 ± 0.22	<0.001
Binge episodes / 2 weeks	1.40 ± 0.23	2.94 ± 0.50	0.37 ± 0.12	<0.001
Age at first drink	15.1 ± 0.3	14.8 ± 0.4	15.3 ± 0.3	0.300
Drinks to feel tipsy [b]	4.17 ± 0.37	4.16 ± 0.34	4.19 ± 0.61	0.972
Family alcohol dependency risk [b]	13.5 ± 1.8	14.8 ± 2.9	12.4 ± 2.3	0.506
T-ACE score [b]	2.08 ± 0.14	2.55 ± 0.20	1.75 ± 0.18	0.005
T-ACE positive [b]	74.3	85.7	66.1	0.026
T-ACE severity (%)[b]	11.5 ± 1.4	12.9 ± 2.3	10.5 ± 1.7	0.385
Type Alcohol Preferred (%)	*N = 100*	*N = 43*	*N = 57*	0.534
Beer	45.5	41.9	48.2	
Wine	13.1	16.3	10.7	
Liquor/ Spirits	31.3	27.9	33.9	
Malt liquor/ energy drinks	10.1	14.0	7.1	
Perception of Other Women's Drinking	*N = 212*	*N = 79*	*N = 133*	
Drinks per week	7.65 ± 0.67	8.91 ± 1.14	6.87 ± 0.82	0.140
Drinks per occasion	3.49 ± 0.23	4.11 ± 0.31	3.13 ± 0.31	0.036
Difference Between Other Women's and Own Drinking	*N = 205*	*N = 78*	*N = 127*	
Drinks per week	4.52 ± 0.69	2.05 ± 1.12	6.06 ± 0.85	0.004
Drinks per occasion	1.48 ± 0.26	0.07 ± 0.35	2.35 ± 0.34	<0.001
Current Drinkers	*N = 121*	*N = 86*	*N = 35*	
Drinks per week	7.67 ± 0.93	9.16 ± 1.25	4.10 ± 0.70	0.013
Drinks per occasion	4.44 ± 0.40	4.77 ± 0.50	3.64 ± 0.65	0.207
Binge episodes / 2 weeks	2.50 ± 0.38	2.94 ± 0.50	1.37 ± 0.39	0.059
Age at first drink	14.9 ± 0.3	14.8 ± 0.4	15.3 ± 0.5	0.430
Drinks to feel tipsy [c]	3.93 ± 0.30	4.16 ± 0.34	3.08 ± 0.51	0.137
Family alcohol dependency risk[c]	13.9 ± 2.3	14.8 ± 2.9	10.7 ± 1.7	0.459
T-ACE score [c]	2.26 ± 0.19	2.55 ± 0.20	1.25 ± 0.31	0.003
T-ACE positive [c]	77.8	85.7	50.0	0.009
T-ACE severity (%)[c]	11.5 ± 1.8	12.9 ± 2.3	6.6 ± 1.5	0.151
Type Alcohol Preferred (%)	*N = 56*	*N = 43*	*N = 13*	0.678
Beer	44.6	41.9	53.8	
Wine	17.9	16.3	23.1	
Liquor/ Spirits	25.0	27.9	15.4	
Malt liquor/ energy drinks	12.5	14.0	7.7	
Perception of Other Women's Drinking	*N = 114*	*N = 79*	*N = 35*	
Drinks per week	8.69 ± 0.89	8.91 ± 1.14	8.19 ± 1.30	0.715
Drinks per occasion	3.91 ± 0.26	4.11 ± 0.31	3.49 ± 0.43	0.264
Difference Between Other Women's and Own Drinking	*N = 112*	*N = 78*	*N = 34*	
Drinks per week	2.86 ± 0.88	2.05 ± 1.12	4.78 ± 1.25	0.156
Drinks per occasion	0.14 ± 0.29	0.07 ± 0.35	0.31 ± 0.51	0.704

Table 2.4: Drinking pattern of 218 non-pregnant women by AEP risk status, continued

[a] n = Comparing At High Risk to Not At High Risk non-pregnant women using ANOVA for continuous variables and chi-square test for categorical variables; missing data on values for 16 women; sample size varies from one variable to the next because only a subset was selected to complete the web-based questionnaire and due to missing variables.

[b] n = 101/42/59

[c] n = 54/42/12

Characteristics of contraceptive use, also part of the criteria for vulnerability to AEP, are shown in **Table 2.5**. A quarter of participants use no birth control, including abstinence. Of those participants using contraceptives, 18.2% reported using highly effective contraceptives.

Table 2.5: Contraceptive use and effectiveness among 218 non-pregnant women by AEP risk status

Contraceptive Use	Total Population *N = 218*	At High Risk *N = 81*	Not At High Risk *N = 137*	p-value [a]
Use Birth Control [b] (%)	75.2	71.6	77.4	
Abstinent (%)	9.2	0	14.6	
Birth Control Effectiveness	*N = 198*	*N = 81*	*N = 117*	<0.001
High (%)	18.2	0	30.8	
Medium High (%)	30.8	42.0	23.1	
Medium Low (%)	23.2	28.4	19.7	
Low (%)	0.5	1.2	0	
No birth control (%)	27.3	28.4	26.5	

[a] Comparison between At High Risk and Not At High Risk using chi-square test. Missing values on contraceptive use for 16 women.

[b] Includes abstinence

The level of knowledge regarding the risks of alcohol consumption to women and unborn children was high as shown in **Table 2.6**; non-pregnant participants answered an average of 83% of all questions correctly. However, while 94% of non-pregnant women were aware of risks of alcohol consumption during pregnancy, only 34% were aware of risks of alcohol consumption to women themselves.

A high percent of all participants (72%) had heard of FASD. Nearly a third knew someone affected by prenatal alcohol exposure and an additional 9% were not sure whether they did or did not.

Table 2.6: Knowledge questions by AEP risk status

Knowledge Questions (Percent Answering Correctly)	At High Risk	Not At High Risk	p-value [a]
Questions Relating to Pregnancy	N = 43	N = 63	
When a woman drinks alcohol when she is pregnant, the alcohol enters the baby's bloodstream. (T)	100.0	100.0	
Just having a FEW drinks (1-3) during pregnancy is safe for the baby. (F)	83.3	92.1	0.168
Babies of women who drink alcohol during pregnancy are at risk for developing physical, mental and behavioral problems. (T)	100.0	98.4	0.406
Drinking alcohol is OK during the last 3 months of pregnancy. (F)	95.2	95.2	1.000
If a woman is already pregnant but does not know it yet and she is drinking alcohol, she can have a child with an Alcohol Related Birth Defect. (T)	88.1	95.2	0.177
During pregnancy, it is OK to drink during the morning. (F)	97.7	100.0	0.224
If you are breastfeeding and you drink alcohol, the alcohol can be passed to the baby through the milk. (T)	95.2	92.1	0.523
It is OK to drink wine during pregnancy. (F)	76.2	90.5	0.046
If you are nauseous or feel sick to your stomach during pregnancy, you should drink a beer. (F)	97.6	100.0	0.218
Question Relating to Women's Health	N = 43	N = 63	
Women are at a greater risk for developing alcohol-related problems than men. (T)	46.5	65.0	0.061
Summary Measures	N = 43	N = 63	
Percent correct overall	79.7 ± 1.8	85.4 ± 1.1	0.005
Percent correct relating to baby's health	91.2 ± 2.0	95.9 ± 1.0	0.024
FASD Awareness	N = 88	N = 141	
Heard of FASD (%)	67.0	76.6	0.191
Know someone affected by FASD (%)	31.0	34.0	0.836
Not sure if know someone affected by FASD (%)	10.3	8.5	

[a] Comparison between At High Risk and Not At High Risk using chi-square test.

Factors predicting vulnerability to AEP, other than alcohol consumption and contraceptive use, are presented in **Table 2.7**. Model 1 is based on all variables available for the final subset that completed both the paper-based and the web-based surveys, whereas Model 2 is based on the paper and pencil questionnaire variables alone. No two-way interaction terms tested in the models were significant. The five variables in Model 1 taken together accounted for 38.5% of the variability in vulnerability to AEP. Instability was introduced by the small number of participants in two of three possible religiosity responses; 15 participants self-reported as "very" religious, 65 as "somewhat" religious, and 8 as "not at all" religious. Model 1 shows that, among those participants in the web-based subset, controlling for the other variables in the model, being somewhat religious as opposed to very religious was associated with a 68 fold increased odds of vulnerability (95% CI 3.6, 1253.2) and being not at all religious was associated with a 23 fold increased odds (95% CI 2.4, 229.0). Older age and believing other women drank more alcohol were associated with a slight increase in risk, whereas having had more pregnancies and answering more knowledge questions correctly was associated with decreased risk. In Model 2, a similar picture emerged except that age was no longer a significant predictor and religiosity was less strongly associated. While the overall model is still highly significant ($p = 0.002$), the model is estimated to explain only 12.8% of the variance in the dependent variable (at high risk of vulnerability to an AEP).

Table 2.7: Multivariate analysis of factors predicting vulnerability to AEP in 234 non-pregnant women

	Odds Ratio (95% CI)	p-value
Model 1[a] n=88		
Percent of knowledge questions correct	0.95 (0.90, 0.99)	0.040
Perception of other women's drinking (number drinks per week)	1.11 (1.02, 1.20)	0.019
Religiosity		0.013
Very religious (ref)	1	
Somewhat religious	67.49 (3.63, 1253.24)	0.005
Not at all religious	23.28 (2.37, 228.99)	0.007
Gravidity	0.65 (0.43, 0.96)	0.033
Age (years)	1.10 (1.02, 1.20)	0.036
Model 2[b] n=198		
Perception of other women's drinking (number drinks per week)	1.12 (1.02, 1.24)	0.020
Religiosity		0.043
Very religious (ref)	1	
Somewhat religious	6.34 (1.48, 27.18)	0.013
Not at all religious	4.41 (1.21, 16.10)	0.025
Gravidity	0.79 (0.65, 0.96)	0.015
Age (years)	1.04 (0.99, 1.09)	0.094

[a]Model 1: All variables included. Pseudo R^2 = 38.5%. Overall model significance = <0.001. N=88 (35/53).

[b]Model 2: Paper and pencil variables only. Pseudo R^2 = 12.8%. Overall model significance = 0.002. N=198 (74/124).

Discussion

Among our sample of non-pregnant AIAN women of childbearing age, approximately a third was vulnerable to an AEP. Despite the fact that half of all participants did not drink alcohol, a subset of women binge drank and used less than highly effective contraceptive methods.

Protective factors against vulnerability to AEP among this sample of AIAN women included having more knowledge regarding risks associated with alcohol consumption, being very religious, and having experienced more pregnancies and having more children. Scoring higher on the T-ACE screening tool for risky drinking was associated with vulnerability.

Misperceptions of cultural norms or peer behavior relating to alcohol consumption may provide promising opportunities for intervention. We found that women overestimate the amount of alcohol consumed by their peers and that this perception may be used as a comparator for their own drinking. Regardless of vulnerability to AEP, drinking patterns and variables other than amount of alcohol consumed were remarkably similar; drinks needed to feel tipsy, age at first drink, drinks per occasion among drinkers, and family dependency risk were not different among groups. These findings reflect a narrow social norm of alcohol consumption where the abstaining from alcohol and binge drinking are the most commonly accepted patterns. These data confirm previous studies where, despite substantial differences across inherently diverse AIAN populations in alcohol consumption patterns and alcohol abstinence rates, among AIAN drinkers there is a tendency to drink more than is defined

as binge drinking in the present study on each drinking occasion [17, 44, 162]. Our results cannot easily be compared with national binge drinking data as our definition used a lower threshold to define binge drinking (≥3 drinks/occasion). A previous study showed that reducing the definition from ≥5 drinks to ≥4 drinks per occasion increased the prevalence of binge drinking by 36% [172].

The protective aspects of religiosity in this population deserve further exploration in future studies. There is evidence that interventions among AIANs to reduce risky drinking that include spirituality and traditional aspects may be more effective [45, 59, 173-180]. Unfortunately, this study did not ask questions regarding spirituality or traditional practices. Religiosity may be a proxy for spirituality.

Among women selected to answer the web-based questions, 74% of 101 participants and 78% of 54 currently drinking (non-pregnant) participants tested positive for risky drinking with T-ACE (Table 4). These results may be compared to those from studies of women attending prenatal visits including three large [181-183] studies in non-Native populations (27.4% to 55% positive) and one small study among AIAN women from the Northern Plains [171] (71% positive). One difference between these studies and the present study is pregnancy status; the results we present are from non-pregnant women. However, among the small number of pregnant women participating in our study who completed the T-ACE diagnostic, a comparable proportion, 69.2% (9 of 13) tested positive for risky drinking (**Table 2.2**). In this sample, screening positive for risky drinking was associated with how much a woman drank, how much she thought other women drank, and showed a trend toward an association with earlier age at first drink

(14.36 vs. 15.71 years, p=0.070). Family risk of alcohol dependency, smoking, illegal drug use, and age were not associated.

It is important to note that the success of recruitment in this special population was largely due to the inclusion of community members in all aspects of the study, culturally modifying the survey tools, addressing confidentiality concerns (CoC, training, data storage), and conducting community awareness events.

Limitations and advantages

Participants were recruited from AIAN health clinics and findings may not be generalizable to AIAN women choosing not to utilize such clinics. Participants were self-selected and data was self-reported and therefore it was impossible to validate the accuracy of the responses. Women may have under-reported (or over-reported) alcohol use and other behaviors due to associated stigma, recall bias (including alcohol-induced impairment), and the effects of some types of questions including forced choice, scale, and closed[184]. However, in view of the sensitive nature of the data collected, steps were taken to ensure confidentiality, and to gain the support of the participants and the community. Trusted community members were trained as study research assistants, and they recruited participants and collected the data. Approval and support of the Tribal IRB was obtained.

Implications for prevention

Risky alcohol consumption prior to the recognition of pregnancy may result in an AEP. The present study explores risky alcohol consumption among an AIAN population where data was previously unavailable. Results indicate that a subset of women in this community is vulnerable to AEPs. In addition, these findings support a targeted

intervention for non-pregnant AIAN women who currently drink alcohol incorporating awareness of FASDs and the risks of alcohol consumption, efforts to shift cultural norms, and contraceptive counseling.

Acknowledgements

This research was supported by the National Institutes of Health Grant U26IHS300292/01. We would like to express our appreciation to the AIAN women, Southern California Tribal Health Clinic staff, and project consultants for their valuable input and participation, and to our wonderful, insightful, patient, and hard-working research assistants without whom this project would not be possible.

Chapter 2, in full, has been submitted for publication of the material as it may appear in Maternal and Child Health Journal, 2014, Montag, A, Brodine, S, Alcaraz, J, Clapp, J, Allison, M, Calac, D, Hull, A, Gorman, J, Jones, K, Chambers C. *Vulnerability to Alcohol-Exposed Pregnancy among a Population of AIAN Women.* The dissertation author was the primary investigator and author of this paper.

CHAPTER 3 PREVENTING ALCOHOL-EXPOSED PREGNANCY AMONG AN AIAN POPULATION: EFFECT OF A SBIRT INTERVENTION.

Annika C. Montag[1,3,6], Stephanie K. Brodine[1], John E. Alcaraz[1], John D. Clapp[2], Matthew A. Allison[3], Dan J. Calac[4], Andrew D. Hull[5], Jessica R. Gorman[6], Kenneth Lyons Jones[6], Christina D. Chambers[3,6]

[1]SDSU Graduate School of Public Health, [2]Ohio State University School of Social Work [3]UCSD Department of Family and Preventive Medicine, , [4]Southern California Tribal Health Clinic, [5]UCSD Department of Reproductive Medicine, [6]UCSD Department of Pediatrics

Abstract

Background: Fetal Alcohol Spectrum Disorders (FASD) are the result of alcohol-exposed pregnancies (AEP) and believed to be the leading known cause of developmental disabilities in the U.S. Our objective was to determine whether a culturally targeted Screening, Brief Intervention, & Referral to Treatment (SBIRT) intervention may reduce risky drinking and vulnerability to alcohol-exposed pregnancy (AEP) among American Indian/Alaska Native (AIAN) women in Southern California. **Methods:** Southern California AIAN women of childbearing age completed a survey including questions regarding alcohol consumption and contraceptive use, were randomized into intervention or treatment as usual groups where the former group completed an on-line SBIRT intervention, and were followed-up at 1, 3, and 6 months post-intervention. **Results:** Of 263 women recruited and 247 with follow-up data, one-

third were at high risk of having an AEP at baseline. Both treatment groups decreased self-reported risky drinking behavior (drinks per week, p=0.000; frequency of heavy episodic (binge) drinking episodes per 2 weeks, p=0.017 and risk of AEP p=0.000 at six months post-intervention) in the follow-up period. There was no difference between treatment groups. Baseline factors associated with decreased risk of an AEP at follow-up included the perception that other women in their peer group consumed a greater number of drinks per week, having reported a greater number of binge episodes in the past two weeks, and depression/impaired functionality. **Conclusions:** Participation in assessment alone may have been sufficient to encourage behavioral change even without the web-based SBIRT intervention. Randomization to the SBIRT did not result in a significantly different change in risky drinking behaviors. The importance of perception of other women's drinking and one's own depression/ functionality may have implications for future interventions. **Keywords:** Fetal Alcohol Spectrum Disorders (FASD), Native American women, Alcohol, Prevention Research, SBIRT

This research was supported by the National Institute of General Medical Sciences grant U26IHS300292/01.

Introduction

Fetal Alcohol Spectrum disorders (FASD), a range of conditions resulting from prenatal alcohol exposure, are the leading known cause of preventable developmental disabilities and learning disabilities. In the most severe form of FASD, Fetal Alcohol Syndrome (FAS), fetal development is so affected as to result in neurobehavioral dysfunction, growth restriction, microcephaly, and characteristic facial features [1]. FASDs result in persistent deficits in cognitive and motor functions including learning

and memory, complex thought, attention, and motor control, as well as psychosocial behavior [7, 185]. Less severe forms of FASD are more difficult to identify but thought to be more prevalent. Specifically, current estimates are that FASD affects 2-5% of young elementary school children in the U.S. and that FAS may affect 0.2-0.7% [161]. Significant variation in FASD prevalence among populations is associated with differences in magnitude and prevailing patterns of alcohol consumption as well as variability in how prevalence is measured. In addition, there may be modification of risk by nutritional status, maternal age, and genetics [18].

There is no known safe level of alcohol consumption during pregnancy. A recent study evaluating prenatal alcohol exposure and a number of outcomes including growth parameters, facial dysmorphology characteristic of prenatal alcohol exposure, and minor structural malformations found a linear relationship and no evidence of a threshold [25]. A review of well controlled studies including six published studies examining the effect of low to moderate alcohol consumption on the cognitive, social, and emotional development of children, found that four of the six showed an association between prenatal alcohol exposure and negative outcome (hyperactivity, behavioral problems, emotional problems, peer relationship problems, and attention deficit disorder) in children from 3-16 years [26]. Despite current controversy[27], there is at best inconclusive evidence of a threshold and the preponderance of data supports that there is no safe dose of prenatal alcohol exposure. One reason for the controversy is the difficulty involved in teasing out neurobehavioral effects of a particular exposure given the myriad potential confounders (nutrition, genetics, etc.). In 2005, the Surgeon General

of the United States issued an advisory for all women who are pregnant or might become pregnant to not consume alcohol [28].

However, the pattern of prenatal alcohol consumption associated with the greatest risk of FASDs is heavy episodic drinking or binge drinking [21]. Binge drinking results in higher blood alcohol concentrations which are associated with greater injury to the fetus. Drinking a greater number of drinks per week or month also increases the risk of harm [23].

Timing of alcohol consumption during pregnancy influences the type of injury to the fetus; the particular injury is related to the developmental phase of the fetus at the time of exposure. A particularly sensitive time for the development of the brain and some of the characteristic dysmorphology associated with FAS occurs early in the first trimester [30]. This is relevant as more than half of all pregnancies in the U.S. are unplanned [33] and many women are unaware they are pregnant 4-6 weeks post-conception [35]. To prevent alcohol-exposed pregnancies, it is therefore important to include all women of childbearing age who may consume alcohol in prevention/intervention.

While most women reduce or discontinue alcohol use upon awareness of pregnancy, subgroups of women remain vulnerable to continued use: women who are unmarried, unemployed, depressed, risky drinkers, exposed to violence, or simply confused by health warning messages and the amount of alcohol their drinks contain [67, 70, 72]. Drinking during pregnancy is heavily influenced by social norms and therefore varies widely among populations. For example, the percent of women who report drinking alcohol during pregnancy is 0% in Saudi Arabia, 6% in Sweden [76], 7.4% in

the U.S. [43], and 34% in New Zealand [77]. Similarly, among the limited populations studied, drinking during pregnancy among the heterogeneous AIAN populations of the U.S. differs significantly. May et al. [17] published data from a prenatal clinic among Northern Plains Indians indicating 16.2% of pregnant women consumed alcohol. Other AIAN studies have reported 36% of urban and 14% of reservation residing pregnant women consuming alcohol [80] and 53.4% at one prenatal clinic in the Northern Plains [81]. Risky pre-pregnancy drinking is strong predictor of drinking during pregnancy [61]. Further exacerbating risk are associations of binge drinking with increased risk of unintended pregnancies [64]. Within the population addressed in this study, approximately a third of women between the ages of 18 and 45 years are estimated to be at risk of having an alcohol exposed pregnancy (submitted manuscript Montag et al., 2014).

Effectiveness of FASD prevention strategies implemented among various AIAN populations were recently reviewed [137]. Available evidence suggests that an effective intervention should strive to include local community members in all aspects of the program, create a relevant and understandable intervention recognizing specific risk and protective factors within the community, and address logistic barriers to participation.

Screening, Brief Intervention, and Referral to Treatment (SBIRT) is a prevention and early intervention approach that uses wide screening, education and feedback specific to the participant, and professional treatment for those identified by the screening as positive for alcohol abuse problems [143]. The latter component, the incorporation of specialized treatment as warranted, sets the approach apart from those offering only brief interventions which have demonstrated largely positive but mixed results [147]. Some

reasons for lack of proven benefit may be that assessment alone may have a mitigating effect on risky drinking (although this has been controlled for in some studies) or that extreme risky drinking may decrease over time due to "regression toward the mean". Valuable lessons learned from Brief Intervention studies include that protocols with multiple contacts are more likely to alter behavior than single contact protocols [148] and that effectiveness may be related to the severity of the underlying condition [150]. SBIRT has been used to motivate a reduction in alcohol consumption in a number of populations including emergency room and other healthcare setting patients [154], college freshmen [159], and WIC participants [160].

Within the Native American Research Centers for Health (NARCH) framework, this intervention sought to develop and test an SBIRT adaptation for reducing risky drinking in AIAN women of childbearing potential in Southern California. NARCH is an initiative funded through a partnership between the National Institutes of Health and the Indian Health Service. As a NARCH project, the overarching goals go beyond the specific aims of any single study to address tribally identified health priorities, reduce distrust of research by the community, and develop future competitive AIAN researchers.

Methods:

Sample source: The population sample consisted of AIAN women from 18 to 45 years of age, of childbearing potential, recruited from one of three AIAN health clinics located in Southern California between April 2011 and September 2012. The sample used for each analysis will vary and is described in association with the particular analysis.

Ethics: This protocol was approved by University of California, San Diego, San Diego State University, and Southern California Tribal Health Clinic Institutional Review Boards. A Certificate of Confidentiality was obtained from the NIH to further protect the confidentiality of participants' data. All research staff complete human research subject protections training.

Recruitment and study protocol: Potential participants were approached in waiting areas of health clinics and screened for eligibility. (See **Figure 3.1** for study flowchart). Interested and eligible participants were brought to a private room where, following the consenting procedure, they were assigned a unique identification number, completed a paper-based self-administered baseline survey, and were randomized into the intervention or control group. Randomization was accomplished by the research assistant, in blinded fashion, pulling a label preprinted with either "intervention" or "control" from a single study randomizing container containing equal numbers of each label. Participants randomized into the intervention group completed a web-based survey which provided personalized feedback that could be printed out in a confidential manner. Participants randomized into the control group received "treatment as usual" which consisted of access to educational brochures about health but did not include specific FASD information. All participants had the opportunity to request referral for treatment to a professional substance abuse counselor. At one, three, and six months following baseline assessment, participants were contacted by telephone to complete follow-up surveys. At each follow-up, participants were again offered referrals to treatment. Participants were provided incentives in the form of a $10 gift card and the choice of a fan or t-shirt emblazoned with the project logo at enrollment and a $15 gift card

following completion of the final follow-up questionnaire. Additional retention incentives were added during the study to improve follow-up completion rates. Participants received one raffle ticket representing a chance to win a $100 prize for each completed follow-up interview.

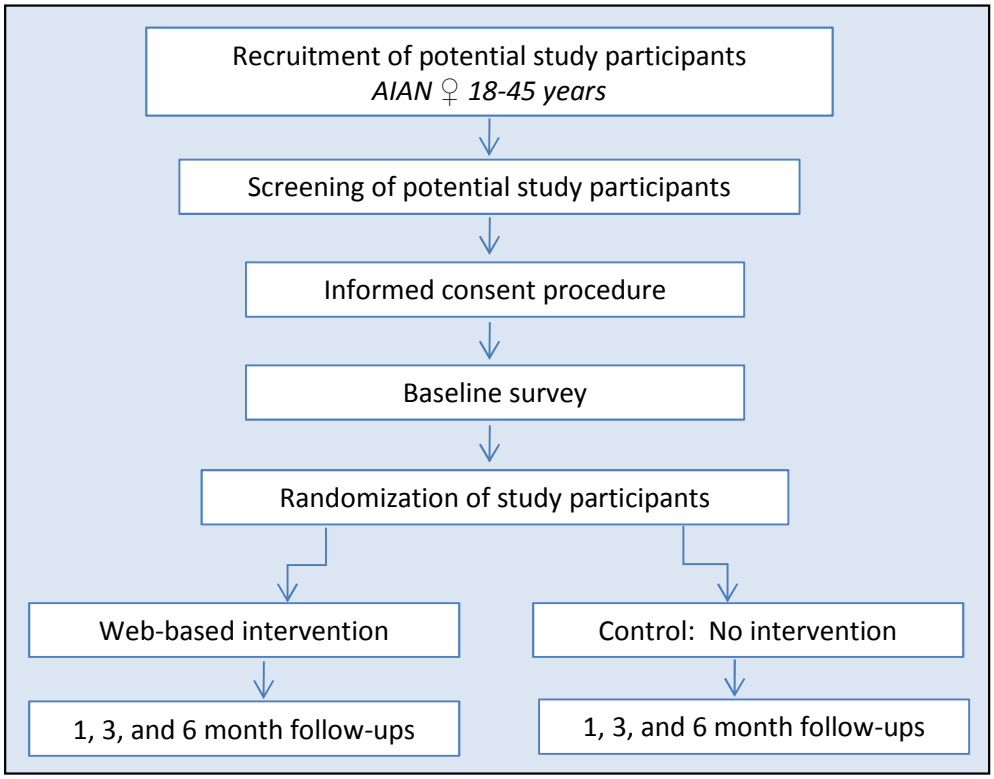


Figure 3.1: Study Flowchart

Data collection: Data was collected on three separate occasions during the study: at recruitment (all participants), during the web-based intervention (participants randomized into the intervention arm of the study), and during each follow-up (all participants able to be contacted for follow-up).

Baseline questionnaire: The self-administered, questionnaire included questions regarding current relationship situation, employment, religiosity, income,

gravidity, parity, birth control use, current use of prescription and non-prescription medications, smoking, illegal drug use, depression and functionality, awareness of FASD, knowledge regarding the risks of alcohol consumption to women and to pregnancy, and alcohol consumption including number of drinks consumed per week and per occasion, and number of binge episodes in the past two weeks (binge defined as consuming ≥ 3 drinks/occasion).

Web-based questionnaire: Participants randomized into the intervention arm of the study self-reported information by computer regarding alcohol consumption over the past two weeks, current use of prescription or non-prescription medications, pregnancy status, the age they began drinking alcohol, and contraceptive use. Illustrations of various alcoholic beverage containers were used to prompt recall. They were asked to complete a series of true or false knowledge questions about risks associated with alcohol consumption.

Follow-up questionnaire: In the follow-up telephone questionnaire, research assistants asked questions regarding current relationship status, pregnancy status, birth control use, and alcohol consumption, including binge drinking, over the past two weeks.

Intervention: eCHECKUP TO GO, a web-based brief assessment and intervention tool based on the e-CHUG web tool developed for college students by Drs. Van Sickle and Moyer at San Diego State University, was tailored to the population participating in this study (Gorman ref). Participants answered questions in a confidential manner at their own pace and received individualized web-based feedback at the end of the session regarding their risk for an alcohol-exposed pregnancy, the impact

of alcohol exposure to the fetus, the physical and financial cost of their alcohol consumption, and how their drinking compared with that of other Native women. A resource page at the end of the web session provided information on resources for additional information or assistance and could be printed out. The intervention took approximately 20 minutes to complete.

Study Measures: The "Vulnerability to Alcohol-Exposed Pregnancy" variable was defined in two categories: not at high risk and at high risk. Being "at high risk" for an AEP was defined as 1) currently drinking 3 or more standard drinks per occasion and/or 8 or more standard drinks per week, and 2) using a less than a highly effective contraceptive method. We defined "binge" or "risky" drinking as 3 or more standard drinks per occasion and/or 8 or more drinks per week as this level of consumption has been defined as either risky for women or predictive of risk of adverse pregnancy outcomes in other studies [186]. We defined standard drinks as shown in **Figure 3.2**.

12 fl. oz. beer (~ 5% alcohol) | 5 oz. wine (~ 12% alcohol) | 1.5 fl. oz. liquor/spirits (~ 40% alcohol)

Figure 3.2: Definition of a "Standard Drink"

Contraceptive effectiveness was defined as: High (less than one pregnancy per 100 women per year), Medium High (2-9 pregnancies per 100 women per year), Medium Low (15-24 pregnancies per 100 women per year), and Low (≥25 pregnancies per 100 women per year) [168].

The 9-item Patient Health Questionnaire (PHQ-9) was used to measure depression and functionality [187]. Depression variables derived from this measure included treatment recommendation for depression (treatment recommended or not recommended), minor depression (yes/no), major depression (yes/no), and functionality (impaired or not impaired).

As only the intervention group responded to the web-based questions, questions from the paper-based baseline questionnaire were used in the analysis where possible. However, where a question in the intervention group was left blank in the paper

questionnaire, the web-based answer was used. Primary outcome variables included the number of drinks consumed per week, the number of binge episodes over the past two weeks, and vulnerability to AEP.

Statistical Analyses: Comparisons were conducted using t-tests (continuous), χ^2 (dichotomous), Fisher's exact test (dichotomous with small cell sizes), and nonparametric analyses (for data not normally distributed and not transformed). Normality in continuous variables was investigated through skewness and kurtosis. ANOVA was used to examine associations among population characteristics. The vulnerability to AEP outcome variable was tested as dichotomous ("at high risk" vs. "not at high risk"). Change over time analyses were conducted in two ways: 1) using only the subjects available at all follow-ups and 2) multiple imputation methods. Linear regression was used to test reduction of some drinking parameters from baseline. Repeated ANOVA or mixed-model methods were used to estimate individual change over time and compare trajectories. Change was assessed in two ways: 1) using a dichotomous scale where participants were improved or not, and 2) using a three category system where participants were categorized as improved, remaining not at risk, and remaining at risk or at increased risk. Regression was used to test for predictors of positive change. First, each predictor was tested to determine whether there were significant independent associations with that one factor and change. Then, multiple regression analysis was used examine all variables previously found to be significant. All two-way interactions among significant variables were tested.

Additional analyses explored the effect of the intervention on high risk drinkers alone, the effect of missing (or completing) a follow-up session on final outcome,

differences between participants lost to follow-up and remaining participants, and the effect of controlling for baseline drinking or risk status on final outcome.

Statistical significance was defined as 2-sided, p-value of <0.05. Statistical analyses were carried out using SPSS (PASW 18, SPSS Inc., Chicago, IL).

Results

A total of 263 women were recruited into the study; of these 16 (6.1%) were lost to follow-up. **Figure 3.3** shows the study recruitment diagram.

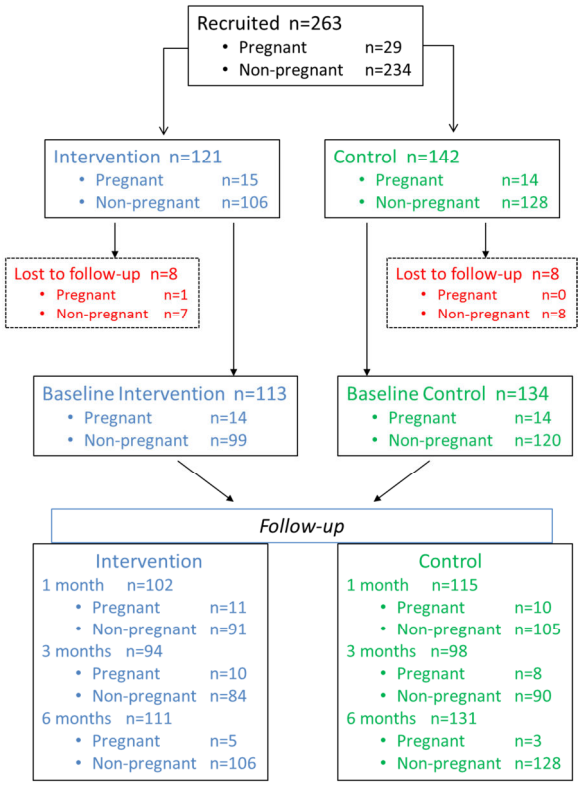


Figure 3.3: Recruitment Flowchart

Baseline characteristics of the sample population are shown in **Table 3.1** by randomized group. Randomized groups were similar in all aspects with the exception of a higher percent of women in the control group having previously had a child.

Table 3.1: Baseline Demographics of Total Population with Follow-up by Randomized Group

Variable	Total (Mean±SE or %) *n=247*[a]	Intervention (Mean±SE or %) *n=113*	Control (Mean±SE or %) *n=134*	p-value[b]
Maternal Characteristics				
Age (years)	28.6 ± 0.5	27.7 ± 0.8	29.4 ± 0.7	0.114
Pregnant currently (%)	11.3	12.4	10.4	0.632
Has had at least one child (%)	64.2	57.1	70.1	0.045
Children (number previous)	1.5 ± 0.1	1.3 ± 0.2	1.6 ± 0.1	0.058
Pregnancies (number previous)	2.0 ± 0.1	1.9 ± 0.2	2.2 ± 0.2	0.293
Wants more children (%)	61.2	63.8	59.1	0.459
Cohabitating (%)	45.7	41.4	49.2	0.224
Employed (%)	42.8	43.1	38.9	0.511
Religious (%)	86.6	88.6	85.0	0.431
Current smoker (%)	29.7	26.8	32.1	0.364
Current use of illegal drugs (%)	12.1	11.9	12.2	0.946
Depression				
Treatment recommended (%)	35.7	35.1	36.2	0.869
Minor Depressive Syndrome (%)	29.4	26.8	31.6	0.412
Major Depressive Syndrome (%)	2.9	2.7	3.1	0.855
Functionality Impaired (%)	7.2	10.5	4.4	0.090
FASD Awareness				
Heard of FASD (%)	71.5	72.3	70.9	0.161
Know someone affected by FASD (%)	32.2	28.8	35.1	0.531
Not sure if know someone affected (%)	9.4	9.0	9.7	

[a] Sample size varies due to inclusion of selected variables in the web-based survey and missing values.

[b] comparing Intervention to Control using ANOVA for continuous variables and chi-square test for categorical variables.

Alcohol consumption and related variables were not different between randomized groups at baseline (**Table 3.2**) nor was contraceptive use (**Table 3.3**) or vulnerability to AEP (**Table 3.4**). Half of participants reported not currently drinking any alcohol. Among those currently consuming alcohol, there was a high proportion of binge drinkers (84%). The social norm, i.e., perception of other women's drinking, on average was reported as 4 drinks per drinking occasion.

Table 3.2: Alcohol Consumption and Related Parameters by Randomized Group

Alcohol Consumption Variable	Total Population	Intervention	Control	p-value
All Women	*N = 247*	*N = 113*	*N = 134*	
Ever drank alcohol (%)	94.7	94.7	94.7	0.993
Currently consume alcohol (%)	50.0	48.7	51.1	0.700
Age at first drink	15.2 ± 0.2	14.8 ± 0.3	15.6 ± 0.3	0.076
Drinks per week	3.80 ± 0.52	4.11 ± 0.94	3.53 ± 0.53	0.576
Drinks per occasion	2.22 ± 0.25	2.01 ± 0.33	2.40 ± 0.38	0.443
Binge episodes / 2 weeks	1.22 ± 0.21	1.40 ± 0.42	1.06 ± 0.16	0.415
Current binge drinker (%)	42.9	42.0	43.7	0.793
Current risky drinker (%)	42.0	42.5	41.7	0.898
Perception of other women's drinking				
Drinks per week	7.40 ± 0.63	7.04 ± 0.92	7.71 ± 0.87	0.599
Drinks per occasion	3.40 ± 0.21	3.28 ± 0.27	3.50 ± 0.32	0.614
Current Drinkers	*N = 122*	*N = 55*	*N = 67*	
Age	29.0 ± 0.7	27.8 ± 1.0	30.0 ± 1.0	0.118
Drinks per week	7.60 ± 0.92	8.38 ± 1.74	6.94 ± 0.84	0.436
Drinks per occasion	4.39 ± 0.41	4.06 ± 0.53	4.66 ± 0.62	0.476
Binge episodes / 2 weeks	2.34 ± 0.38	2.78 ± 0.78	1.98 ± 0.25	0.299
Current binge drinker (%)	83.6	85.5	82.1	0.617
Current risky drinker (%)	84.4	87.3	82.1	0.432
Age at first drink	14.8 ± 0.3	14.6 ± 0.5	15.0 ± 0.3	0.450
Perception of Other Women's Drinking	*N = 114*	*N = 51*	*N = 63*	
Drinks per week	8.70 ± 0.89	8.90 ± 1.55	8.53 ± 1.00	0.837
Drinks per occasion	3.85 ± 0.26	3.85 ± 0.36	3.85 ± 0.36	1.000
Difference Between Other Women's and Own Drinking	*N = 111*	*N = 50*	*N = 61*	
Drinks per week	2.85 ± 0.88	3.79 ± 1.14	2.02 ± 1.31	0.315
Drinks per occasion	0.17 ± 0.28	0.51 ± 0.38	-0.10 ± 0.41	0.288

Table 3.3: Baseline Contraceptive Use by Randomized Group (non-pregnant participants)

Contraceptive Use	Total Population *N = 219*	Intervention *N = 99*	Control *N = 120*	p-value [a]
Use Birth Control [b] (%)	61.2	65.7	57.5	0.218
Abstinent (%)	8.7	11.5	6.3	0.183
Birth Control Effectiveness	*N = 190*	*N = 85*	*N = 105*	0.073
High (%)[c]	13.7	11.8	15.2	
Medium High (%)	30.5	40.0	22.9	
Medium Low (%)	24.2	24.7	23.8	
Low (%)	0.5	0	1.0	
No birth control (%)	31.1	23.5	37.1	

[a] Comparison between Intervention and Control using chi-square test.
[b] Excludes abstinence
[c] Comparison between Intervention and Control for Highly Effective Birth Control or not: p = 0.302

Figure 3.4 A through C show changes over time in various measurements: a) number drinks consumed per week, b) number binge episodes in past two weeks, and c) at high risk for AEP. Regardless of variable, all outcomes show a statistically significant time effect but no intervention effect.

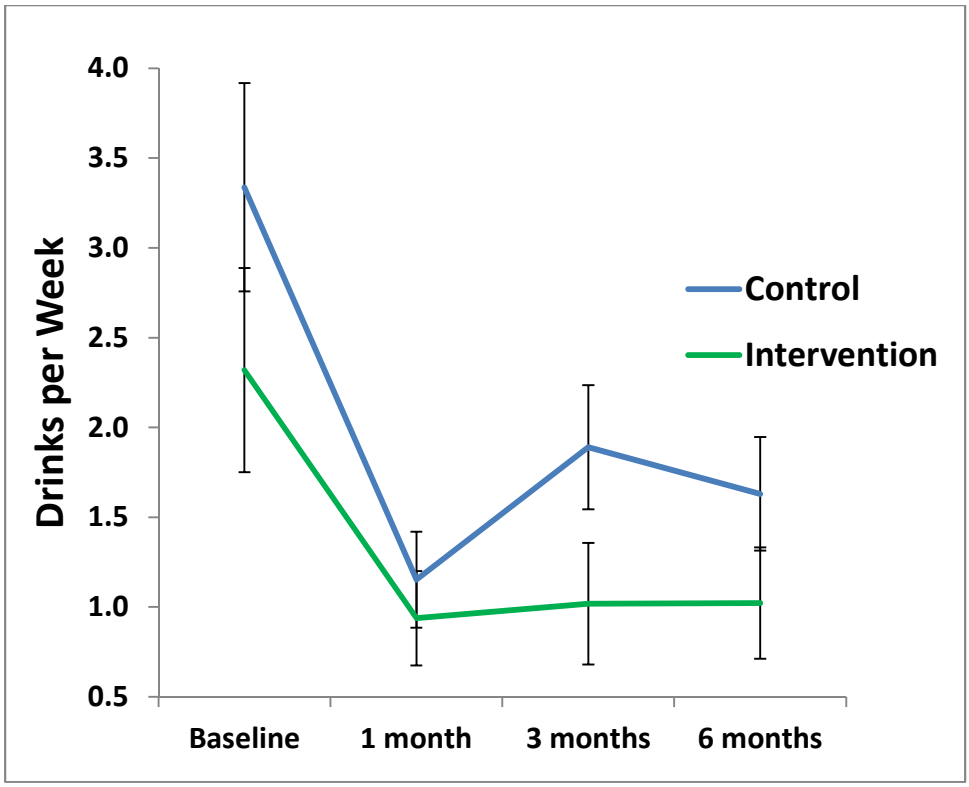


Figure 3.4 A, B, and C. Change over time in primary outcome variables (estimated marginal means and SE)

A. Average Number Drinks per Week, Total Population without Missing Values (n= 157, 80 Control /77 Intervention).
Treatment by time interaction p = 0.687; Time effect p = 0.000

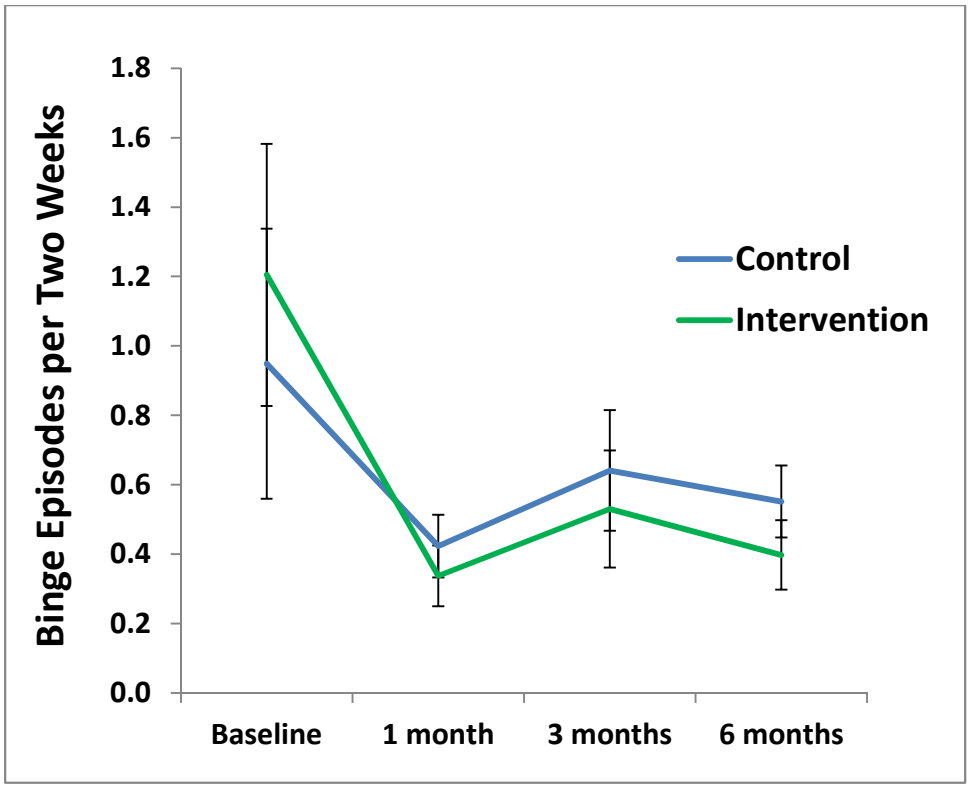


Figure 3.4 A, B, and C. Change over time in primary outcome variables (estimated marginal means and SE), continued

B. Number Binge Episodes in the Past Two Weeks, Total Population without Missing Values (n=161, 83 Control/ 78 Intervention)
Treatment by time interaction p = 0.551; Time effect p = 0.017

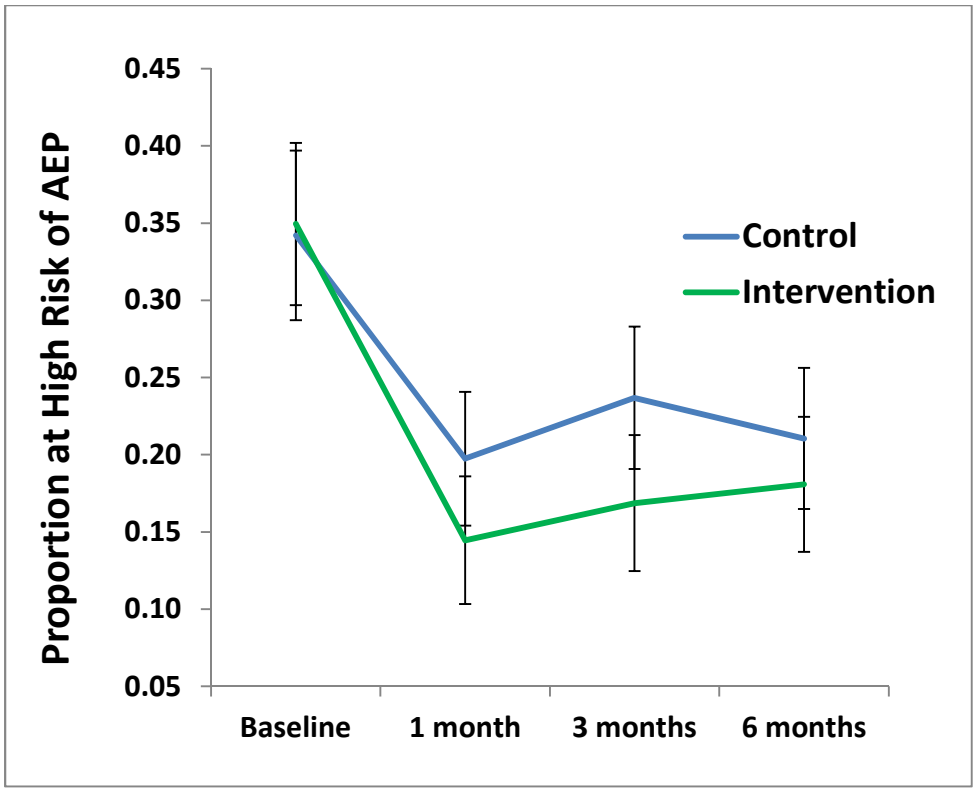


Figure 3.4 A, B, and C. Change over time in primary outcome variables (estimated marginal means and SE), continued

C. Proportion of Population at High Risk of AEP, Total Population without Missing Values (n=159, 83 Control / 76 Intervention)
Treatment by time interaction p = 0.716; Time effect p = 0.000

Table 3.4 further illustrates change over time by presenting means of all available data at each time point. As in **Figure 3.4** A through C representing estimated marginal means of complete data sets, a strong positive time effect is evident. There is a steep reduction in risky behavior evident at the first follow-up. Using multiple imputation methods, the outcome remains the same: a strong time effect but no difference between treatment groups.

Table 3.4: Change over Time in Primary Outcome Variables –mean (SE) or %. N shown is Intervention group/ Treatment group.

	Time Period			
	Baseline	1 month	3 months	6 months
Drinks per week (all available data)	N=116/130	102/115	91/97*	110/131
Intervention	4.40±0.94	0.89±0.21	0.98±0.26	1.64±0.55
Control	3.38±0.50	1.34±0.24	1.94±0.38	1.99±0.46
Binge Episodes / 2 weeks (all available data)	N=115/132	102/115	94/98	111/131
Intervention	1.47±0.40	0.36±0.08	0.49±0.17	0.50±0.12
Control	1.06±0.16	0.49±0.09	0.62±0.13	0.72±0.14
High Risk of AEP(%) (all available data)	N=121/137	101/114	90/92	111/131
Intervention	36.4	18.8	16.7	18.9
Control	33.6	21.9	21.7	22.1

*p=0.037 at 3-month follow-up; drinks per week

Predictors of change (variables associated with a decrease in alcohol consumption) are shown in **Table 3.5**. The more likely participants were to need treatment for depression (or to feel that their functionality was impaired), the more they thought other women drink, and the more binge episodes they had in the past 2 weeks, the more likely they were to reduce alcohol consumption. In the present study, depression and functionality variables often functioned similarly in analyses. Many women in our study expressed surprise regarding both other women's drinking (that half do not drink) and their own (that they were engaging in binge drinking).

Table 3.5: Variables Associated with a Decrease in Drinks per Week from Baseline to 6 Months (n=164).

	β[a]	B[b] ± SE	sig	Partial R^2
Predictor Variables				
Binge episodes per 2 weeks at baseline (number)	0.563	1.31±0.15	0.000	0.575
Functionality (impaired vs. not impaired)	0.171	5.13±1.89	0.008	0.210
Perception of other women's drinking (number drinks per week)	0.127	0.11±0.06	0.050	0.154
Cohabitating (yes vs. no)	0.093	1.52±1.02	0.139	0.118
R^2	0.411			
Adjusted R^2	0.396			
ANOVA sig	0.000			

[a] Standardized coefficient
[b] Unstandardized coefficient

Discussion

In this randomized controlled study, risky drinking behavior and vulnerability to AEP were reduced in both the intervention and control groups. For each primary outcome variable (number drinks per week, number binge episodes per 2 weeks, vulnerability to AEP) there was evidence of a time effect but no statistically significant treatment effect. Effects were sustained over the six month follow-up period.

Assessment reactivity (particularly in participants already considering change), regression to the mean, and effects related to our mixed mode design may have contributed to the reduction in alcohol consumption in the control group. Our findings emphasize the need to include control groups in similar studies. In controlled studies, similar effects are not uncommon observations [188]. The finding that assessment, in

and of itself, is associated with a positive change in behavior has important implications for future interventions in this population. An assessment strategy may prove appropriate in situations where more time-intensive approaches are impractical.

AIAN tribes vary significantly in alcohol consumption [45, 189]. Our findings regarding the pattern of drinking among our participants supports previous work by May[37] , among others, where binge drinking is the primary pattern of drinking among a number of AIAN populations. Overestimation of other women's alcohol consumption may contribute to increased drinking [56] and increased perception of risks associated with drinking may reduce consumption [57]. Social norms that tolerate risky drinking may prevent women from recognizing and addressing problems. According to the 2007 National Survey of Drug Use and Health, the vast majority of people needing treatment for alcohol abuse were unaware that they needed it [58]. Nonetheless, attempts to shift social norms relating to alcohol consumption have been used in interventions among non-AIAN populations with mixed results [52, 54]. The present results indicate that, among AIAN women in our source group, interventions addressing social norms may prove effective. Findings support narrow social norms among variables such as drinks per occasion among drinkers, drinks needed to feel tipsy, and age at first drink. These variables were not different among groups with different vulnerability to AEP. The perception of how much other women drink was an important predictor of reduced drinking during follow-up.

In addition to perceiving social norms of higher alcohol consumption, the present study revealed two other predictors of reduction in alcohol use: testing positive for depression or impaired functionality and a greater number of binge drinking episodes

over a two week period. Treatment for depression was recommended for a third of the women in our sample (36%). This proportion is striking when compared to the prevalence of depression among U.S. women (14% in 2006) [86] and among 2,289 adult Alaska Native women (20%) [91] measured using the same PHQ-9 instrument. In women, as opposed to men, depression appears to predate alcohol problems [69]. Screening for depression may facilitate identification of women vulnerable to AEP. Furthermore, addressing depression in this population may be a helpful independent approach to preventing FASD.

The finding that a greater magnitude of change was predicted by higher number of binge episodes at baseline is somewhat unexpected in that the strategy of SBIRT is geared toward a broader population of relatively lower risk. However, recognition of the extent of one's binge drinking may be sobering (and motivating) for women who are more likely to frequently binge drink.

Controlling for baseline alcohol consumption only served to improve the predictive power of our model (adjusted R^2 increased to 75.2%). In addition, binge drinking, perception of social norms, and depression/functionality were consistently predictive of primary variable change at each follow-up time point. Variables that were, perhaps unexpectedly, not significantly predictive of change were age, smoking, income, illegal drug use, and religiosity.

Previous research has found that the effect of an intervention may be intensified or extended by multiple contacts (Longabaugh, 2001). In the present study, whether or not the one-month follow-up contact was completed did not affect the three- or six-month

follow-up results (data not shown). Similarly, missing the three-month follow-up did not affect findings in the six-month follow-up.

The present intervention did not include a contraceptive intervention component beyond assessment. Contraceptive use was not different among treatment groups or follow-up time points. As vulnerability to AEP may be decreased by preventing pregnancy as well as preventing risky drinking, this would be a valuable addition to future interventions. Relevant examples of such interventions are project CHOICES[190] and EARLY [191]. It is of note that exposure to the EARLY intervention was associated with a greater change in contraceptive use than in alcohol consumption [191].

Limitations and strengths

Participants in this study were self-selected volunteers so that it is unknown to what extent they represent the entire population of women of reproductive potential in these settings. However, we recruited potential subjects at various locations and publicized the study broadly. Another limitation was that data was self-reported and therefore not feasible to validate. "Social presence" may have played a role as the self-administered paper-based and web-based questionnaires were completed with a researcher in the same room. Therefore it is possible that participants may have under or over-reported sensitive behaviors due to social acceptability / desirability.

In addition, a mixed mode design for data collection was used where baseline data was collected using a paper-and-pencil based format and follow-up data was obtained by telephone interview. Participants randomized to the intervention, completed an additional web-based survey where a subset of questions were repeated from the baseline

survey. We compared responses on questions that occurred in both the paper-based and web-based modes, and found no significant differences.

We sought to minimize these potential biases by assuring participants of confidentiality, using well trained interviewers who were community members, establishing private environments for all data collection modes, using equivalent questions across modes, and ensuring that participants could ask questions or request clarification of questions in all modes.

Not all participants completed all follow-up interviews. Missing follow-up data may introduce bias but, whether data was analyzed using only complete data sets, all available data, or using multiple imputation methods, the results did not differ.

Alcohol consumption data was collected in increments of 2 weeks; a relatively short time period selected for the purpose of obtaining the most precise data on daily drinking habits. As the number of drinks consumed per occasion (or drinking day) remained relatively consistent and reductions in risky drinking were largely due to changes in the frequency of drinking days, the brief assessment period may have introduced bias. This threat to validity could be lessened in future studies by expanding the assessment time periods.

Initial and continuing efforts to gain the support of the community and to ensure confidentiality increased participation and retention. All recruitment and data collection was carried out by trusted community members trained as research assistants. Approval and support of the Tribal IRB was obtained. Efforts were made to adapt the SBIRT intervention to make it as relevant and understandable to this particular community as possible.

Implications for prevention

Our finding that assessment alone, even without intervention, may be sufficient to decrease risky drinking and vulnerability to AEP indicate a value to providing assessment even if time constraints prevent an accompanying intervention. Furthermore, the study supports targeted interventions for AIAN women who currently drink alcohol that incorporate efforts to shift cultural norms, recognition of depression, and assessment of alcohol consumption and vulnerability to AEP.

Acknowledgements

This research was supported by the National Institutes of Health Grant U26IHS300292/01.

Chapter 3, in full, has been submitted for publication of the material as it may appear in Alcoholism: Clinical and Experimental Research, 2014, Montag, A, Brodine, S, Alcaraz, J, Clapp, J, Allison, M, Calac, D, Hull, A, Gorman, J, Jones, K, Chambers C. *Preventing Alcohol-Exposed Pregnancy among an AIAN Population: Effect of a SBIRT Intervention.* The dissertation author was the primary investigator and author of this paper.

CHAPTER 4 INFLUENCE OF DEPRESSION ON VULNERABILITY TO ALCOHOL-EXPOSED PREGNANCY AND RESPONSE TO INTERVENTION.

Annika C. Montag[1,3,6], Stephanie K. Brodine[1], John E. Alcaraz[1], John D. Clapp[2], Matthew A. Allison[3], Dan J. Calac[4], Andrew D. Hull[5], Jessica R. Gorman[6], Kenneth Lyons Jones[6], Christina D. Chambers[3,6]

[1]SDSU Graduate School of Public Health, [2]Ohio State University School of Social Work [3]UCSD Department of Family and Preventive Medicine, , [4]Southern California Tribal Health Clinic, [5]UCSD Department of Reproductive Medicine, [6]UCSD Department of Pediatrics

Abstract

Objectives: To investigate the association of depression with risk factors for alcohol-exposed pregnancy (AEP) and to explore modification of the effect of a Screening Brief Intervention and Referral to Treatment (SBIRT) intervention by depression in a population of American Indian Alaska Native (AIAN) women. **Methods:** Between 2011 and 2012, 263 AIAN women of childbearing age completed a baseline questionnaire including the PHQ-9 depression diagnostic, an SBIRT intervention if randomized into the treatment group, and follow-up surveys at 1, 3, and 6 months post-intervention. **Results:** Depression was associated with risk factors for AEP; increased alcohol consumption and decreased effective contraceptive use (*P*'s <.001). Women identified as depressed at baseline experienced greater reduction in risky behavior with

the intervention than non-depressed women. **Conclusions:** Screening for depression may assist in targeting FASD prevention interventions. Depressed women may benefit to a greater extent than non-depressed women from interventions incorporating personalized feedback.

Keywords: Fetal Alcohol Spectrum Disorders (FASD), AIAN women, Alcohol, Prevention Research, SBIRT

Introduction

Alcohol-exposed pregnancies (AEPs) can result in broad array of conditions that together are referred to as Fetal Alcohol Spectrum Disorders (FASD). They are the leading known cause of developmental physical, neurological, and behavioral disabilities [1-12].

The pattern of prenatal alcohol consumption influences the risk of FASDs. The pattern of drinking associated with the highest risk of FASDs is heavy episodic, or binge, drinking [21, 22]. Binge drinking results in the high blood alcohol concentrations associated with greater injury to the fetus. Among pregnant women who drink alcohol, the greater the number of drinks over the period of a month or two weeks, the more likely their children will incur negative effects [23].

Risk factors associated with FASD in the general population, beyond magnitude and pattern of alcohol consumption, are older age, high parity, use of other drugs including tobacco and illegal substances, unemployment, family history of alcohol abuse, alcohol abuse by partner, tenuous marital status (cohabitation without marriage, separated, divorced), community tolerance of risky drinking, and mood disorders including depression and anxiety [16-18, 37-41].

Pre-pregnancy drinking is a robust predictor of AEP [61]. Binge drinking is associated with an increased risk of unintended pregnancies, further amplifying the risk of an AEP [64]. Naimi also found that women who binge drank were more likely to smoke and experience violence prior to pregnancy, and to drink alcohol and smoke during pregnancy [64].

The relationship between depression and alcohol problems (including binge drinking) in women has long been recognized [69, 105-112]. In women, as opposed to men, depression appears to predate [69, 116] and perhaps predict [192] alcohol problems. Treatment of depression in women may help prevent risky drinking [193, 194].

Depression and alcohol consumption also appear to be associated in pregnancy [117-120]. Depressed pregnant women are more likely to drink alcohol, binge drink, and smoke than non-depressed pregnant women, and less likely to receive prenatal care [119, 121-124]. Additionally, antenatal depression is associated with poor obstetric and fetal outcomes [125, 126]. Due to the potentially catastrophic consequences of untreated depression in pregnancy, it is important to identify and treat maternal depression as early as possible [127-129]. A 2003 study found that among women identified as being in need of treatment for depression, 86% did not receive treatment [130].

Within AIAN populations, risk factors for FASD are less well known [166]. The heterogeneity of AIAN populations in terms of alcohol consumption [37, 44-47]) further complicates characterization. In a study among Navajos, risk factors for female problem drinking included depression[50]. Alcohol disorders have been found to be more prevalent among some American Indian Alaska Native (AIAN) populations than in the general population[51] and similar to the general population in others [45]. The

dominant factors associated with quitting or reducing drinking are pregnancy and childcare [62]. The prevalence and pattern of drinking among the AIAN populations addressed in the present study are unknown.

As with alcohol consumption, depression varies among different AIAN communities [88, 89]. Beals et al. [90] found less depression in an AIAN population than in the general population. O'Connell et al. [44] describes a prevalence of 16% for mood disorders among female drinkers in two AIAN populations. Perhaps most relevant to our study, 20% of 2,289 adult Alaska Native women tested positive for depression using the PHQ-9 instrument [91].

One prevention and early intervention approach is Screening, Brief Intervention, and Referral to Treatment (SBIRT). It uses broad screening and education incorporating personalized feedback to the participant, followed by professional treatment for those screening positive for alcohol abuse problems [143-145]. SBIRT has been used to reduce risky drinking in population groups including emergency room and other healthcare venue patients [151-158], college freshmen [159], and WIC participants [160].

Working within the Native American Research Centers for Health (NARCH) structure, the aim of the parent study of this paper was to reduce risky drinking and, ultimately, prevent FASDs among AIAN women in Southern California using a culturally modified SBIRT intervention [195]. To determine prevalence estimates and correlates of risky drinking and potential AEPs, recruitment was not limited by risky drinking profile. The web-based intervention portion of the randomized controlled study screened participants for risky drinking and provided individualized advice regarding the risks of alcohol consumption and FASD.

Data from this parent study indicated that a third of this population was at risk of an AEP and that vulnerability was associated with a lower level of knowledge regarding risks of alcohol consumption, being less religious, having had fewer pregnancies, and believing that other women among their peers consumed a greater number of drinks per week [196]. Vulnerability to having an AEP was significantly reduced in both the intervention and control groups but there was no additional benefit of the intervention above that of assessment alone (the control group). A high proportion of participants, 36%, were identified as depressed using the PHQ-9. Furthermore, depression, or feeling that one's functionality was impaired, was a strong predictor of a reduction in risky drinking during the course of the study.

The aim of the present study is to better understand the effect of depression on risk factors for having an AEP and on the response to an FASD prevention intervention among AIAN women. This understanding may help focus future prevention efforts.

Methods:

The population sample was composed of AIAN women from 18 to 45 years of age, of childbearing potential, recruited from one of three AIAN Southern California health clinics between April 2011 and September 2012. Methods and intervention are described in detail in earlier publications [195, 196]. Briefly, potential participants were recruited as per the study flowchart in **Figure 4.1**. Following completion of the baseline questionnaire, randomization into intervention or control group, and completion of a web-based survey providing personalized feedback if relevant, participants were followed-up with brief surveys by telephone at 1, 3, and 6 months post-baseline.

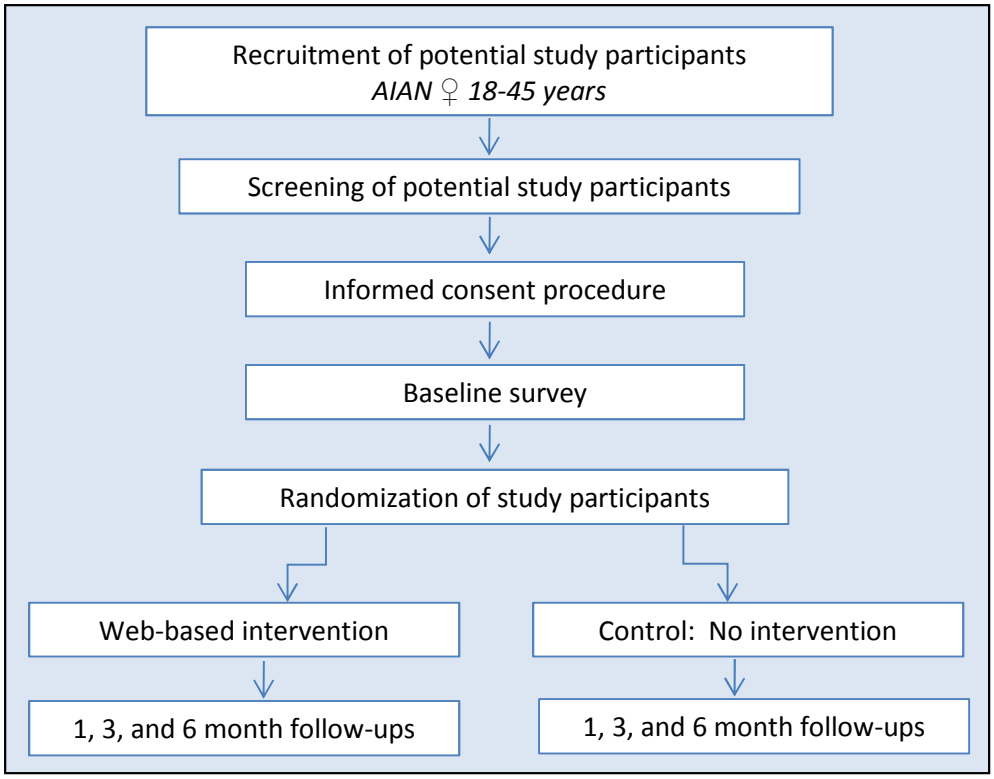


Figure 4.1: Study Flowchart

Primary outcome variables were drinks per week, number of binge drinking episodes in the past two weeks, and vulnerability to AEP.

"Vulnerability to Alcohol-Exposed Pregnancy" was defined in two categories: not at high risk and at high risk. Being "at high risk" for an AEP was defined as 1) currently drinking ≥3 standard drinks per occasion and/or ≥8 standard drinks per week, and 2) using a less than a highly effective contraceptive method. We defined "binge" drinking as ≥3 standard drinks per occasion and "risky" drinking as binge drinking and/or ≥8 drinks per week as this level of consumption has been defined as either risky for women or predictive of risk of adverse pregnancy outcomes in other studies [186]. Standard drinks were defined as shown in **Figure 4.2**.

Figure 4.2: Definition of a "Standard Drink"

Contraceptive effectiveness was defined as: High (<1 pregnancy per 100 women per year), Medium High (2-9 pregnancies per 100 women per year), Medium Low (15-24 pregnancies per 100 women per year), and Low (≥25 pregnancies per 100 women per year) [168]. "Using Birth Control Correctly" was defined as responding that birth control was used correctly every time or most of the time, as opposed to some of the time or none of the time.

The 9-item Patient Health Questionnaire (PHQ-9) was used to measure depression and functionality. In a variety of studies it has been found to have a sensitivity of 73% and specificity of 94% for major depression [187, 197, 198]. Variables derived from this measure included depression and functionality (impaired or not impaired) and were calculated as described by Kroenke et al. [197].

T-ACE (Tolerance, Annoyed, Cut down, Eye-opener) is a screening instrument of four questions structured to identify risky drinking [170] previously found effective in an

AIAN population [171]. Sensitivity and specificity of this instrument has been estimated at 80-90% sensitivity and 40-70% specificity [182, 199-202] .

Family dependency risk was calculated from the number of blood relatives the participant indicates as having alcohol problems (parents, siblings, grandparents, uncles/aunts, cousins).

Knowledge variables were true or false questions regarding drinking norms and risks to women and unborn children exposed to alcohol. See eleven knowledge questions shown in Appendix C.

Analyses: Comparison of continuous, dichotomous, or categorical variables were conducted using t-tests (continuous), $\chi 2$ (dichotomous), or ANOVA. Normality in continuous variables was investigated by looking at skewness and kurtosis. ANOVA was used to examine associations among population characteristics. Repeated measures ANOVA and mixed-model methods were used to estimate change over time and compare trajectories. Adjustment was made for multiple comparisons. Change over time analyses were conducted in two ways: 1) using only the subjects available at all follow-ups and 2) multiple imputation methods.

Statistical significance was defined as 2-sided, P value of $<.05$. Statistical analyses were carried out using SPSS (PASW 18, SPSS Inc., Chicago, IL).

Results

Between April 2011 and September 2012, a total of 263 AIAN women were recruited into the study; of these 29 were pregnant at recruitment and 16 (6.1%) were subsequently lost to follow-up. **Figure 4.3** shows the study recruitment diagram.

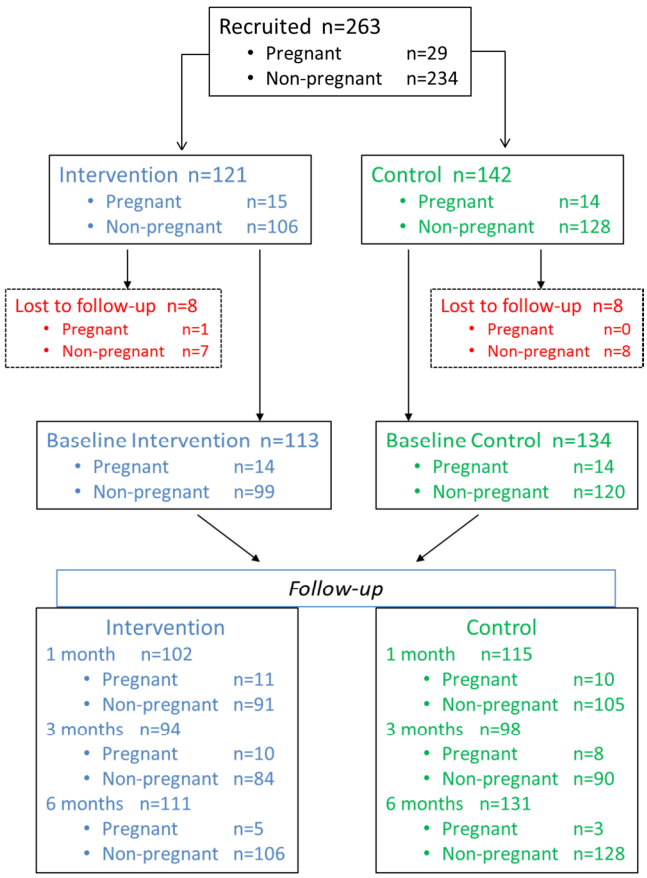


Figure 4.3: Recruitment Flowchart

Baseline characteristics of the total sample by pregnancy status and randomized group are shown in **Table 4.1**. A third of all participants were identified as depressed. Nearly three-quarters of participants were identified as vulnerable to risky drinking by the T-ACE screen. A quarter of participants had not heard of FASD or FAS, but more than a third knew someone affected by an AEP. Pregnant and non-pregnant samples varied in terms of cohabitation status, alcohol use, smoking, and illegal drug use. Because alcohol and birth control use were not comparable between pregnant and non-pregnant women, pregnant participants were excluded from subsequent analyses. Randomization was largely successful; intervention and control groups differed significantly only in parity.

Table 4.1: Characterization of population demographics (Mean ± SE or %)

Variable	Total	Not Pregnant	Pregnant	*P* value[e]	Intervention (Non-pregnant)	Control (Non-pregnant)	*P* value[e]
	n=263[a]	*n=234*	*n=29*		*n=106*	*n=128*	
Demographic characteristics							
Age (years)	28.4 ± 0.5	28.6 ± 0.5	26.7 ± 1.2	.214	27.7 ± 0.7	29.3 ±0.7	.133
Has had a child (%)	65.6	63.9	79.3	.100	57.1	69.5	.050
Children (number)	1.50 ± 0.09	1.50 ± 0.10	1.55 ± 0.26	.744	1.26 ± 0.15	1.68 ± 0.13	.034
Pregnancies (number)	2.05 ± 0.13	1.96 ± 0.14	2.71 ± 0.32	.070	1.75 ± 0.21	2.14 ±0.18	.155
Wants more children (%)	60.5	60.2	63.0	.780	61.2	59.3	.777
Cohabitating (%)	45.2	42.2	69.0	.006	37.5	46.0	.192
Employed (%)	40.2	41.4	31.0	.283	42.2	40.8	.836
Religious (%)	85.9	86.4	81.5	.486	88.6	85.0	.431
Smoker (%)	29.8	31.8	13.8	.046	29.5	33.6	.507
Illegal drugs (%)	12.1	13.7	0	.034	12.7	14.4	.718
Alcohol Consumption Variables							
Ever drank alcohol	95.0	95.2	93.1	.666	95.3	95.2	.989
Currently consume alcohol	49.2	54.3	7.1	<.001	53.8	54.8	.880
Age at first drink [b]	15.1 ± 0.2	15.0 ± 0.2	15.9 ± 0.7	.331	14.7 ±0.3	15.3 ± 0.4	.208
Drinks per week [b]	3.86 ± 0.51	4.32 ± 0.57	0.25 ± 0.22	.012	5.04 ± 1.06	3.70 ±0.55	.245
Drinks per occasion [b]	2.18 ± 0.24	2.45 ± 0.27	0.07 ± 0.05	.002	2.30 ± 0.35	2.58 ± 0.39	.598
Binge episodes / 2 weeks [b]	1.25 ± 0.20	1.41 ± 0.23	0.04 ± 0.04	.032	1.68 ±0.46	1.18 ± 0.17	.270
Current binge drinker (%)[b]	42.5	47.3	3.6	<.001	46.7	47.9	.849
Family dependency risk [c]	14.1 ± 1.7	13.3 ± 1.8	19.7 ± 5.5	.206			
T-ACE [c]	2.08 ± 0.13	2.08 ± 0.14	2.08 ± 0.40	.994			
T-ACE severity (mean %)[c]	11.6 ± 1.3	11.5 ± 1.4	12.5 ± 4.4	.812			
Perception of other women's drinking							
Drinks per week [d]	7.43 ± 0.61	7.63 ± 0.66	5.37 ± 1.20	.292	7.65 ± 1.01	7.61 ± 0.87	.980
Drinks per occasion [d]	3.41 ± 0.21	3.44 ± 0.22	3.05 ± 0.50	.578	3.41 ± 0.29	3.48 ± 0.32	.877
FASD Awareness							
Heard of FASD (%)	74.5	75.0	70.4	.602	72.1	77.5	.353
Know someone affected (%)	34.6	35.2	29.6	.564	29.8	39.7	.137
Depressed (%)	35.4	36.1	29.6	.507	35.2	36.8	.806
Functionality Impaired (%)	7.3	8.1	0	.166	11.0	5.6	.166

[a] Sample size varies due to inclusion of selected variables in the web-based survey and missing values.

Table 4.1: Characterization of population demographics (Mean ± SE or %), continued

[b] n = 249/221

[c] n = 113

[d] n = 238/216

[e] comparing non-pregnant to pregnant participants using ANOVA for continuous variables and chi-square test for categorical variables

In **Table 4.2**, the non-pregnant population is characterized by depression status. Depressed participants were more likely to have had a child (although there was no difference in parity or gravidity), more likely to take illegal or prescription drugs, and more likely to believe their functionality was impaired. There was a trend toward depressed participants using less birth control ($P = .072$). In addition, they were less likely to use birth control correctly most of the time or all of the time. A quarter of participants use no birth control, including abstinence. Only 16.5% of those identified as depressed reported taking anti-depressants. The level of knowledge regarding the risks of alcohol consumption in pregnancy and to women was high and not different between groups. However, nearly half of participants were unaware that women are at greater risk for developing alcohol-related problems than men. A similar percent of participants with and without symptoms of depression were vulnerable to an AEP as defined in this study.

Table 4.2: Characterization of non-pregnant sample by Depression status (Mean ± SE or %)

Variable	Not Depressed	n	Depressed	n	*P* value[a]
Age (years)	28.3 ± 0.6	147	29.3 ± 0.8	83	.358
Has had a child (%)	59.6	146	73.5	83	.034
Pregnancies (number)	1.92 ± 0.19	142	2.11 ± 0.21	82	.522
Children (number)	1.42 ± 0.13	146	1.66 ± 0.16	83	.241
Wants more children (%)	61.4	140	58.2	79	.642
Employed (%)	44.4	144	36.3	80	.233
Religious (%)		140		79	.850
Not at all	12.9		13.9		
Somewhat	74.3		70.9		
Very	12.9		15.2		
Cohabitating (%)	46.2	145	35.4	82	.112
Use Birth Control [b] (%)	63.9	147	51.8	84	.072
Abstinent (%)	10.0		7.6		
Birth Control Effectiveness		125		73	.069
High (%)	14.4		13.7		
Medium High (%)	33.6		26.0		
Medium Low (%)	26.4		16.4		
Low (%)	0		1.4		
No birth control (%)	25.6		42.5		
Using Birth Control Correctly (%)	78.3		55.0		<.001
Smoker (%)	29.3	147	34.9	83	.372
Taking illegal drugs (%)	9.0	145	20.3	79	.016
Taking prescription drugs (%)	32.9	146	57.5	80	<.001
Taking depression medication (%)	5.5	146	16.5	79	.007
Taking anxiety medication (%)	5.5	145	8.9	79	.332
Functionality impaired (%)	1.8	112	16.7	83	<.001
Knowledge Questions (% correct)		67		37	
Pregnancy related	95.0 ± 1.3		92.5 ± 1.8		.246
Women's health related	35.1 ± 3.5		33.3 ± 5.6		.784
Total	84.1 ± 1.2		81.6 ± 1.8		.232
Heard of FASD/FAS (%)	77.1	140	71.6	81	.359
Know someone affected by FASD/FAS (%)	34.1	132	36.8	76	.689
At High Risk of AEP (%)	38.5	143	39.0	82	.934

[a] Comparison between Depressed and Not Depressed using chi-square test or ANOVA.
[b] Includes abstinence

There were significant differences between depressed and non-depressed participants in alcohol consumption related variables (**Table 4.3**). Depressed participants, on average, drank more drinks per week, experienced more binge episodes in the past two weeks, and had a greater family dependency risk than non-depressed participants. Among participants currently consuming alcohol, depressed participants consumed significantly more drinks per week, binge drank more often, started drinking at an earlier age, had a greater family dependency risk and a higher risk of "risky drinking" as determined by the T-ACE screen, and estimated the drinks per week consumed by other women to be higher than did non-depressed participants. Interestingly, the cultural norm of how many drinks women typically consume per occasion was approximately 4 and did not differ between groups.

Table 4.3: Alcohol consumption variables among non-pregnant sample by Depression status

Variable	Not Depressed (Mean ± SE or %)	n	Depressed (Mean ± SE or %)	n	*P* value
All Non-pregnant Women					
Drinks per week	2.93 ± 0.39	136	6.72 ± 1.41	78	.002
Drinks per occasion	2.38 ± 0.33	138	2.57 ± 0.47	79	.738
Binge episodes / 2 weeks	0.94 ± 0.14	136	2.20 ± 0.58	79	.008
Age at first drink	15.5 ± 0.3	138	14.5 ± 0.45	79	.136
Family dependency risk	10.1 ± 1.1	64	19.4 ± 4.7	33	.014
T-ACE	1.92 ± 0.17	64	2.35 ± 0.27	33	.157
T-ACE severity (mean %)	10.3 ± 1.3	65	14.1 ± 3.2	34	.195
Perception of Other Women's Drinking					
Drinks per week	6.61 ± 0.71	138	9.20 ± 1.36	72	.063
Drinks per occasion	3.41 ± 0.30	137	3.33 ± 0.30	76	.862
Current Drinkers					
Drinks per week	5.18 ± 0.56	77	13.45 ± 2.39	39	<.001
Drinks per occasion	4.16 ± 0.48	79	5.07 ± 0.75	40	.292
Binge episodes / 2 weeks	1.58 ± 0.20	81	4.35 ± 1.03	40	.001
Age at first drink	15.4 ± 0.3	81	13.8 ± 0.5	41	.007
Family dependency risk	9.46 ± 1.24	39	22.6 ± 6.8	16	.008
T-ACE	1.92 ± 0.20	39	3.14 ± 0.36	14	.003
T-ACE severity (mean %)	8.82 ± 0.74	39	19.7 ± 6.3	14	.008
Perception of Other Women's Drinking					
Drinks per week	6.22 ± 0.61	78	13.6 ± 2.3	35	<.001
Drinks per occasion	3.49 ± 0.28	76	4.39 ± 0.48	37	.088

Figure 4.4 shows changes in drinks per week by treatment group as analyzed by repeated measures ANOVA. It includes all available data (n=123, 67 Control and 56 Intervention) using multiple imputation analysis. Alcohol consumption decreased in both treatment groups, with the greatest reduction in drinking occurring between the baseline assessment and the 1 month follow-up assessment. There was a statistically significant time effect ($P < .001$) but no intervention effect (treatment by time, $P = .127$).

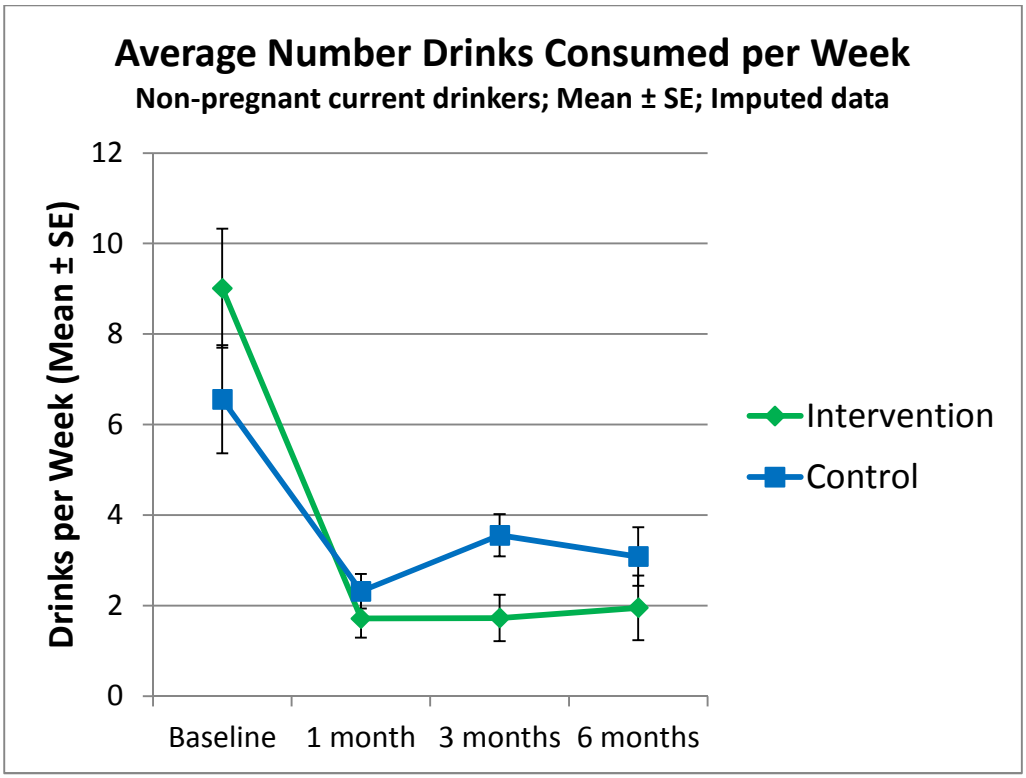
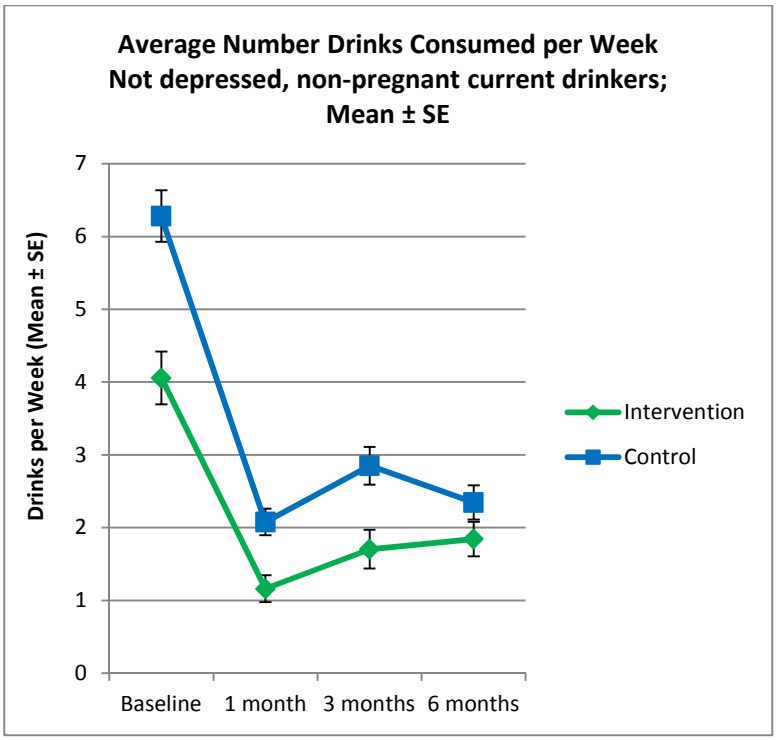
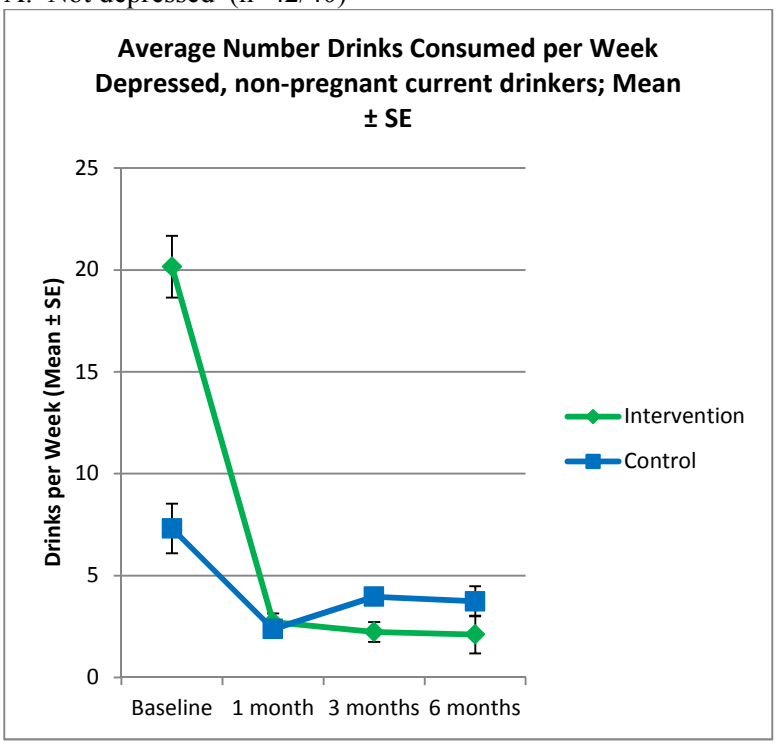


Figure 4.4. Drinks consumed per week over time by treatment group (estimated marginal means and SE). Repeated measures ANOVA with Imputed data (n=123, 67/56).

In **Figure 4.5**, the sample is split by the presence or absence of depression and the analysis is repeated. **Figure 4.5** shows marginal means over time for drinks consumed per week among participants who are not depressed (left) and depressed (right). As in analysis of the full sample, there is a significant time effect. However, among the depressed sample, as opposed to the full sample or the non-depressed sample, there is a significant treatment by time (or intervention) effect. Among the depressed, the intervention is significantly more effective than just the assessment alone ($P < .001$).



A. Not depressed (n=42/40)



B. Depressed (n=25/16)

Figures 4.5 A &B. Number of drinks consumed per week split into separate graphs for depressed and non-depressed samples

Among participants in the intervention group, depressed and non-depressed participants respond differently ($P < .001$) with depressed participants responding more enthusiastically to the intervention. Both depressed and non-depressed participants reduce their drinking significantly in the follow-up period ($P < .001$).

There are significant interactions between depression and time ($P < .001$), depression and intervention ($P = 0.021$), and among depression, intervention, and time ($P < .001$).

Discussion

The two main findings from this analysis are that depression appears to be associated with risk factors for vulnerability to AEP, particularly alcohol consumption related risk factors, and modifies the response to an SBIRT intervention. Depressed women were more likely to consume alcohol is a risky manner and showed a trend toward using less birth control ($P = .072$) and using birth control less correctly ($P < .001$). Among participants currently consuming alcohol, depressed women were significantly less likely to report using birth control (n=123, $P = 0.30$) and to report using it correctly "every time" or "most of the time" (n=120, $P = .006$). This more inconsistent use of contraceptives, as previously described in the literature [203], potentially further increases vulnerability to AEP. Despite the fact that this intervention did not target contraceptive use, the follow-up trajectories of contraceptive use mirror those of the alcohol consumption variables. The lack of impact of depression on our "at risk" of AEP variable at baseline (table 2) may be related to the prevalence of risky drinking among those consuming any alcohol and to the low use of highly effective contraception methods. While similar numbers of depressed and not depressed participants are

vulnerable to an AEP, depressed participants are vulnerable to a more severe AEP. As seen in previously published analyses from this study, following both assessment alone and assessment plus SBIRT intervention, risky drinking behavior was significantly reduced [195]. However, there was no additional effect of the intervention above that of assessment alone. In this analysis of the data, we show that among women identified as depressed, the intervention had a positive effect in reducing risky drinking above that of assessment alone.

There are previous studies reporting similar results, albeit in somewhat different, primarily alcoholic, populations, which may not be relevant to our population of women of childbearing age some of whom engage in risky drinking. Rounsaville reported in 1987 that among alcoholic women, those with major depression had a comparatively better treatment outcome than those with alcoholism alone [204]. The authors proposed that alcoholism was not the primary diagnosis among these women but secondary to depression, making it a different and more treatable type of alcoholism. Similarly, Thase et al. [205] found patients with comorbid depression and alcoholism, who are treated for both, may experience better outcome. Penberthy et al. provide the most applicable comparison although their reanalysis of the EARLY study included only women who had recently engaged in risky drinking and sex using ineffective contraception, and excluded women presenting with untreated major depressive disorder [206]. The EARLY study includes a birth control component which the present study does not. They report a significant effect of a "motivational interviewing plus feedback" intervention on drinks consumed per drinking day among depressed women when compared to interventions incorporating a video or brochures to convey educational information. The treatment

effect was not evident among non-depressed women. The person-to-person interaction component of the MI-based intervention was proposed as a possible responsible factor. It is interesting to note that drinks consumed per drinking day (or drinks per occasion) change in the EARLY study whereas drinks consumed per week and binge episodes per two-week period change with intervention in the present study. Among our study sample there is a strong cultural norm of binge drinking when consuming alcohol.

Depressed participants, on average, engaged in more risky drinking at baseline than their non-depressed counterparts. Part of the reason for the greater effect of the intervention among the depressed may lie in their alcohol consumption starting point which allows for greater change. In addition, greater readiness to change is associated with greater alcohol misuse severity [207]. When the sample is divided by magnitude of consumption or limited to risky drinkers, there is no significant effect of the intervention above that of the assessment (results not shown).

Depressed participants may be more aware of the discrepancy between their current condition and their desired state. They are more likely to self-report functional impairment ($P < .001$). Responses to the question asking "If you checked off any problem on this questionnaire so far, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?" are "Not difficult at all", "Somewhat difficult", "Very difficult", and "Extremely difficult". Analysis of these responses indicate that, among those indicating any problem on the depression screen (n=195), there is a clear and significant dose response in follow-up trajectory of alcohol consumption with more functional impairment associated with higher baseline alcohol consumption and lower follow-up alcohol consumption ($P < .001$

for change over time and difference among groups). There is evidence that depression may encourage self-awareness [208] and a more realistic understanding of personal risk [209] which may contribute to readiness for change. In the present study, the assessment may facilitate self-reflection and prevent avoidance of self-awareness, enabling recognition of the link between risky alcohol consumption and negative consequences. Depression may also motivate problem solving [210]. An intriguing article by Andrews and Thomson in 2009 [211] posits that depression may actually be an "evolved stress response mechanism" allowing us to focus and sustain our problem solving efforts. If our assessment facilitates readiness to change, the web-based intervention with personalized feedback providing an analysis of personal risk, relevant information, and strategies to help achieve change may support and stabilize this change.

Perhaps, for the reasons discussed above, depressed participants are more prepared to take advantage of the personalized feedback.

Implications of the present study are that depressed women may benefit from an intervention incorporating personalized feedback to a greater extent than non-depressed women. Screening for depression may be particularly important in FASD prevention as first onset of depression in women [84] and prevalence of depression [85] peak during childbearing years. Among some AIAN populations, women are at increased risk for depression as a result of the living conditions they experience. For example, AIAN women are at increased risk of violence including domestic violence, rape, stalking, and assault[92-98], less than optimal health, accidents, smoking, obesity, low high school and college graduation rates, and living in poverty [99, 100]. Some of these conditions are a legacy of the long history of oppression, marginalization, and systematic persecution

experienced by AIANs. In addition to these factors, AIAN women may be at greater risk of depression due to historical trauma, loss of culture, lingering discrimination issues, and conflicts between traditional and modern culture [101-104]. A higher percent of women screened positive for depression in our study (35%) than in a national study in 2006 using the same screening tool (14%) [86]. It is therefore particularly important that future interventions among this population screen for depression to facilitate identification of those vulnerable to AEP and to determine what type intervention might prove most effective. Interventions of assessment alone may be sufficient to achieve significant reductions in risky behavior among non-depressed women.

Limitations and strengths

Participants were self-selected and may not represent the source population. All data were self-reported and not validated by biomarkers or other means. The taboo nature of some questions may have caused participants to estimate risky behaviors in a more socially acceptable light.

There are missing data, as not all participants answered all questions. We analyzed the follow-up trajectories in three ways: using all available data, only complete sets of data, and using multiple imputation methods. Results were similar, differing in power not outcome.

The two-week time period assessing alcohol consumption was selected for accuracy. A longer time period may have provided more valid data as changes to drinking were more likely to occur from a reduction in frequency of binge drinking episodes than a reduction in the number of drinks per occasion.

Depression and functionality were not assessed during follow-up. It is therefore unknown whether these variables were affected by the intervention or by the change in behavior subsequent to assessment or intervention. The present study design did not address whether depression preceded an increase in risky drinking or vice versa.

Recruitment and data collection were made possible by ensuring confidentiality, respecting cultural etiquette, and having them carried out by trusted community members trained as research assistants.

Future studies

Future studies will be needed to explore mediators of response to SBIRT interventions. One aspect may be pursued by testing more intensive personalization of feedback using motivational interviewing.

Following participants longer than 6 months might test whether reductions in risky behavior are maintained.

The incorporation of biomarkers would provide important validation of self-reported alcohol consumption.

The source community for the present study places an emphasis on family. Future interventions could include family members. There is precedent for doing so; programs such as Alcoholics Anonymous have had success expanding meetings to include family members [212]. In addition, the extent of family influence on outcome might be explored.

In the present study contraceptive use was assessed but there was no contraceptive component of the intervention. There are two ways to prevent FASDs: prevent drinking during pregnancy or prevent pregnancy. In view of this, incorporating information

regarding contraception in a manner respectful of traditional mores might be a valuable addition to a future intervention [190, 191].

Conclusions

The present study indicates that depression is associated with risk factors for AEP and may be a modifying factor in how AIAN women in Southern California responded to a culturally tailored SBIRT intervention. Women identified by the PHQ-9 as in need of treatment for depression decreased risky drinking to a greater extent in response to the intervention than women not identified as depressed. The results suggest that women who are depressed may benefit from a more personalized intervention whereas assessment alone and information via non-personalized routes (brochures) may provide maximal results for non-depressed women.

Acknowledgements

This research was supported by the National Institutes of Health Grant U26IHS300292/01.

Chapter 4 is currently being prepared for submission for publication of the material in The American Journal of Public Health. Montag, A, Brodine, S, Alcaraz, J, Clapp, J, Allison, M, Calac, D, Hull, A, Gorman, J, Jones, K, Chambers C. *Influence of Depression on Vulnerability to Alcohol-Exposed Pregnancy and Response to Intervention.* The dissertation author was the primary investigator and author of this paper.

CHAPTER 5 OVERALL CONCLUSIONS AND DISCUSSION

The baseline study for this dissertation found that approximately a third of our sample of non-pregnant AIAN women of childbearing age was vulnerable to having an AEP. A large proportion of the participants, approximately half, did not drink alcohol and was therefore not vulnerable to AEP. However, among the participants who currently consumed alcohol, the prevailing pattern of drinking was binge drinking. A quarter of participants did not use any birth control, including abstinence, and few among those using contraception (<20%) reported using highly effective contraception.

In the course of conducting this initial study, issues with recruitment and retention came to light. This was not unexpected given the pervasive and well founded distrust of research, the incomplete understanding of cultural differences between the community and the researchers, and the unknown nature of the underlying causes of potential disparities being addressed. Changes were made in response to the issues encountered and may be considered "lessons learned". Chief among our lessons learned was that solutions to problems may be found within the community. Community involvement is required in all aspects of the study; staff should be composed of local trusted community members, focus groups may be used to create tools, the intervention itself, and to culturally modify all aspects, consulting with local experts is best continued throughout the study, and the Tribal IRB can be a valued resource. It is important to take the time to develop local partnerships and seek approval from as many influential groups as possible. Each community develops its own strengths that should be harnessed for successful interventions. The source population for these studies has a high proportion of alcohol abstainers compared to the general population, marked resiliency, a family or community

focus as opposed to individual, a deep sense of altruism where the desire to help the community is a potent motivator, and respect for Tribal elders. We found education and outreach to increase awareness crucial. In attending or hosting community events we were able to decrease distrust and skepticism toward the project, decrease the stigma of the topics it addressed, and increase community ownership of the project. We tackled confidentiality concerns by emphasizing that data collected is owned by the Tribal organization, not non-Native researchers or academic institutions, by hiring and training Tribal members, by obtaining a Certificate of Confidentiality, by maintaining records separately from the health clinic, and by addressing risks as they are seen by the community. Offering referrals both within and outside the community would have been an appreciated addition to the project but proved untenable. Logistics repeatedly proved to be a barrier to recruitment. Transportation will be written into future grants as much as possible. To avoid potentially disrespectful situations, local team members determined the places and times to recruit. We expanded our recruiting sites to ameliorate transportation limitations. Our initial recruitment incentives (gift cards) were not as incentivizing as hoped. They were augmented by the addition of a project t-shirt and hand fan emblazoned with our project logo. Retention in AIAN studies, particularly those involving follow-up interviews by telephone, has historically been variable and often too low to allow clear conclusions [213-215]. Reaching participants for follow-up initially proved challenging for us primarily due to the frequency with which some participants change their telephone numbers, the unwillingness of some participants to answer calls from the health clinic, and the potential for loss of confidentiality during a telephone call. We countered these challenges by collecting multiple methods of contact,

including phone numbers other than the primary cell through which we might reach them, asking permission to email or text, asking best times and methods for communication, and asking who we might reach them through if our primary methods fail. One effective contact conduit proved to be grandmothers. Each research assistant was provided a project cell phone and a direct line was set up to the project office. In addition, we matched incentives to each project step by adding raffle tickets for a chance to win a prize for each completed follow-up interview. Our loss to follow-up rate, despite low initial numbers, was 6.1% reflecting 16 participants lost.

Among our sample of women, protective factors against vulnerability to AEP included knowledge regarding the risks associated with alcohol consumption, increased parity and gravidity, and being very religious. A higher score on the T-ACE screen for risky drinking was associated with a greater vulnerability to AEP. Patterns of drinking reflected a cultural norm of drinks per occasion among current drinkers, drinks needed to feel tipsy, age at first drink, and family dependence risk. The most common drinking patterns appear to be abstaining from alcohol or binge drinking. A positive T-ACE screen was associated with how much the woman herself drank and how much she thought other women like her drank.

A third of all participants were identified as in need of treatment for depression. Depressed women were more likely to have had a child, to take illegal or prescription drugs, and to perceive their functionality as impaired. While a higher percent of them was taking medication for depression than those identified as not depressed, that amounted to only 16.5% reflecting a high unmet need and that depression is not always controlled by medication. They were not different from non-depressed women in age,

parity, gravidity, employment, religiosity, or in their desire for more children. Almost all alcohol consumption variables were significantly different between depressed and non-depressed women. The difference became even more striking among current drinkers. Women identified as depressed were significantly more likely to drink in a risky manner and to perceive of other women as doing so. There was a trend toward depressed women using less birth control but this is an area where the cultural norm comes into play and may confound usage. Depressed women were less likely to report using contraception correctly.

Risky drinking and vulnerability to AEP were significantly reduced in the follow-up period in both the intervention and control groups. There was no significant difference between treatment groups and the effects were sustained through six months. A strong response to assessment may be obscuring the effect of the intervention. It is also possible that our study was insufficiently powered to detect a difference between treatment groups. This project targeted all women of childbearing age without specifying behavioral criteria in order to determine vulnerability of the population. Using retrospective analysis we determine our power to detect a treatment effect, given our sample size and results for all non-pregnant participants, to be approximately 31% for drinks per week. Increasing the sample size to 380/group is recommended for future studies. Predictors of reduced alcohol use included more binge drinking episodes over two weeks, testing positive for depression or impaired functionality, and a higher perception of how much peers drink.

In our population sample, depression modifies the response to the SBIRT intervention. There were significant interactions among depression, time, and

intervention. Both depressed and non-depressed women significantly reduced risky drinking in the follow-up period but only in depressed women did the intervention reduce risky drinking above the reduction experienced with assessment alone. There are several reasons why screening for depression should be a part of any intervention to prevent FASD in our source population: it may help to identify women vulnerable to an AEP; it may help determine what type of intervention to allocate participant to as while assessment alone may be sufficient for most women, depressed women may benefit from personalized feedback; and treating depression and alcohol consumption simultaneously may enhance the effectiveness of both treatments.

To create effective future interventions to prevent FASD and improve health disparities the following are areas for consideration gleaned from the present study:

- Ensure that potential contributions of AIAN insights and perspectives, as well as community strengths are embraced and incorporated
- Culturally tailor
- Screen for depression and impaired functionality, and provide relevant treatment
- Expand psychological screening to include trauma and anxiety
- Incorporate motivational interviewing into intervention to further enhance the personalized feedback
- Target misperceptions regarding cultural norms or peer practices relating to alcohol consumption
- Explore whether religiosity and spirituality have different effects and what role traditional religious practices may have
- Provide contraceptive counseling

- Incorporate biomarkers to provide validation of self-reported alcohol consumption
- Design the intervention to include family members
- Follow the participants further in time to determine whether the effect wanes or is maintained, and whether periodic assessment extends the effect
- Reduce barriers to participation such as transportation

References

1. Jones, K.L., et al., *Pattern of malformation in offspring of chronic alcoholic mothers.* The Lancet, 1973. **301**(7815): p. 1267-1271.

2. Jones, K. and D. Smith, *RECOGNITION OF THE FETAL ALCOHOL SYNDROME IN EARLY INFANCY.* The Lancet, 1973. **302**(7836): p. 999-1001.

3. Floyd, R.L., et al., *Recognition and prevention of fetal alcohol syndrome.* Obstetrics & Gynecology, 2005. **106**(5, Part 1): p. 1059-1064.

4. Sokol, R.J., V. Delaney-Black, and B. Nordstrom, *Fetal alcohol spectrum disorder.* JAMA: The Journal of the American Medical Association, 2003. **290**(22): p. 2996-2999.

5. Riley, E., M.A. Infante, and K. Warren, *Fetal Alcohol Spectrum Disorders: An Overview.* Neuropsychology Review, 2011. **21**(2): p. 73-80.

6. Jones, K.L., *The effects of alcohol on fetal development.* Birth Defects Research Part C: Embryo Today: Reviews, 2011. **93**(1): p. 3-11.

7. Streissguth, A.P., C.S. Herman, and D.W. Smith, *Intelligence, behavior, and dysmorphogenesis in the fetal alcohol syndrome: A report on 20 patients.* The Journal of pediatrics, 1978. **92**(3): p. 363-367.

8. Streissguth, A., S. Clarren, and K. Jones, *NATURAL HISTORY OF THE FETAL ALCOHOL SYNDROME: A 10-YEAR FOLLOW-UP OF ELEVEN PATIENTS.* The Lancet, 1985. **326**(8446): p. 85-91.

9. Streissguth, A., *Offspring effects of prenatal alcohol exposure from birth to 25 years: The Seattle Prospective Longitudinal Study.* Journal of Clinical Psychology in Medical Settings, 2007. **14**(2): p. 81-101.

10. Spohr, H.L., J. Willms, and H.C. Steinhausen, *Prenatal alcohol exposure and long-term developmental consequences.* The Lancet, 1993. **341**(8850): p. 907-910.

11. Streissguth, A.P., et al., *Fetal alcohol syndrome in adolescents and adults.* JAMA: The Journal of the American Medical Association, 1991. **265**(15): p. 1961-1967.

12. United States, N.I.o.A.A. and Alcoholism, *10th Special Report to the U.S. Congress on Alcohol and Health: Highlights from Current Research*. 2001: U.S. Government Printing Office.

13. May, P.A., et al., *Prevalence and epidemiologic characteristics of FASD from various research methods with an emphasis on recent in school studies.* Developmental Disabilities Research Reviews, 2009. **15**(3): p. 176-192.

14. Sampson, P.D., et al., *Incidence of fetal alcohol syndrome and prevalence of alcohol-related neurodevelopmental disorder.* Teratology, 1997. **56**(5): p. 317-326.

15. Keen, C.L., et al., *The plausibility of maternal nutritional status being a contributing factor to the risk for fetal alcohol spectrum disorders: The potential influence of zinc status as an example.* BioFactors, 2010. **36**(2): p. 125-135.

16. Jacobson, J.L., et al., *Relation of maternal age and pattern of pregnancy drinking to functionally significant cognitive deficit in infancy.* Alcoholism: Clinical and Experimental Research, 1998. **22**(2): p. 345-351.

17. May, P.A., 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): p. 10-20.

18. May, P.A., et al., *Maternal risk factors predicting child physical characteristics and dysmorphology in fetal alcohol syndrome and partial fetal alcohol syndrome.* Drug and alcohol dependence, 2011.

19. Jones, K.L., et al., *Fetal alcohol spectrum disorders: extending the range of structural defects.* American Journal of Medical Genetics Part A, 2010. **152**(11): p. 2731-2735.

20. Astley, S., *Diagnosing fetal alcohol spectrum disorders (FASD).* Prenatal Alcohol Use and Fetal Alcohol Spectrum Disorders: Diagnosis, Assessment and New Directions in Research and Multimodal Treatment, 2011: p. 3-29.

21. Paintner, A., A.D. Williams, and L. Burd, *Fetal Alcohol Spectrum Disorders—Implications for Child Neurology, Part 1: Prenatal Exposure and Dosimetry.* Journal of Child Neurology, 2012. **27**(2): p. 258-263.

22. Viljoen, D.L., et al., *Fetal alcohol syndrome epidemiology in a South African community: a second study of a very high prevalence area.* Journal of studies on alcohol, 2005. **66**(5): p. 593.

23. Maier, S.E. and J.R. West, *Drinking patterns and alcohol-related birth defects.* Alcohol Research and Health, 2001. **25**(3): p. 168-174.

24. May, P., et al., *Prevalence of Children with Severe Fetal Alcohol Spectrum Disorders in Communities Near Rome, Italy: New Estimated Rates Are Higher*

than Previous Estimates. International Journal of Environmental Research and Public Health, 2011. **8**(6): p. 2331-2351.

25. Sawada Feldman, H., et al., *Prenatal Alcohol Exposure Patterns and Alcohol-Related Birth Defects and Growth Deficiencies: A Prospective Study.* Alcoholism: Clinical and Experimental Research, 2012.

26. Holmgren, S., *Low dose alcohol exposure during pregnancy - does it harm?* Swedish National Institute of Public Health, 2009. **R2009:14**.

27. Kesmodel, U.S., et al., *The effect of different alcohol drinking patterns in early to mid pregnancy on the child's intelligence, attention, and executive function.* BJOG: An International Journal of Obstetrics & Gynaecology, 2012. **119**(10): p. 1180-1190.

28. Services, U.D.o.H.a.H. *US Surgeon General releases advisory on alcohol use in pregnancy.* Washington, DC: US Department of Health and Human Services 2005 [cited 2013 2/21]; Available from: http://www.surgeongeneral.gov/news/2005/02/sg02222005.html.

29. Lebel, C., et al., *A longitudinal study of the long-term consequences of drinking during pregnancy: heavy in utero alcohol exposure disrupts the normal processes of brain development.* The Journal of Neuroscience, 2012. **32**(44): p. 15243-15251.

30. Roussotte, F.F., et al., *Regional brain volume reductions relate to facial dysmorphology and neurocognitive function in fetal alcohol spectrum disorders.* Human brain mapping, 2012.

31. Goodlett, C.R. and K.H. Horn, *Mechanisms of Alcohol-Induced Damage to the Developing Nervous System.* Alcohol Research & Health, 2001. **25**(3): p. 175.

32. Finer, L.B. and K. Kost, *Unintended pregnancy rates at the state level.* Perspectives on Sexual and Reproductive Health, 2011. **43**(2): p. 78-87.

33. Finer, L.B. and M.R. Zolna, *Unintended pregnancy in the United States: incidence and disparities, 2006.* Contraception, 2011. **84**(5): p. 478-485.

34. Goldsmith, K.A., et al., *Unintended childbearing and knowledge of emergency contraception in a population-based survey of postpartum women.* Maternal and child health journal, 2008. **12**(3): p. 332-341.

35. Floyd, R.L., P. Decouflé, and D.W. Hungerford, *Alcohol use prior to pregnancy recognition.* American journal of preventive medicine, 1999. **17**(2): p. 101-107.

36. Edwards, E.M. and M.M. Werler, *Alcohol consumption and time to recognition of pregnancy.* Maternal and child health journal, 2006. **10**(6): p. 467-472.

37. May, P.A. and J.P. Gossage, *New data on the epidemiology of adult drinking and substance use among American Indians of the northern states: male and female data on prevalence, patterns, and consequences.* American Indian and Alaska Native Mental Health Research, 2001. **10**(2): p. 1-26.

38. West, J.H., et al., *Correlates of Continued Alcohol Consumption During Pregnancy: Implications for Health Promotion.* Californian Journal of Health Promotion, 2011. **9**(1): p. 56-61.

39. Stratton, K.R., C.J. Howe, and F.C. Battaglia, *Fetal alcohol syndrome: Diagnosis, epidemiology, prevention, and treatment*. 1996: National Academies.

40. Abel, E.L., *An update on incidence of FAS: FAS is not an equal opportunity birth defect.* Neurotoxicology and teratology, 1995. **17**(4): p. 437-443.

41. Abel, E.L., *Fetal alcohol syndrome: the 'American Paradox'.* Alcohol and Alcoholism, 1998. **33**(3): p. 195-201.

42. Substance Abuse and Mental Health Services Administration, *The NSDUH Report: Substance Use among American Indian or Alaska Native Adults.* , in *OAS, Rockville, MD.* 2010.

43. Marchetta, C.M.e.a., *Alcohol Use and Binge Drinking Among Women of Childbearing Age —United States, 2006–2010.* MMWR, 2012. **61**(28): p. 534.

44. O'Connell, J.M., et al., *Disparities in Patterns of Alcohol Use Among Reservation-based and Geographically Dispersed American Indian Populations.* Alcoholism: Clinical and Experimental Research, 2005. **29**(1): p. 107-116.

45. Spicer, P., et al., *The Prevalence of DSM-III-R Alcohol Dependence in Two American Indian Populations.* Alcoholism: Clinical and Experimental Research, 2003. **27**(11): p. 1785-1797.

46. May, P.A., *Fetal alcohol effects among North American Indians: Evidence and implications for society.* Alcohol Health & Research World, 1991. **15**(3): p. 239-248. .

47. May, P.A., et al., *Epidemiology of fetal alcohol syndrome among American Indians of the southwest.* Biodemography and Social Biology, 1983. **30**(4): p. 374-387.

48. Beals, J., et al., *Racial disparities in alcohol use: Comparison of 2 American Indian reservation populations with national data.* American journal of public health, 2003. **93**(10): p. 1683.

49. May, P., *The prevention of alcohol and other drug abuse among American Indians: A review and analysis of the literature.* The Challenge of Participatory

Research: Preventing Alcohol Related Problems in Ethnic Communities. Rockville, MD, Center for Substance Abuse Prevention, Dept. of Health and Human Services, pp, 1995: p. 185-243.

50. Kunitz, S., *Life Course Observations of Alcohol Use among Navajo Indians: Natural History or Careers?* Medical Anthropology Quarterly, 2006. **20**(3): p. 279-296.

51. Beals, J., et al., *Prevalence of DSM-IV disorders and attendant help-seeking in 2 American Indian reservation populations.* Archives of General Psychiatry, 2005. **62**(1): p. 99.

52. Lewis, M.A. and C. Neighbors, *Social norms approaches using descriptive drinking norms education: A review of the research on personalized normative feedback.* Journal of American College Health, 2006. **54**(4): p. 213-218.

53. Borsari, B. and K.B. Carey, *Descriptive and injunctive norms in college drinking: A meta-analytic integration.* Journal of studies on alcohol, 2003. **64**(3): p. 331.

54. Clapp, J.D., et al., *A failed norms social marketing campaign.* Journal of studies on alcohol and drugs, 2003. **64**(3): p. 409.

55. Schultz, P.W., et al., *The constructive, destructive, and reconstructive power of social norms.* Psychological Science, 2007. **18**(5): p. 429-434.

56. Dunnagan, T., et al., *Support for social norms programming to reduce alcohol consumption in pregnant women.* Addiction Research & Theory, 2007. **15**(4): p. 383-396.

57. Testa, M. and A. Reifman, *Individual differences in perceived riskiness of drinking in pregnancy: antecedents and consequences.* Journal of studies on alcohol and drugs, 1996. **57**(4): p. 360.

58. Substance Abuse and Mental Health Services Administration, *Results from the 2007 National Survey on Drug Use and Health: National Findings.* , O.o.A.S. Substance Abuse and Mental Health Services Administration, Editor. 2008, Office of Applied Statistics: Rockville.

59. Guillory, B., E. Willie, and E. Duran, *Analysis of a community organizing case study: Alkali Lake.* Journal of Rural Community Psychology, 1988. **9**(1): p. 27-35. .

60. Ehlers, C.L., et al., *The clinical course of alcoholism in 243 Mission Indians.* American journal of Psychiatry, 2004. **161**(7): p. 1204.

61. Ethen, M.K., et al., *Alcohol consumption by women before and during pregnancy.* Maternal and child health journal, 2009. **13**(2): p. 274-285.

62. Bezdek, M., C. Croy, and P. Spicer, *Documenting Natural Recovery in American-Indian Drinking Behavior: A Coding Scheme*.* Journal of studies on alcohol, 2004. **65**(4): p. 428-435.

63. Tenkku, L., et al., *Racial Disparities in Pregnancy-Related Drinking Reduction.* Maternal and child health journal, 2009. **13**(5): p. 604-613.

64. Naimi, T.S., et al., *Binge Drinking in the Preconception Period and the Risk of Unintended Pregnancy: Implications for Women and Their Children.* Pediatrics, 2003. **111**(Supplement 1): p. 1136-1141.

65. Alvik, A., et al., *Alcohol use before and during pregnancy: a population-based study.* Acta Obstetricia et Gynecologica Scandinavica, 2006. **85**(11): p. 1292-1298.

66. Kitsantas, P., et al., *Determinants of alcohol cessation, reduction and no reduction during pregnancy.* Archives of gynecology and obstetrics, 2013: p. 1-9.

67. Havens, J.R., et al., *Factors associated with substance use during pregnancy: Results from a national sample.* Drug and alcohol dependence, 2009. **99**(1–3): p. 89-95.

68. Helzer, J., *Psychiatric diagnoses and substance abuse in the general population: the ECA data.* NIDA Res Monogr, 1988. **81**: p. 405-415.

69. Helzer, J.E. and T.R. Pryzbeck, *The co-occurrence of alcoholism with other psychiatric disorders in the general population and its impact on treatment.* Journal of studies on alcohol and drugs, 1988. **49**(03): p. 219.

70. Kaskutas, L., *Understanding drinking during pregnancy among urban American Indians and African Americans: health messages, risk beliefs, and how we measure consumption.* Alcoholism: Clinical and Experimental Research, 2000. **24**(8): p. 1241-1250.

71. Meschke, L.L., et al., *Correlates of prenatal alcohol use.* Maternal and child health journal, 2008. **12**(4): p. 442-451.

72. Skagerström, J., G. Chang, and P. Nilsen, *Predictors of drinking during pregnancy: a systematic review.* Journal of Women's Health, 2011. **20**(6): p. 901-913.

73. Caetano, R., et al., *The epidemiology of drinking among women of child-bearing age.* Alcoholism: Clinical and Experimental Research, 2006. **30**(6): p. 1023-1030.

74. Palma, S., et al., *Weekday but not weekend alcohol consumption before pregnancy influences alcohol cessation during pregnancy.* The European Journal of Public Health, 2007. **17**(4): p. 394-399.

75. Branco, E. and L. Kaskutas, *If it burns going down…": how focus groups can shape fetal alcohol syndrome (FAS) prevention.* Substance Use & Misuse, 2001. **36**(3): p. 333-345.

76. Nilsen, P., et al., *Alcohol use before and during pregnancy and factors influencing change among Swedish women.* Acta Obstetricia et Gynecologica Scandinavica, 2008. **87**(7): p. 768-774.

77. Mallard, S.R., J.L. Connor, and L.A. Houghton, *Maternal factors associated with heavy periconceptional alcohol intake and drinking following pregnancy recognition: A post-partum survey of New Zealand women.* Drug and Alcohol Review, 2013: p. n/a-n/a.

78. Croxford, J. and D. Viljoen, *Alcohol consumption by pregnant women in the Western Cape.* S Afr Med J, 1999. **89**(9): p. 962-965.

79. Kesmodel, U., et al., *Use of alcohol and illicit drugs among pregnant Danish women, 1998.* Scandinavian Journal of Public Health, 2003. **31**(1): p. 5-11.

80. Warren, C.W., et al., *Assessing the reproductive behavior of on-and off-reservation American Indian females: Characteristics of two groups in Montana.* Biodemography and Social Biology, 1990. **37**(1-2): p. 69-83.

81. Bad Heart Bull, L., et al., *Validation of a self-administered questionnaire to screen for prenatal alcohol use in Northern Plains Indian women.* American journal of preventive medicine, 1999. **16**(3): p. 240-243.

82. Martin, J.A. and N.C.f.H. Statistics, *Births: final data for 2002.* 2003.

83. Watt, T.T., *Alcohol Use and Cigarette Smoking During Pregnancy Among American Indians/Alaska Natives.* Journal of Ethnicity in Substance Abuse, 2012. **11**(3): p. 262-275.

84. Weissman, M.M. and M. Olfson, *Depression in Women: Implications for Health Care Research.* Science, 1995. **269**(5225): p. 799-801.

85. Hasin, D.S., et al., *Epidemiology of major depressive disorder: results from the National Epidemiologic Survey on Alcoholism and Related Conditions.* Archives of General Psychiatry, 2005. **62**(10): p. 1097-1106.

86. Farr, S.L., et al., *Mental health and access to services among US women of reproductive age.* American Journal of Obstetrics and Gynecology, 2010. **203**(6): p. 542. e1-542. e9.

87. Clark, T.C.a.B., D, *Percentage of Adults Aged ≥18 Years Who Often Felt Depressed,* by Sex and Age Group — National Health Interview Survey, United States, 2010–2011.* MMWR, 2013. **62**(7).

88. Gone, J.P. and J.E. Trimble, *American Indian and Alaska Native mental health: Diverse perspectives on enduring disparities.* Annual Review of Clinical Psychology, 2012. **8**: p. 131-160.

89. Duran, B., et al., *Prevalence and correlates of mental disorders among Native American women in primary care.* Journal Information, 2004. **94**(1).

90. Beals, J., et al., *Prevalence of major depressive episode in two American Indian reservation populations: unexpected findings with a structured interview.* American journal of Psychiatry, 2005. **162**(9): p. 1713-1722.

91. Dillard, D.A., et al., *Depression prevalence and associated factors among Alaska Native people: The Alaska education and research toward health (EARTH) study.* Journal of affective disorders, 2012. **136**(3): p. 1088-1097.

92. Evans-Campbell, T., et al., *Interpersonal violence in the lives of urban American Indian and Alaska Native women: Implications for health, mental health, and help-seeking.* Journal Information, 2006. **96**(8).

93. Tjaden, P. and N. Thoennes, *Full report of the prevalence, incidence, and consequences of violence against women: findngs from the National Violence Against Women Survey.* Washington, DC: United States Department of Justice, 2000: p. 71.

94. Bohn, D.K., *Lifetime physical and sexual abuse, substance abuse, depression, and suicide attempts among Native American women.* Issues in Mental Health Nursing, 2003. **24**(3): p. 333-352.

95. Malcoe, L.H., B.M. Duran, and J.M. Montgomery, *Socioeconomic disparities in intimate partner violence against Native American women: a cross-sectional study.* BMC medicine, 2004. **2**(1): p. 20.

96. Bachman, R., et al., *Estimating the magnitude of rape and sexual assault against American Indian and Alaska Native (AIAN) women.* Australian & New Zealand Journal of Criminology, 2010. **43**(2): p. 199-222.

97. USA, A.I., *Maze of Injustice: The Failure to Protect Indigenous Women from Sexual Violence in the USA*. No.: ISBN 978-1-887204-47-7, 2006: p. 112.

98. Sapra, K.J., et al., *Family and partner interpersonal violence among American Indians/Alaska Natives.* Injury epidemiology, 2014. **1**(1): p. 7-7.

99. Barnes PM, e.a., *Health characteristics of the American Indian or Alaska Native adult population: United States, 2004–2008.* National health statistics reports, 2010. **20**.

100. Sondik, E., et al., *Summary Health Statistics for the U.S. Population: National Health Interview Survey, 2011.* Vital and health statistics. , 2013. **Series 10**(Number 255).

101. Davis DD, K.K., *A brief history of and future considerations for research in American Indian and Alaska Native Communities.* ERIC Database # ED473270, 2002.

102. Walters, K.L., J.M. Simoni, and T. Evans-Campbell, *Substance use among American Indians and Alaska natives: incorporating culture in an" indigenist" stress-coping paradigm.* Public Health Reports, 2002. **117**(Suppl 1): p. S104.

103. Whitbeck, L., et al., *Discrimination, Historical Loss and Enculturation: Culturally Specific Risk and Resiliency Factors for Alcohol Abuse among American Indians*.* Journal of studies on alcohol, 2004. **65**(4): p. 409-419.

104. Aguirre, R.T. and T.D. Watts, *Suicide and alcohol use among American Indians: toward a transactional–ecological framework.* Journal of Comparative Social Welfare, 2010. **26**(1): p. 3-11.

105. Grant, B.F. and T.C. Harford, *Comorbidity between DSM-IV alcohol use disorders and major depression: results of a national survey.* Drug and alcohol dependence, 1995. **39**(3): p. 197-206.

106. Swendsen, J.D. and K.R. Merikangas, *The comorbidity of depression and substance use disorders.* Clinical Psychology Review, 2000. **20**(2): p. 173-189.

107. Mackie, C.J., P. Conrod, and K. Brady, *Depression and Substance Use 21.* Drug Abuse and Addiction in Medical Illness: Causes, Consequences and Treatment, 2012: p. 275.

108. Mushquash, A.R., et al., *Depressive Symptoms are a Vulnerability Factor for Heavy Episodic Drinking: A Short-Term, Four-Wave Longitudinal Study of Undergraduate Women.* Addictive Behaviors, 2012.

109. Parker, T., et al., *Psychological distress among Plains Indian mothers with children referred to screening for Fetal Alcohol Spectrum Disorders.* Substance abuse treatment, prevention, and policy, 2010. **5**(1): p. 1-9.

110. Tsai, J., et al., *Alcohol use and serious psychological distress among women of childbearing age.* Addictive Behaviors, 2009. **34**(2): p. 146-153.

111. Kessler, R.C., et al., *LIfetime co-occurrence of dsm-iii-r alcohol abuse and dependence with other psychiatric disorders in the national comorbidity survey.* Archives of General Psychiatry, 1997. **54**(4): p. 313-321.

112. Schutte, K.K., J. Hearst, and R.H. Moos, *Gender differences in the relations between depressive symptoms and drinking behavior among problem drinkers: a three-wave study.* Journal of consulting and clinical psychology, 1997. **65**(3): p. 392.

113. Rodgers, A.E.e.a., *Nonlinear relationships in associations of depression and anxiety with alcohol use.* Psychological Medicine, 2000. **30**(2): p. 421-432.

114. Gea, A., et al., *A longitudinal assessment of alcohol intake and incident depression: the SUN project.* BMC public health, 2012. **12**(1): p. 954.

115. Alati, R., et al., *Is there really a 'J-shaped'curve in the association between alcohol consumption and symptoms of depression and anxiety? Findings from the Mater-University Study of Pregnancy and its outcomes*.* Addiction, 2005. **100**(5): p. 643-651.

116. Slade, T., et al., *Onset and temporal sequencing of lifetime anxiety, mood and substance use disorders in the general population.* Epidemiology and psychiatric sciences, 2013: p. 1-9.

117. Zuckerman, B., et al., *Depressive symptoms during pregnancy: relationship to poor health behaviors.* American Journal of Obstetrics and Gynecology, 1989. **160**(5 Pt 1): p. 1107.

118. Flynn, H.A. and S.T. Chermack, *Prenatal alcohol use: the role of lifetime problems with alcohol, drugs, depression, and violence.* Journal of studies on alcohol and drugs, 2008. **69**(4): p. 500.

119. O'Connor, M.J. and S.E. Whaley, *Health care provider advice and risk factors associated with alcohol consumption following pregnancy recognition.* Journal of studies on alcohol and drugs, 2006. **67**(1): p. 22.

120. Meschke, L.L., J.A. Holl, and S. Messelt, *Assessing the risk of fetal alcohol syndrome: understanding substance use among pregnant women.* Neurotoxicology and teratology, 2003. **25**(6): p. 667-674.

121. O'Keane, V. and M.S. Marsh, *Depression during pregnancy.* Bmj, 2007. **334**(7601): p. 1003-1005.

122. Leis, J., et al., *Associations Between Depressive and Anxious Symptoms and Prenatal Alcohol Use.* Maternal and child health journal, 2012. **16**(6): p. 1304-1311.

123. Munafò, M.R., J. Heron, and R. Araya, *Smoking patterns during pregnancy and postnatal period and depressive symptoms.* Nicotine & Tobacco Research, 2008. **10**(11): p. 1609-1602.

124. Zuckerman, B., et al., *Depressive symptoms during pregnancy: relationship to poor health behaviors.* American Journal of Obstetrics and Gynecology, 1989. **160**(5): p. 1107-1111.

125. Alder, J., et al., *Depression and anxiety during pregnancy: A risk factor for obstetric, fetal and neonatal outcome? A critical review of the literature.* Journal of Maternal-Fetal & Neonatal Medicine, 2007. **20**(3): p. 189-209.

126. Bansil, P., et al., *Maternal and fetal outcomes among women with depression.* Journal of Women's Health, 2010. **19**(2): p. 329-334.

127. Bonari, L., et al., *Perinatal risks of untreated depression during pregnancy.* Can J Psychiatry, 2004. **49**(11): p. 726-735.

128. Muzik, M., et al., *Depression during pregnancy: detection, comorbidity and treatment.* Asia-Pacific Psychiatry, 2010. **2**(1): p. 7-18.

129. Marcus, S.M. and J.E. Heringhausen, *Depression in childbearing women: when depression complicates pregnancy.* Primary Care: Clinics in Office Practice, 2009. **36**(1): p. 151-165.

130. Marcus, S.M., et al., *Depressive symptoms among pregnant women screened in obstetrics settings.* Journal of Women's Health, 2003. **12**(4): p. 373-380.

131. Mengel, M.B., et al., *Increasing FASD knowledge by a targeted media campaign: Outcome determined by message frequency.* Journal of FAS International, 2005. **3**: p. 1-14.

132. Ingersoll, K.S., et al., *Preconceptional motivational interviewing interventions to reduce alcohol-exposed pregnancy risk.* Journal of Substance Abuse Treatment, 2012.

133. Dunlop, A.L., et al., *Change in Women's Knowledge of General and Personal Preconception Health Risks Following Targeted Brief Counseling in Publicly Funded Primary Care Settings.* American Journal of Health Promotion, 2013. **27**(sp3): p. S50-S57.

134. Schwarz, E.B., et al., *Computerized Counseling for Folate Knowledge and Use: A Randomized Controlled Trial.* American journal of preventive medicine, 2008. **35**(6): p. 568-571.

135. Williams, L., et al., *Associations Between Preconception Counseling and Maternal Behaviors Before and During Pregnancy.* Maternal and child health journal, 2012. **16**(9): p. 1854-1861.

136. Elsinga, J., et al., *The effect of preconception counselling on lifestyle and other behaviour before and during pregnancy.* Women's Health Issues, 2008. **18**(6): p. S117-S125.

137. Montag, A., et al., *A review of evidence-based approaches for reduction of alcohol consumption in native women who are pregnant or of reproductive age.* The American journal of drug and alcohol abuse, 2012. **38**(5): p. 436-443.

138. Caldwell JY, D.J., Du Bois B, Echo-Hawk H, Erickson JS, Goins RT, Hill, C, Hillabrant W, Johnson SR, Kendall E, Keemer K, Manson SM, Marshall CA, Running Wolf P, Santiago RL, Schacht R, Stone JB *Culturally Competent Research with American Indians and Alaska Natives: Findings and Recommendations of the First Symposium of the Work Group on American Indian Research and Program Evaluation Methodology.* American Indian and Alaska Native Mental Health Research: The Journal of the National Center, 2005. **12**(1): p. 1-21.

139. Manson, S.M. and D.S. Buchwald, *Enhancing American Indian and Alaska Native health research: a multi-faceted challenge.* Journal of interprofessional care, 2007. **21**(S2): p. 31-39.

140. Mitchell, T.L. and E. Baker, *Community-building versus career-building research: the challenges, risks, and responsibilities of conducting research with Aboriginal and Native American communities.* Journal of Cancer Education, 2005. **20**(S1): p. 41-46.

141. Walters, K.L., et al., *Indigenist" collaborative research efforts in Native American communities.* The field research survival guide, 2009: p. 146-173.

142. Caldwell, J.Y., et al., *Culturally competent research with American Indians and Alaska Natives: findings and recommendations of the first symposium of the work group on American Indian Research and Program Evaluation Methodology.* American Indian & Alaska Native Mental Health Research: The Journal of the National Center, 2005. **12**(1).

143. Babor, T.F., et al., *Screening, Brief Intervention, and Referral to Treatment (SBIRT): toward a public health approach to the management of substance abuse.* Substance Abuse, 2007. **28**(3): p. 7.

144. Babor, T.F., et al., *Screening, Brief Intervention, and Referral to Treatment (SBIRT): Toward a Public Health Approach to the Management of Substance Abuse.* Focus, 2011. **9**(1): p. 130-148.

145. Keough, V. and J. Jennrich, *Including a Screening and Brief Alcohol Intervention Program in the Care of the Obstetric Patient.* Journal of Obstetric, Gynecologic, & Neonatal Nursing, 2009. **38**(6): p. 715-722.

146. Nilsen, P., *Brief alcohol intervention to prevent drinking during pregnancy: an overview of research findings.* Current Opinion in Obstetrics and Gynecology, 2009. **21**(6): p. 496-500 10.1097/GCO.0b013e328332a74c.

147. Whitlock, E., et al., *Behavioral counseling interventions in primary care to reduce risky/harmful alcohol use by adults: a summary of the evidence for the US Preventive Services Task Force.* Annals of internal medicine, 2004. **140**(7): p. 557.

148. Longabaugh, R., et al., *Evaluating the effects of a brief motivational intervention for injured drinkers in the emergency department.* Journal of studies on alcohol and drugs, 2001. **62**(6): p. 806.

149. Daeppen, J.-B., et al., *Brief alcohol intervention and alcohol assessment do not influence alcohol use in injured patients treated in the emergency department: a randomized controlled clinical trial.* Addiction, 2007. **102**(8): p. 1224-1233.

150. Bernstein, E. and J. Bernstein, *Effectiveness of alcohol screening and brief motivational intervention in the emergency department setting.* Annals of emergency medicine, 2008. **51**(6): p. 751-754.

151. Woodruff, S.I., et al., *Evaluation of California's Alcohol and Drug Screening and Brief Intervention (CASBIRT) Project for Emergency Department Patients.* Western Journal of Emergency Medicine, 2013. **0**(0).

152. Gentilello, L.M., et al., *Alcohol interventions in a trauma center as a means of reducing the risk of injury recurrence.* Annals of Surgery, 1999. **230**(4): p. 473.

153. Love, A.C., et al., *Emergency department screening and intervention for patients with alcohol-related disorders: a pilot study.* JAOA: Journal of the American Osteopathic Association, 2008. **108**(1): p. 12.

154. Madras, B., et al., *Screening, brief interventions, referral to treatment (SBIRT) for illicit drug and alcohol use at multiple healthcare sites: comparison at intake and 6 months later.* Drug and alcohol dependence, 2009. **99**(1-3): p. 280-295.

155. Manwell, L.B., et al., *Treatment of problem alcohol use in women of childbearing age: results of a brief intervention trial.* Alcoholism: Clinical and Experimental Research, 2000. **24**(10): p. 1517-1524.

156. Cherpitel, C.J., et al., *Screening, brief intervention, and referral to treatment (SBIRT) in a Polish emergency department: three-month outcomes of a randomized, controlled clinical trial.* Journal of studies on alcohol and drugs, 2009. **70**(6): p. 982.

157. D'Onofrio, G., et al., *A brief intervention reduces hazardous and harmful drinking in emergency department patients.* Annals of emergency medicine, 2012.

158. D'Onofrio, G., et al., *Brief intervention for hazardous and harmful drinkers in the emergency department.* Annals of emergency medicine, 2008. **51**(6): p. 742.

159. Bezilla, W.A., *Assessing Fidelity and Use of Core Implementation Components in the Implementation of a Brief Motivational Intervention to Reduce Binge Drinking Among College Students: A Systematic Review of the Literature*. 2010, University of Pittsburgh.

160. Delrahim-Howlett, K., et al., *Web-Based Assessment and Brief Intervention for Alcohol Use in Women of Childbearing Potential: A Report of the Primary Findings.* Alcoholism: Clinical and Experimental Research, 2011. **35**(7): p. 1331-1338.

161. May, P., et al., *Prevalence and epidemiologic characteristics of FASD from various research methods with an emphasis on recent in school studies.* Developmental Disabilities Research Reviews, 2009. **15**(3): p. 176-192.

162. Beals, J., et al., *Racial disparities in alcohol use: Comparison of 2 American Indian reservation populations with national data.* American journal of public health, 2003. **93**(10): p. 1683.

163. NIAAA. *Women and Alcohol*. 2011; Available from: http://pubs.niaaa.nih.gov/publications/womensfact/womensfact.htm

164. May, P.A., et al., *Maternal risk factors for fetal alcohol syndrome and partial fetal alcohol syndrome in South Africa: a third study.* Alcoholism: Clinical and Experimental Research, 2008. **32**(5): p. 738-753.

165. May, P.A., et al., *The epidemiology of fetal alcohol syndrome and partial FAS in a South African community.* Drug and alcohol dependence, 2007. **88**(2): p. 259-271.

166. May, P.A. and J. Phillip Gossage, *Maternal risk factors for fetal alcohol spectrum disorders: Not as simple as it might seem.* Alcohol Research and Health, 2011. **34**(1): p. 15.

167. May, P.A., et al., *Approaching the Prevalence of the Full Spectrum of Fetal Alcohol Spectrum Disorders in a South African Population-Based Study.* Alcoholism: Clinical and Experimental Research, 2013. **37**(5): p. 818-830.

168. WHO, C., *Family planning: a global handbook for providers (2011 update)*. 2011, CCP and WHO: Baltimore and Geneva.

169. Howlett, K.D., *Web-based intervention for alcohol use in women of childbearing potential*. 2010, UC San Diego: San Diego.

170. Sokol, R.J., S.S. Martier, and J.W. Ager, *The T-ACE questions: practical prenatal detection of risk-drinking.* American Journal of Obstetrics and Gynecology, 1989. **160**(4): p. 863.

171. Gale, T., J. White, and T. Welty, *Differences in detection of alcohol use in a prenatal population (on a Northern Plains Indian Reservation) using various methods of ascertainment.* South Dakota Journal of Medicine, 1998. **51**(7): p. 235.

172. Chavez, P.R., et al., *Impact of a new gender-specific definition for binge drinking on prevalence estimates for women.* American journal of preventive medicine, 2011. **40**(4): p. 468-471.

173. Torres Stone, R.A., et al., *Traditional practices, traditional spirituality, and alcohol cessation among American Indians.* Journal of studies on alcohol, 2006. **67**(2).

174. LaFromboise, T.D., J.E. Trimble, and G.V. Mohatt, *Counseling Intervention and American Indian Tradition An Integrative Approach.* The Counseling Psychologist, 1990. **18**(4): p. 628-654.

175. Berkowitz, G., et al., *Community and treatment program challenges for chemically dependent American Indian and Alaska Native women.* Contemporary Drug Problems, 1998. **25**: p. 347.

176. Jilek, W., *Traditional healing in the prevention and treatment of alcohol and drug abuse.* Transcultural Psychiatry, 1994. **31**(3): p. 219-258.

177. Prue, R.E., *King Alcohol to Chief Peyote: A grounded theory investigation of the supportive factors of the Native American Church for drug and alcohol abuse recovery*. 2009, University of Kansas.

178. Pascarosa, P. and S. Futterman, *Ethnopsychedelic Therapy for Alcoholics: Observations In the Peyote Ritual of the Native American Church.* Journal of psychoactive drugs, 1976. **8**(3): p. 215-221.

179. Albaugh, B. and P. Anderson, *Peyote in the treatment of alcoholism among American Indians.* American journal of Psychiatry, 1974. **131**(11): p. 1247.

180. Gray, N., et al., *A Culturally Focused Wellness Intervention for American Indian Women of a Small Southwest Community: Associations With Alcohol Use, Abstinence Self-Efficacy, Symptoms of Depression, and Self-Esteem.* American Journal of Health Promotion, 2010. **25**(2): p. 1-10.

181. Alvik, A., et al., *Alcohol Consumption Before and During Pregnancy Comparing Concurrent and Retrospective Reports.* Alcoholism: Clinical and Experimental Research, 2006. **30**(3): p. 510-515.

182. Chang, G., et al., *Alcohol use and pregnancy: improving identification.* Obstetrics & Gynecology, 1998. **91**(6): p. 892-898.

183. Chang, G., et al., *Brief intervention for prenatal alcohol use: a randomized trial.* Obstetrics and gynecology, 2005. **105**(5 Pt 1): p. 991.

184. Del Boca, F.K. and J. Darkes, *The validity of self-reports of alcohol consumption: state of the science and challenges for research.* Addiction, 2003. **98**(s2): p. 1-12.

185. Secretary of Health and Human Services, *10th Special Report to the US Congress on Alcohol and Health* 2000, National Institute on Alcohol Abuse and Alcoholism.

186. May, P.A., et al., *Maternal alcohol consumption producing fetal alcohol spectrum disorders (FASD): Quantity, frequency, and timing of drinking.* Drug and alcohol dependence, 2013. **133**(2): p. 502-512.

187. Kroenke, K. and R.L. Spitzer, *The PHQ-9: a new depression diagnostic and severity measure.* Psychiatric Annals, 2002. **32**(9): p. 509-515.

188. Bernstein, J.A., E. Bernstein, and T.C. Heeren, *Mechanisms of change in control group drinking in clinical trials of brief alcohol intervention: implications for bias toward the null.* Drug and Alcohol Review, 2010. **29**(5): p. 498-507.

189. May, P.A. and J.P. Gossage, *Estimating the prevalence of fetal alcohol syndrome: A summary.* Alcohol Research and Health, 2001. **25**(3): p. 159-167.

190. Floyd, R.L., et al., *Preventing Alcohol-Exposed Pregnancies:: A Randomized Controlled Trial.* American journal of preventive medicine, 2007. **32**(1): p. 1-10.

191. Ingersoll, K.S., et al., *Preconceptional motivational interviewing interventions to reduce alcohol-exposed pregnancy risk.* Journal of Substance Abuse Treatment, 2013. **44**(4): p. 407-416.

192. KUO, P.-H., et al., *The temporal relationship of the onsets of alcohol dependence and major depression: using a genetically informative study design.* Psychological Medicine, 2006. **36**(08): p. 1153-1162.

193. Wang, J. and S.B. Patten, *A prospective study of sex-specific effects of major depression on alcohol consumption.* Canadian journal of psychiatry, 2001. **46**(5): p. 422-425.

194. Moscato, B.S., et al., *Gender differences in the relation between depressive symptoms and alcohol problems: a longitudinal perspective.* American Journal of Epidemiology, 1997. **146**(11): p. 966-974.

195. Montag, A., Brodine, A., Alcaraz, J., Clapp, J., Allison, M., Calac, D., Hull, A., Gorman, J., Jones, K., Chambers, C., *Preventing Alcohol-Exposed Pregnancy among an AIAN Population: Effect of a SBIRT Intervention.* submitted to Alcoholism: Clinical & Experimental Research, 2014.

196. Montag, A., Brodine, A., Alcaraz, J., Clapp, J., Allison, M., Calac, D., Hull, A., Gorman, J., Jones, K., Chambers, C., *Vulnerability to Alcohol-Exposed Pregnancy among a Population of AIAN Women.* submitted to Maternal and Child Health Journal, 2014.

197. Kroenke, K., R.L. Spitzer, and J.B. Williams, *The PHQ-9.* Journal of general internal medicine, 2001. **16**(9): p. 606-613.

198. Spitzer, R.L., K. Kroenke, and J.B. Williams, *Validation and utility of a self-report version of PRIME-MD.* JAMA: The Journal of the American Medical Association, 1999. **282**(18): p. 1737-1744.

199. Russell, M., et al., *Screening for Pregnancy Risk-Drinking.* Alcoholism: Clinical and Experimental Research, 1994. **18**(5): p. 1156-1161.

200. Russell, M., et al., *Detecting risk drinking during pregnancy: a comparison of four screening questionnaires.* American journal of public health, 1996. **86**(10): p. 1435-1439.

201. Chang, G., *Alcohol screening instruments for pregnant women.* Alcohol Research and Health, 2001. **25**(3): p. 204-209.

202. Chiodo, L.M., et al., *Validity of the T-ACE in pregnancy in predicting child outcome and risk drinking.* Alcohol, 2010. **44**(7–8): p. 595-603.

203. Berenson, A.B., C.R. Breitkopf, and Z.H. Wu, *Reproductive correlates of depressive symptoms among low-income minority women.* Obstetrics and gynecology, 2003. **102**(6): p. 1310-1317.

204. Rounsaville, B.J., et al., *Psychopathology as a predictor of treatment outcome in alcoholics.* Archives of General Psychiatry, 1987. **44**(6): p. 505-513.

205. Thase, M.E., I.M. Salloum, and J.D. Cornelius, *Comorbid alcoholism and depression: Treatment issues.* Journal of Clinical Psychiatry, 2001. **62**(SUPPL. 20): p. 32-41.

206. Penberthy, J.K., et al., *Depressive symptoms moderate treatment response to brief intervention for prevention of alcohol exposed pregnancy.* Journal of Substance Abuse Treatment, 2013. **45**(4): p. 335-342.

207. Williams, E.C., et al., *Readiness to change in primary care patients who screened positive for alcohol misuse.* The Annals of Family Medicine, 2006. **4**(3): p. 213-220.

208. Pyszczynski, T. and J. Greenberg, *Self-regulatory perseveration and the depressive self-focusing style: a self-awareness theory of reactive depression.* Psychological bulletin, 1987. **102**(1): p. 122.

209. Alloy, L.B. and L.Y. Abramson, *Judgment of contingency in depressed and nondepressed students: Sadder but wiser?* Journal of experimental psychology: General, 1979. **108**(4): p. 441.

210. Carver, C.S. and M.F. Scheier, *Origins and functions of positive and negative affect: a control-process view.* Psychological review, 1990. **97**(1): p. 19.

211. Andrews, P.W. and J.A. Thomson Jr, *The bright side of being blue: depression as an adaptation for analyzing complex problems.* Psychological review, 2009. **116**(3): p. 620.

212. Shore, J. and B. Von Fumetti, *Three alcohol programs for American Indians.* American journal of Psychiatry, 1972. **128**(11): p. 1450.

213. Evans, E., et al., *Outcomes of drug and alcohol treatment programs among American Indians in California.* American journal of public health, 2006. **96**(5): p. 889.

214. Chong, J. and M. Herman-Stahl, *Substance abuse treatment outcomes among American Indians in the Telephone Aftercare Project.* Journal of psychoactive drugs, 2003. **35**(1): p. 71-77.

215. Hanson, J.D., et al., *Prevention of Alcohol-Exposed Pregnancies Among Nonpregnant American Indian Women.* American Journal of Health Promotion, 2013. **27**(sp3): p. S66-S73.

216. Westermeyer, J. and E. Peake, *A ten-year follow-up of alcoholic Native Americans in Minnesota.* American journal of Psychiatry, 1983. **140**(2): p. 189.

217. Kivlahan, D., et al., *Detoxification recidivism among urban American Indian alcoholics.* American journal of Psychiatry, 1985. **142**(12): p. 1467.

218. Walker, R., et al., *American Indian alcohol misuse and treatment outcome.* Alcohol Use Among U.S. Ethnic Minorities, 1989: p. 301–311.

219. Evans, E., et al., *Outcomes of Drug and Alcohol Treatment Programs Among American Indians in California.* Am J Public Health, 2006. **96**(5): p. 889-896.

220. Dickerson, D.L., et al., *American indians/alaska natives and substance abuse treatment outcomes: positive signs and continuing challenges.* Journal of addictive diseases, 2011. **30**(1): p. 63.

221. O'Malley, S.S., et al., *Naltrexone Alone and With Sertraline for the Treatment of Alcohol Dependence in Alaska Natives and Non Natives Residing in Rural Settings: A Randomized Controlled Trial.* Alcoholism: Clinical and Experimental Research, 2008. **32**(7): p. 1271-1283.

222. Masis, K. and P. May, *A comprehensive local program for the prevention of fetal alcohol syndrome.* Public Health Reports, 1991. **106**(5): p. 484.

223. May, P., et al., *Enhanced case management to prevent fetal alcohol spectrum disorders in Northern Plains communities.* Maternal and child health journal, 2008. **12**(6): p. 747-759.

224. Ferguson, F., *A treatment program for Navaho alcoholics: results after four years.* Quarterly journal of studies on alcohol, 1970. **31**(4): p. 898.

APPENDIX

Appendix A. CDC FASD Guidelines

Table 3: Brief Outline of Diagnostic criteria for Fetal Alcohol Syndrome

Facial dysmorphia

Based on racial norms, individual exhibits all three characteristic facial features:

- Smooth philtrum (University of Washington Lip-Philtrum Guide rank 4 or 5)
- Thin vermillion border (University of Washington Lip-Philtrum Guide rank 4 or 5)
- Small palpebral fissures (at or below 10th percentile)

Growth problems

Confirmed prenatal or postnatal height or weight, or both, at or below the 10th percentile, documented at any one point in time (adjusted for age, sex, gestational age, and race or ethnicity).

Central Nervous System Abnormalities

I. Structural

1) Head circumference (OFC) at or below the 10th percentile adjusted for age and sex.
2) Clinically significant brain abnormalities observable through imaging.

II. Neurological

Neurological problems not due to a postnatal insult or fever, or other soft neurological signs outside normal limits.

III. Functional

Performance substantially below that expected for an individual's age, schooling, or circumstances, as evidenced by:

1. *Global cognitive or intellectual deficits representing multiple domains of deficit (or significant developmental delay in younger children) with performance below the 3rd percentile (2 standard deviations below the mean for standardized testing)*
   or
2. *Functional deficits below the 16th percentile (1 standard deviation below the mean for standardized testing) in at least three of the following domains:*
   a) cognitive or developmental deficits or discrepancies
   b) executive functioning deficits
   c) motor functioning delays
   d) problems with attention or hyperactivity
   e) social skills
   f) other, such as sensory problems, pragmatic language problems, memory deficits, etc.

Maternal Alcohol Exposure

I. Confirmed prenatal alcohol exposure
II. Unknown prenatal alcohol exposure

Criteria for FAS Diagnosis

Requires all three of the following findings:

1 Documentation of all three facial abnormalities (smooth philtrum, thin vermillion border, and small palpebral fissures);
2. Documentation of growth deficits
3. Documentation of CNS abnormality

Appendix B: Quantitatively evaluated interventions to reduce risky drinking among AIAN women.

Author / Year	*Title* / program description	Study description	Results	Lessons learned
Westermeyer J and Peake E 1983 [216]	*A ten-year follow-up of alcoholic Native Americans in Minnesota*	10 year interview follow-up of previously hospitalized alcoholics n=45 (37♂8♀	42 located: 7 abstinent (5♂2♀, 9 died, 26 drinking. 17% stable abstinence	High relapse rate; ≤17% success rate
Kivlahan D et al 1985 [217]	*Detoxification recidivism among urban American Indian alcoholics.*	2 year follow-up interview of detoxification graduates n=50 urban AI (45♂5♀	None sober at follow-up. 74% readmitted	Detoxification alone doesn't work
Walker RD et al 1989 [218]	*American Indian Alcohol Misuse and Treatment Outcome* 3 separate studies from Seattle Treatment Outcome Project	2 year interview and state monitoring follow-up of 3 urban AI samples: 1. detox (n=50) 2. inpatient or half-way house (90) 3. AI focus (46) or not (27)	80% follow-up total: 1. 0/50 abstinent 2. 9% inpatient and 16% halfway house reported less alcohol abuse or dependence 3. AI programs no more successful	Little or no success with any program
Evans E et al 2006 [219]	*Outcomes of drug and alcohol treatment programs among American Indians in California*	Pre and post admission assessment; 3 and 9 month post interviews; 1 year pre and post driving (DUI), arrest, and mental health records n=368 AI and 368 non-AI	Both AI and non-AI reduced alcohol related problems somewhat. AI received fewer services and had shorter retention in residential treatment.	Service intensity needed for retention in residential treatment

Ferguson F 1970 [224]	Shore J and Von Fumetti B 1972 [212]	May PA et al 2008 [223]	Masis & May 1991 [222]	O'Malley SS et al 2008 [221]	Dickerson DL et al 2011 [220]
A treatment program for Navaho alcoholics: results after four years.	*Three alcohol programs for American Indians*	*Enhanced Case Management to Prevent Fetal Alcohol Spectrum Disorder in Northern Plains Communities*	*program for the prevention of fetal alcohol syndrome.* Primary prevention: community awareness / training providers; Secondary prevention: screening at prenatal clinics; Tertiary prevention: case	*Naltrexone Alone and With Sertraline for the Treatment of Alcohol Dependence in Alaska Natives and Non Natives Residing in Rural Settings: A Randomized Controlled Trial.*	*American Indians/Alaska Natives and substance abuse treatment outcomes: positive signs and continuing challenges.*
Hospitalization, disulfiram, counseling, vocational training; 2-year follow-up; multiple sources n=115 (4 ♀ AI/AN arrested ≥10x for drunkenness	All created within AI communities, involved casework, vocational training, AI tailored n=642 AI/AN	Case management with motivational interviewing and questionnaires at start, shorter at 6 month intervals n=131 AI women	High risk women referred to case management: counseling, personal support, social services and medical services a) detoxification and follow-up and b) voluntary birth control n=48 women referred	Randomized controlled clinical trial with 3 treatment arms. n=68 AI (27 ♀ and 33 non-AI	TSI (Treatment Impact System) project. Treatment by licensed CA programs instead of incarceration /probation. 12 month telephone follow-up. n=245 AI and non-AI
43% drinking less at 12 and 23% at 24 months; 78% decline in arrests; employment increased; low follow-up rate	Overall, 28% showed clear improvement at 1-4 years; 47% ♀ and 26% ♂ improved in one of three programs	Mixed but significant benefit for at risk women; pregnancies protected: 149, data on 119 with 76% normal births, 2 FASD	39 women participated. At 18 months, 18 abstinent, 4 drinking less, 10 still drinking, 7 lost to follow-up; 8 pregnant, 4 using birth control, 6 voluntarily sterilized, 14 at risk for pregnancy.	AI and non-AI had higher abstinence with naltrexone only (35%) vs. placebo (12%) but not longer time to heavy drinking. Medicinal compliance 67% and 60% respectively.	AI and matched controls (~40% female) had no significant outcome differences. 18.8% completed treatment.
Disulfiram may be helpful. Less educated, older, with high arrest rates and less English skills responded best.	Methods and philosophy need to be matched to population. Involve community in planning and execution.	It is feasible to incorporate CM as part of community based prevention program.	Good acceptance of program possibly related to: "prevention" designation, based in hospital / clinic, community members as staff, family-oriented approach.	Naltrexone may be helpful in remote communities	High AI and non-AI dropout rates. Baselines differ suggesting need for culturally tailored, comprehensive programs

Hanson JD et al 2013 [215]	Chong J and Herman-Stahl M 2003 [214]	Torres Stone RA et al 2006 [173]
Prevention of alcohol-exposed pregnancies among non-pregnant American Indian women	*Substance abuse treatment outcomes among American Indians in the Telephone Aftercare Project.*	*Traditional practices, traditional spirituality, and alcohol cessation among American Indians*
Telephone intervention of motivational interview, personalized feedback, and 12-month follow-up. n=231 AI ♀	Enrolled if successfully completed residential program and returning to reservation. Monthly telephone interviews for 6 months. n=30 AI	3 year interview study n=732 AI/AN (≥60% ♀
Self-reported drinking was reduced. No control. Self-selected sample. Loss-to-follow-up 78-87% at 12 months.	30 (21 ♀ recruited of 41 eligible. Drinking from baseline to 3mo 91 to 18%, 6mo 92 to 15%. No control. ASI alcohol score improved.	Women, older, married, or active in traditional practices or spirituality more likely to cease drinking
Project CHOICES may be effectively modified as a telephone based intervention.	High loss to follow-up (63% 3mo, 57% 6mo). Telephone aftercare may be alternative where in-person aftercare is unavailable.	Traditional activities and spirituality had significant positive effects on alcohol cessation.

Appendix C: Questions regarding knowledge of the risks of alcohol consumption

1. When a woman drinks alcohol when she is pregnant, the alcohol enters the baby's bloodstream (blood system).

   ○ True
   ○ False
   ○ Decline to Answer

2. Women are at a greater risk for developing alcohol-related problems than men.

   ○ True
   ○ False
   ○ Decline to Answer

3. Just having a FEW drinks (1-3) during pregnancy is safe for the baby.

   ○ True
   ○ False
   ○ Decline to Answer

4. Babies of women who drink alcohol during pregnancy are at risk for developing physical, mental and behavioral problems.

   ○ True
   ○ False
   ○ Decline to Answer

5. Drinking alcohol is OK during the last 3 months of pregnancy.

   ○ True
   ○ False
   ○ Decline to Answer

6. If a woman is already pregnant but does not know it yet and she is drinking alcohol, she can have a child with an Alcohol Related Birth Defect.

   ○ True
   ○ False
   ○ Decline to Answer

7. Most women aged 18-44 who are members of Southwestern (California, Arizona, New Mexico, Utah, Colorado, Nevada) Tribes currently drink alcohol.

   ○ True
   ○ False
   ○ Decline to Answer

8. During pregnancy, it is OK to drink during the morning.

   ○ True
   ○ False
   ○ Decline to Answer

9. If you are breastfeeding and you drink alcohol, the alcohol can be passed to the baby through the milk.

   ○ True
   ○ False
   ○ Decline to Answer

10. It is OK to drink wine during pregnancy.

   ○ True
   ○ False
   ○ Decline to Answer

11. If you are nauseous or feel sick to your stomach during pregnancy, you should drink a beer.

   ○ True
   ○ False
   ○ Decline to Answer