PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Comparison and Validation of Screening Tools for Substance Use in Pregnancy: A Cross-Sectional Study conducted in Maryland Prenatal Clinics
AUTHORS	Coleman-Cowger, Oga, Emmanuel; V; Peters, Erica; Trocin, Kathleen; Koszowski, Bartosz; Mark, K

VERSION 1 – REVIEW

REVIEWER	Prabhakar Kocherlakota Maria Fareri Children's Hospital at Westchester Medical Center, New York Medical College, Valhalla, NY 10595
REVIEW RETURNED	12-Nov-2017

GENERAL COMMENTS	Number of hair and urine samples are too small

REVIEWER	Michael K Lindsay MD, MPH Department Gynecology Obstetrics Emory University, Atlanta, Georgia , USA
REVIEW RETURNED	14-Nov-2017

GENERAL COMMENTS	Study Protocol Validating Screening Tool for Illicit and Prescription Drug Use in Pregnancy Using Hair and Urine Sample Testing This study addresses an emerging Public Health Problem, the use of illicit and prescription drugs in pregnancy. The study protocol is well designed. The results obtained from this cross sectional study may identify the best tool for clinicians to use to screen for substance use in pregnancy. The results of this study has the potential to add new knowledge to the literature since there is no universally validated screening tool for identifying illicit drug use in pregnancy. The study is designed to examine the sensitivity, specificity and usability of three separate validated substance use screening tools; Alcohol, Smoking and Substance Involvement Screening Test (ASSIST), the 4P's and Substance Use Risk Profile Pregnancy (SURP-P) among a cross section of pregnant women recruited from two obstetric clinics in Baltimore, Maryland. The 3 aims of the study are clearly articulated: 1.To determine the sensitivity, specificity, and usability of 3 screening tool for substance use compared to the gold standard of hair and urine sample testing.

	2. To determine the impact of clinical population variable (age, race, trimester of pregnancy) on the validity of the three screening tools. 3. To determine the birth outcomes (birth weight, gestational age, head circumference) and rate of NICU admission in the populations with most widely used prescription drug and multi-drug exposure. The sites of recruitment were well described and a novel feature of the study design is that two clinics were selected for recruitment, one clinic where the majority of patients most publically insured and the other where the majority of patient were on commercial insurance. This design will enhance the generalizability of the study findings. The authors present recruitment data from previous studies conducted in these clinical settings. The recruitment goals were obtained which provide confidence that the current study would be able to reach its recruitment goal. The eligibility criteria are clearly defined. The study procedures are clear and the research staff will not negatively impact patient flow. The mechanism for the protection of patient information was well described and is appropriate. An added feature was that patient are rewarded for study participation via gift card which is an acknowledgement that the researchers value the importance of the study participant's time. The study procedure is clearly detailed and study instruments are used to study drug detection windows and detection cut off for urine and hair. A protocol is presented on how women with positive drug screens should be triaged. The results from the pilot study is very informative and buttress confidence that the study recruitment goals can be achieved. The power and sample size calculations are sound and based on realistic estimates. The proposed analysis are appropriate and is consistent with the questions being addressed: a. Reliability and validity of each screen via correlation coefficients b. Test/retest reliability c. Sensitivity/specificity of each screening instrument compared to gold standard hair and urine samples d. Logistic Regression to examine difference in screen validity by age, race, trimester of pregnancy e. Prevalence of prescription and illicit drug use f. ANOVA to test for differences in birthweight, gestational age and head circumference stratified by positive hair drug test results. g. Relative Risk of NICU admission, stillbirth and miscarriage based on screening test between those with positive and negative hair drug test This is a novel study that has the potential to add valuable new information to the literature. The study has the potential 1. Enhance the detection of the prevalence of prescription and illicit drug use in pregnancy. 2. Provide a more comprehensive measure of substance use in pregnancy by combining urine and hair drug detection techniques. 3. Compare 3 screening tools for substance use in a head to head comparison. 4. Use EMR to capture prescription drug use and birth outcomes.

	5. Provide evidence for universal substance use screening in pregnancy. If this study is successful in identifying a reliable screening tool for substance use in pregnancy, it will have a profound public health impact for both mothers and infants. However, what is simultaneously important is a public health push for treatment of all substance abuser in pregnancy to enhance their odds of a successful pregnancy outcome.

REVIEWER	Nathan Tauger Unaffiliated, USA
REVIEW RETURNED	11-Dec-2017

GENERAL COMMENTS	This is a very clear study design to compare three screening tools for illicit and prescription drug use during pregnancy at two clinics in Baltimore, Maryland. Could the study referenced on lines 152-154 be cited if it has already been published? From lines 171-175, are there pre-supplied reasons given for patient lack of interest, or just blank space? Is there any reason to expect selection bias for participating? Could those concerns be discussed in the discussion section or study weakness section? The discussion section should mention risk of legal intervention as a result of screening, whether because of state policy or because of unintentional breech of confidentiality. For references to potential negative outcomes resulting from drug screening, see: 1.) Guttmacher Institute: State Laws and Policies -- Substance Use During Pregnancy. 2017. 2.) "Stratified reproduction and kin of last resort" in Knight KR: addicted.pregnant.poor 2016. (particularly page 157)

REVIEWER	Cheryl Currie University of Lethbridge, Canada
REVIEW RETURNED	12-Dec-2017

GENERAL COMMENTS	This study will address a gap in our knowledge regarding evidence-based screens that can be used to asses illicit or prescription drug use among pregnant women. The team completed a pilot study with 42 women to confirm the feasibility of this study. The current study is in the process of recruiting 500 women during their regularly scheduled prenatal appointment to compare 3 drug screeners to gold standard biochemical measures. The study will also strengthen and update our knowledge in other areas including the test-retest reliability of the screeners used; differences in the validity of screeners by age, ethnicity and trimester; the prevalence of prescription and illicit drug use during pregnancy, and the impacts of drug use on birth outcomes. The methodology and analysis strategy is well developed and articulated. Limitations The study is limited to adults. The prevalence of illicit drug use is highest among pregnant adolescents. This study will not identify screens most appropriate for this population.

	This should be noted as a limitation of this study. This study is limited to women who seek prenatal care. Women who do not seek prenatal care are often at the greatest risk for illicit drug use. This study will not identify screens most appropriate for this population. This should be noted as a limitation of this study.

VERSION 1 – AUTHOR RESPONSE

Reviewer #1
"Number of hair and urine samples are too small."

We are collecting hair and urine samples from each participant and are enrolling 500 participants. This is a convenience sample of pregnant women and is not a national sample; we recognize this is a limitation and have acknowledged this in our Limitations section. However, for the population of pregnant women, this sample size of 500 is quite sizeable and results will be generalizable given the numbers of positive screens we are seeing (27-31% with n=480 to date).

Reviewer #2:
"…what is simultaneously important is a public health push for treatment of all substance abuser in pregnancy to enhance their odds of a successful pregnancy outcome."

Response: We agree with the reviewer and have added this important point to the Discussion.

Reviewer #3
"Could the study referenced on lines 152-154 be cited if it has already been published?

Response: This paper was very recently accepted for publication, pending revisions, therefore we did not include it since it is not yet officially "in press."

"From lines 171-175, are there pre-supplied reasons given for patient lack of interest, or just blank space?

Response: There is space to note reasons for lack of interest but no pre-supplied reasons.

"Is there any reason to expect selection bias for participating?"

Response: As in most studies, selection bias is possible and we have noted this in the study limitations section.

"The discussion section should mention risk of legal intervention as a result of screening…"

Response: The reviewer makes an excellent point and we have included discussion of this issue in the Discussion.

Reviewer #4
"…The prevalence of illicit drug use is highest among pregnant adolescents. This study will not identify screens most appropriate for this population. This should be noted as a limitation of this study."

Response: This is an important limitation to note. In our original protocol adolescents were included, but the University of Maryland IRB did not allow for inclusion of pregnant adolescents in a “no-benefit” study.

“Women who do not seek prenatal care are often at the greatest risk for illicit drug use. This study will not identify screens most appropriate for this population.”

Response: While it is true that women who do not seek prenatal care are at higher risk of illicit drug use, the purpose of this study is to determine which screeners work best to identify substance use in a clinic setting. Our target is therefore only women who present to clinics.
We appreciate the opportunity to revise and resubmit our paper and look forward to seeing our manuscript in print.

VERSION 2 – REVIEW

REVIEWER	Michael K Lindsay MD, MPH Emory University, United States
REVIEW RETURNED	09-Jan-2018

GENERAL COMMENTS	The authors diligently addressed all reviewers concern about their manuscript and revised the manuscript accordingly. The resultant manuscript is more comprehensive and informative. The authors should be congratulated on this excellent work product.

REVIEWER	Cheryl Currie University of Lethbridge, Canada
REVIEW RETURNED	22-Dec-2017

GENERAL COMMENTS	I have no additional editing suggestions.