The Trajectory of Fetal Alcohol Spectrum Disorders (FASD) Across the Life Span: Continuing Prevention and Longitudinal Epidemiology

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PROTOCOL

Complete Title: The Trajectory of Fetal Alcohol Spectrum Disorders (FASD) Across the Life Span: Continuing Prevention and Longitudinal Epidemiology

Short Title: Motivational Enhancement Therapy

Drug or Device Name(s): Not Applicable

FDA IND/IDE (if applicable): Not Applicable

Sponsor: National Institute on Alcohol Abuse and Alcoholism

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Abbreviations and Definitions of Terms

Abbreviation	Definition
AUDIT	Alcohol Use Disorder Identification Test
FASD	Fetal alcohol spectrum disorders
MET	Motivational Enhancement Therapy
PAE	Prenatal Alcohol Exposure
PEth	Phosphatidyl ethanol
SA	South Africa
USDTL	United States Drug Testing Laboratories, Inc.

PROTOCOL SYNOPSIS

Study Title	The Trajectory of Fetal Alcohol Spectrum Disorders (FASD) Across the Life Span: Continuing Prevention and Longitudinal Epidemiology
Principal Investigator	Philip A. May, PhD, UNC Nutrition Research Institute
Funder	National Institute on Alcohol Abuse and Alcoholism
Clinical Phase	N/A
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Study Rationale	Alcohol is a known teratogen and can cause fetal alcohol spectrum disorders (FASD). Globally, FASD are a leading cause of development delays. The Western Cape Province of South Africa currently has the highest documented prevalence of FASD in the world. Effective prevention interventions are needed to reduce the number of individuals with prenatal alcohol exposure and/or who have a diagnosis within the FASD continuum.
Study Objective(s)	To determine whether there is a greater reduction in AUDIT scores from baseline to follow-up in the intervention group relative to the control group.
Study Design	Randomized trial comparing two behavioral interventions (Motivational Enhancement Therapy vs. Pamphlets Only)
Subject Population key criteria for Inclusion and Exclusion:	Inclusion Criteria 1. Pregnant females, 15 - 44 years of age 2. Gestation age $\leq$20 weeks 3. At risk for an alcohol-exposed pregnancy
Number Of Subjects	Up to 400 pregnant women

BACKGROUND AND RATIONALE

Alcohol is a known teratogen, and prenatal alcohol exposure (PAE) can lead to a variety of physical malformations and cognitive and behavioral impairments and/or delays. The broad range of physical and neurodevelopmental traits associated with prenatal alcohol exposure is captured under the umbrella term of fetal alcohol spectrum disorders (FASD). The prevalence of FASD has been found to be no lower than 1-5% in communities of the United States and 17 - 28% in the Western Cape Province of South Africa (SA).[1–6] Yet there are few brief interventions designed to reduce or eliminate alcohol consumption during pregnancy in order to prevent and/or reduce the number of individuals who are diagnosed within the FASD continuum.

Drinking during pregnancy in parts of the Western Cape Province of South Africa is frequently reported. Croxford and Viljoen (1999) reported that 43% of prenatal patients in Cape metropolitan areas drank during pregnancy.[7] Concern about FASD has grown in South Africa.[8–10] Studying characteristics of Western Cape Province mothers is useful for understanding high risk drinking and for designing prevention programs. FASD prevention programs in the Western Cape Province of SA can and must be built in this area.

According to the US Surgeon General, there is no known safe amount of alcohol during pregnancy. The Host, Agent, and Environment model has guided our thinking from the start of SA research. This mainstream, utilitarian, analytic tool provides a distinctive, multivariate and multi-disciplinary understanding of prenatal alcohol exposure. Principles of Motivational Interviewing[11] and Community-Reinforcement Approach[12,13] have been shown efficacious in promoting behavior change (reduced alcohol consumption) in several settings.[14–18] Ingersoll et al (2005) reported that a one-session motivational interview-based interview reduced risk for alcohol-exposed pregnancies compared to controls who received a pamphlet on women's health. Others reported greater reduction in alcohol consumption following brief interventions.[18] Potential benefits of this intervention include: women reduce or stop alcohol consumption during pregnancy which results in less or no prenatal alcohol exposure to the developing fetus. Therefore, the public health burden associated with prenatal alcohol exposure is reduced.

STUDY OBJECTIVE

The purpose of the study is to determine the efficacy of a one-session, motivational enhancement therapy intervention to reduce Alcohol Use Disorder Identification Test (AUDIT) scores compared to a comparison group which only receives pamphlets on the risks associated with alcohol consumption during pregnancy.

Primary Objective: To determine whether there is a greater reduction (change) in AUDIT scores from baseline to follow-up in the intervention group relative to the comparison group.

STUDY DESIGN

Setting

The study will be carried out in a single Municipal Area and surrounding rural areas in the Western Cape Province of SA. Afrikaans, English, and Xhosa are the dominate languages in the study area.

Procedures

Pregnant women who sought prenatal care at local clinics will be screened for study eligibility. To be eligible females must be 15-44 years of age, ≤ 20 weeks gestation, and at risk for having an alcohol-exposed pregnancy (e.g., drank within the past 30 days). Up to 400 women will be enrolled into the intervention study. Enrolled pregnant participants will be randomly assigned to either an intervention group or a pamphlets-only comparison group.

Intervention Group: a one-on-one session with a project officer using motivational interviewing to examine current lifestyle choices (regarding alcohol consumption) and develop a tailored change plan to identify steps the participant can take to change a current lifestyle choice. Once a participant enrolls into the Motivational Enhancement Therapy (MET) study and is randomized to the Intervention Group, each will be provided a brief MET session, provided a call in number, and monitored up to five times throughout the pregnancy.

Comparison Group (pamphlets only): receive pamphlets on the dangers of alcohol consumption during pregnancy.

Both Groups: Women in both groups will be interviewed at enrollment and 9 months follow-up. All mothers enrolled in the Intervention Group and Comparison Group will be asked to provide blood spot samples at 3 time points: 1) on the same day the antenatal screening questionnaire is completed, 2) once during the third trimester of the pregnancy (between 30- and 34 weeks gestation), and 3) within 30 days after the birth of the baby. Obtaining the blood spot samples will take about 10-15 minutes and will be performed by an experienced research staff member. Blood spots will be collected by pricking the finger with a sterile safety lancet. The collector will wear latex free gloves and use universal precautions (five small drops of blood will be collected). Blood spots will be collected on de-identified, sterile blood spot collection cards and will be shipped to United States Drug Testing Laboratories, Inc (USDTL) for processing for detection of phosphatidylethanol (PEth) levels. Infants of both groups will be assessed with standard neurodevelopmental assessments (Bayley Scales of Infant Development)[20] and standardized physical assessment for growth, development, and dysmorphology.[21,22]

Randomization

Random assignment numbers will be picked via a computerized random number selection program to indicate who is assigned to the Intervention Group and who is assigned to the Comparison Group. The randomization ratio will be 1:1. There is no blinding or masking.

DATA COLLECTION AND MANAGEMENT

Data collection will be carried out in person. Data will be recorded by hand in hard copy. Forms will be kept in locked file cabinets/offices. The offices have restricted access. As needed, data will be translated to English. Data will be entered into an electronic database. Electronic databases will be stored on password-protected computers meeting University security requirements. Standard epidemiological record keeping methods will be used to protect confidentiality. Each participant will be given an identification number. Names and other identifiable information (telephone number, address) will not be included in databases.

Intellectual property and data generated under this project will be administered in accordance with institutional policies, including the NIH Data Sharing Policy and Implementation Guidance. Materials generated under the project will be disseminated in accordance with participating institutional policies.

RECRUITMENT STRATEGY

All recruitment will be carried out in person. As the first step in this process, regular, screening for alcohol problems will occur at prenatal clinics, in the field, and at the local prevention office. Women will be

asked in the screening if they would like to participate in a trial of brief Motivational Enhancement Therapy. Those females found to be in need of assistance with alcohol problems will be referred to the prevention staff for further assessment. A total of up to 400 women who screen positive for drinking will be asked if they want to be enrolled.

CONSENT PROCESS

The informed consent process will begin with the purpose of the study and a description of the study procedures. Study staff will review the consent form and orally explain the consent form to the participant. All participants will read and sign a standard consent form (in Afrikaans and/or English). A translator will be provided, if requested, at no cost to the participant. The consent process will occur in a private location (e.g., study office or another mutually agreed upon location). To ensure that participants comprehend the nature of the study, procedures, and risk/benefits, participants will be encouraged to ask questions and repeat back study expectations. A wavier of parental consent for pregnant females 15-17 is appropriate to keep the process of consent of this study consistent with South African standards of practice and regulations. Pregnant women ages 15-17 will sign the approved informed consent documents. Staff will be acquiring consent according to South African laws and regulations. No information will be withheld while obtaining consent or directing the progress of the study.

ADDITIONAL SAFEGUARDS FOR PREGNANT INDIVIDUALS

By definition, women are the major focus of this study as FASD is caused primarily by women consuming alcohol during the prenatal period. The research focuses on the general health and behavioral factors they possess which put a fetus at risk. Human subjects are protected by using standard and conservative protocols and the protection of privileged medical information. In the feedback process empathic communication is used at all times, and blaming is not allowed. Communication styles will be monitored by the research team.

ADDITIONAL SAFEGUARDS FOR NON-ENGLISH-SPEAKING INDIVIDUALS

All field staff will be bi-lingual in the two primary languages of the study community (Afrikaans and English). All study materials will be available in Afrikaans and English. If another language is requested by a study participant, a translator will be provided at no cost to the participant.

PARTICIPANT SAFETY, PROTECTION, AND CONFIDENALITY

The PI will be responsible for monitoring participant data for safety concerns, adverse events, and serious adverse events. Any unanticipated problems will be reported promptly in compliance with Good Clinical Practice. Staff will notify participants of new safety information as soon as possible. Women requiring additional medical attention will be given the contact information for local providers and guided to referrals by staff.

There is no prospect of benefit for the woman or the fetus involved in this research, the risk to the fetus is not greater than minimal, and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by any other means. The risks to the participants of this project will be minimal. The research focuses on the general health and behavioral factors that participants may possess which put a fetus at risk. When maternal interviews are carried out, a unique consent form is signed by the female interviewee. All information from the interview is confidential. Participants are protected by using standard conservative protocols and the protection of privileged information. Screening, confidential record reviews, and some of the research activities have strict record protection protocols. Communication styles will be monitored by the research team. Consent forms are signed emphasizing the voluntary nature of the services, that they are oriented to research, and that participants can disengage from the study at any time with no penalty.

WITHDRAWL

Participants may withdraw from the study at any point. Participants who voluntarily withdraw may keep previously given incentive amount.

STATISTICAL ANALYSIS PLAN

Primary Endpoint: Change in Alcohol Use Disorder Identification Test (AUDIT) score.

Data Analysis Plan: The primary outcome is the change in AUDIT score from baseline to 9 months follow-up. Between-group mean differences and standard deviations will be compared. Data analysis will include traditional statistical analyses for group differences.

Power Analysis: The primary test is that women in the Intervention Group should show greater reduction of alcohol consumption over time than women in the Comparison Group. Main effects of time are expected because alcohol consumption should be reduced as a result of first contact. Therefore, a group (between) effect, time (within) effect, and a group by time interaction will be explored. With a sample size of 400, alpha = .05, power of 0.95, there is power to detect an effect size (*f*) of .09. With a sample size of 200, there is power to detect an effect size of .13.

Data Integrity: Data will be subjected to standard quality control and assurance measures.

PLANS FOR PUBLICATION

Aggregate, anonymous data will be presented in standard scientific publications and conferences. The utilization of final publication information only in anonymous and aggregate form protects the identity of both individuals and communities. Groups and/or subgroups will not be small enough to allow individuals to be deductively identified.

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