Smoking Reduction in Gravid Women with Substance Use Disorders (SIGS): A Randomized Controlled Trial

Protocol

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1. Study Abstract

In 2018, 12.0% of adult women in the US smoked,[1] and approximately 7% of women continue smoking during pregnancy.[2] Rates of smoking are even higher among women with substance use disorders. While only 16% of the US adult population reports smoking, 66% of those with a substance use disorder report smoking.[3]

Smoking accounts for almost 3,000 stillbirths in high-income countries annually.[4] Any smoking is associated with an 20-40% increase in the odds of stillbirth compared to not smoking, and heavy smoking (defined as ≥10 cigarettes/day) increases the odds of stillbirth by 50-80%.[4,5] Maternal smoking is also associated with an increase in the risk of neonatal death, preterm birth, and low birth weight.[6]

Unfortunately, nicotine replacement therapy has not helped women quit smoking during pregnancy.[7-10] Limited data on other smoking cessation agents such as varenicline and buproprion limit their widespread use in pregnancy[11].

Exhaled carbon monoxide monitors, such as the Smokerlyzer® device, can be used as a motivational tool to encourage women to quit smoking. Studies in non-pregnant populations using this device to encourage smoking cessation have been promising.[12,13] The use of such monitors to measure smoking in pregnancy has also been validated and used in other studies of smoking cessation in pregnancy.[14-17] Exhaled carbon monoxide can also be directly correlated to fetal carboxyhemoglobin levels, a direct byproduct of in utero exposure to cigarette smoke.

Therefore, we propose a randomized controlled trial to evaluate the efficacy of monitoring exhaled carbon monoxide in smoking cessation during pregnancy in women with substance use disorders. We hypothesize that women who undergo exhaled carbon monoxide monitoring will have greater smoking cessation rates that those who do not undergo exhaled carbon monoxide monitoring.

1.1. Primary Hypothesis

Women who receive exhaled carbon monoxide (eCO) monitoring will be more likely to quit heavy smoking prior to delivery than women do not undergo eCO monitoring.

1.2. Secondary Hypotheses

- Women who receive eCO monitoring are more likely to quit smoking prior to delivery than women who do not receive eCO monitoring.
- Women undergoing eCO monitoring will give birth to larger infants and fewer infants that are small for gestational age.
- eCO levels at delivery will correlate to infant birth weight.
- Women undergoing eCO monitoring will give birth to infants closer to term (37 weeks gestation)
- Women using eCO monitoring will have infants with higher APGAR scores at 5 minutes
- Women undergoing eCO monitoring will be more satisfied with their prenatal care and smoking cessation experience.

1.3. Purpose of the Study Protocol

The purpose of this study is to determine whether eCO monitoring will aid in smoking cessation during pregnancy. This protocol describes the rationale, design, and organization of the study.

2. Background

2.1. Smoking in Pregnancy

Pregnancy is considered a time when women are highly motivated to commit to change.[18-20] Therefore, encouraging all pregnant women to quit smoking, even those with substance use disorders, can significantly improve birth outcomes. Although quitting prior to 15 weeks gestation is the most beneficial for the pregnancy, quitting prior to the third trimester improves infant birth weight.[21]

2.2. Substance Use Disorders and Smoking

Women with substance use disorders frequently also smoke. Smoking cessation is not a component of treatment for substance use disorders, and tobacco abuse is all too frequently forgotten in the face of encouraging abstinence from cocaine, heroin, and amphetamines. However, continued tobacco use is associated with relapse.[22,23] Therefore, encouraging smoking cessation during treatment for substance use disorders is essential.

2.3. Smoking Cessation in Pregnancy

Smoking cessation in pregnancy is recommended not only by the U.S Preventative Service Task Force (USPSTF) but also by the American College of Obstetricians and Gynecologists (ACOG). More specifically, the USPSTF recommends that all pregnant women be asked about tobacco use in pregnancy as well as offer intervention to pregnant smokers at their first prenatal visit. Such interventions that are available are using the 5A's (ask, advise, assess, assist, and arrange) as well as the 1-800-QUIT-NOW line[10].

The rate of reduction or cessation for smoking in pregnancy reduced from 18.4% to 13.2% in 1990 to 2006, respectively. Overall, when pregnant, most women are motivated to stop smoking. Of those who desire smoking cessation, 46% of prepregnancy smokers quit successfully before or during pregnancy[7].

The benefits of smoking cessation can improve reduction in low birth weight caused by maternal smoking as well as decrease the risks associated with maternal smoking such as placental abruption, placenta previa, preterm birth, miscarriage and stillbirth[11].

2.4. Exhaled Carbon Monoxide Monitoring

Carbon monoxide is a toxic, odorless, colorless and tasteless gas that is formed by the incomplete combustion of organic materials at high temperatures. This gas is created when smoking tobacco cigarettes and toxic as it displaces oxygen in the bloodstream to form carboxyhemoglobin (Ernst). This displacement restricts the body's tissue of oxygen leading to fatigue and other health problems. Carbon monoxide can remain in the bloodstream for up to 24 hours, has a half-life of 5 hours, and crosses the placenta causing decreased oxygenation to an unborn fetus.

The Smokerlyzer® device is one that has been used to aid in smoking cessation for non-pregnant and male patients, and now has the ability to measure not only maternal carbon monoxide levels but also record the fetal carboxyhemoglobin levels and correlate the percentage of vital oxygen that has been replaced in the bloodstream.

The device works by measuring the carbon monoxide from a 15 second inhaled breath that is blow slowly into a mouth piece until all the air in the lungs are completely exhaled. The screen then displays the maternal carbon monoxide, percent carboxyhemoglobin and percent fetal carboxyhemoglobin levels and is recorded on to the device.

2.5. Exhaled Carbon Monoxide Monitoring in Pregnancy

Expired carbon monoxide levels to aid in smoking cessation have been used in non-pregnant patients. A previous study conducted using a device that measured expired carbon monoxide was completed and reflected accurate smoking levels in the pregnant population. However, no study has been completed using a carbon monoxide test to promote smoking cessation in the pregnant population.

2.6. Rationale for a Clinical Trial

Currently, the management for smoking in pregnancy is to provide patients with resources for cessation and inform them of the risk for the fetus. Despite counseling patients, there is no way to show patients how their smoking is directly affecting their baby. Historically, it has been known that pregnant smokers overall have smaller babies. Although eCO levels can aid non-pregnant patients in smoking cessation, a randomized controlled trial is needed to determine whether measuring the maternal eCO and associated fetal carboxyhemoglobin levels in pregnancy will reduce adverse outcomes associated with smoking in pregnancy.

2.7. Innovation

This novel handheld device can be used in the clinic setting to provide immediate feedback for the patient and provider on smoking; this real time information can be used for biofeedback and counseling on smoking cessation.

3. Study Design

3.1. Primary Research Question

Does eCO monitoring decrease the rate of smoking ≥10 cigarettes day at the time of delivery in women with substance use disorders?

3.2. Secondary Research Questions

- Does eCO monitoring decrease the number of cigarettes smoked per day?
- Does eCO monitoring increase infant birth weight?
- Does maternal eCO at delivery correlate with infant birth weight?
- Does maternal eCO prior to 24 weeks correlate with infant birth weight?
- Does percent fetal carboxyhemoglobin at final measurement correlate with birth weight?
- Does eCO monitoring at delivery correlate with APGAR scores?
- Does eCO monitoring increase gestational age at delivery?
- Does eCO monitoring improve patient satisfaction with prenatal care and smoking cessation?

3.3. Design Summary

This is a randomized control trial. Women with a known substance use disorder who meet inclusion criteria will be offered participation in the study. Both groups will undergo eCO monitoring at enrollment, each prenatal visit and delivery. Women in the intervention group will be informed of their exhaled carbon monoxide measurement at each visit as well as the correlation to fetal carboxyhemoglobin. At each visit, women in the intervention group will receive counseling on fetal impact of smoking based on fetal carboxyhemoglobin level and institutional and state information on smoking cessation will be provided. The control group will not receive any information about their exhaled carbon monoxide or fetal carboxyhemoglobin level. At each visit, women in the control group will be provided institutional and state information on smoking cessation if they report continued smoking. Additional medications to quit smoking (nicotine replacement or other medical therapies) will not be provided to either group (although patients in either group may receive NSRIs as medically indicated for indications other than smoking cessation). The primary outcome is the number of women each group smoking ≥10 cigarettes/day at their final prenatal visit, as determined by exhaled carbon monoxide measurements. Analysis will be on an intent to treat basis.

3.4 Study Population and Eligibility Criteria

The study population of women with substance use disorders was selected for several reasons. First, women with substance use disorders have a significantly higher rate of smoking than women without substance use disorders.[3] Secondly, women with substance use disorders who continue to smoke have a higher rate of relapse than those who quit smoking, [22,23] suggesting that this population will uniquely benefit from smoking cessation during pregnancy.

a. Inclusion criteria:

i. Age 16-45
ii. Singleton gestation
iii. Gestational age at enrollment <24 weeks
iv. Substance use disorder defined as modified NIDA ASSIST ≥4

v. Cigarette smoker using ≥10 cigarettes/day interested in quitting

b. **Exclusion criteria:**
   i. Known or suspected fetal growth restriction at enrollment
   ii. Known fetal anomaly, aneuploidy, or demise
   iii. Not interested in smoking cessation or reduction during pregnancy
   iv. E-cigarette use

3.5 Study groups

There will be two intervention groups:

a. **Group 1 (Standard Care treatment)**
   Patient exhale into Smokerlyzer® device but are blinded to maternal carbon monoxide and subsequent fetal carboxyhemoglobin levels.

b. **Group 2 (Intervention/eCO Monitoring)**
   Patients exhale into Smokerlyzer® device and are informed of the maternal carbon monoxide and subsequent fetal carboxyhemoglobin results. The patient will then view a chart with the levels and correspond them to the current smoking amount as well as counseled on its effects on maternal and fetal health.

3.6 Informed Consent

Institutional Review Board (IRB) approved informed consent forms will be presented to the patient, and informed consent must be obtained prior to enrolling the patient in this randomized controlled trial. The full list of potential risks to the patient and her neonate will be listed in the informed consent. The nature and purpose of the study will also be detailed in the informed consent. The patient will be provided a copy of the signed informed consent. The informed consent will only be in English, and thus, only English-speaking individuals may participate in the study.

4. Study Procedures

4.1 Screening for Eligibility and Consent

All patients will be identified utilizing the IRB-approved UAB Obstetric Automated Recording (OBAR) system (IRB X030604010). This system will be used to identify patients entering prenatal care <24 weeks of pregnancy. Women will be approached at a prenatal care visit, where a member of the research team will confirm eligibility and present the study which will include the risks, benefits, procedures, and alternatives. The informed consent will be signed after all questions have been answered.

4.2 Randomization

Randomization will occur after eligibility/exclusion criteria are confirmed and informed consent is obtained. Randomization will occur by a predetermined computer-generated block randomization scheme prepared by a study statistician. A variable block design will be utilized.

4.3 Management of patients who develop exclusion criteria (stillbirth, new fetal anomaly or aneuploidy diagnosis)

Patients that develop the exclusion criteria of stillbirth, new fetal or aneuploidy diagnosis will continue to be followed for outcomes but will be excluded from any secondary analyses that include infant outcomes.

4.4 Management of intervention group

At each prenatal visit, in addition to receiving standard prenatal care, women randomized to the intervention group will:

1) Be asked to report how many cigarettes they have smoked per day in the last week
2) Measure eCO
3) Be counseled on their exhaled carbon monoxide level and corresponding fetal carboxyhemoglobin level
4) Receive smoking cessation materials if reports continued smoking or eCO indicates continued smoking

4.5. Management of control group

At each prenatal visit, in addition to receiving standard prenatal care, women randomized to the intervention group will:

1) Be asked to report how many cigarettes they have smoked per day in the last week
2) Measure eCO
3) Receive smoking cessation materials if reports continued smoking

4.6 Adherence

Study personnel will monitor each participant at each clinic visit to conduct the exhaled carbon monoxide measurement. Study personnel will record any deviations from the protocol and adherence to the protocol will be reported in the primary manuscript.

4.7 Participant follow-up

Participants will be followed through discharge after delivery. At hospital admission for delivery, a final exhaled carbon monoxide measurement will be obtained. Patients will be asked to complete a survey prior to hospital discharge. Maternal and infant outcomes will be ascertained until discharge.

4.8 Adverse Event Reporting

As this is a low-risk study, an independent data safety monitoring board will not be formed.

We defined an adverse event as an undesirable experience or outcome occurring in a research participant, regardless of whether participation in the research study caused the event to occur. For example, placental abruption and/or stillbirth are known risks of pregnancy, and while not associated with the Smokerlyzer® device, would be considered an adverse event if it occurred during the study. All serious adverse events will be reported to the IRB. A serious adverse event will include the following events.

a. Death
    a. Maternal
    b. Fetal (stillbirth)
b. Life-threatening
c. Prolonged hospitalization
d. Disability or permanent damage
e. Other serious or important medical events:
    a. Placental abruption
    b. Any other serious event necessitating an unanticipated higher level of care, such as a transfer to an intensive-care unit (not including anticipated transfers to neonatal ICU for prematurity, neonatal withdrawal syndrome)
f. Any other event not listed that the investigators believe may have been caused by the intervention.

4.9 Study Outcome Measurements and Ascertainment

4.9.1. Primary outcome

Prevalence of smoking ≥10 cigarettes/day in each group at final measurement (last prenatal visit prior to delivery or at delivery), as measured by exhaled carbon monoxide

4.9.2. Secondary outcomes

1. Average number of cigarettes smoked/day in each group, as measured by exhaled carbon monoxide at final measurement
2. Prevalence of smoking ≥10 cigarettes/day in each group at delivery, per patient report
3. Average number of cigarettes smoked/day in each group, per patient report
4. Average exhaled carbon monoxide at final measurement
5. Average percent fetal carboxyhemoglobin at final measurement
6. Infant birthweight
7. APGAR at 5 minutes
8. Small for gestational age at birth (<10^{th} percentile)
9. Gestational age at delivery

10. Patient satisfaction at final prenatal visit, measured by PANAS scales (positive and negative affect scales) and select questions on Stop Smoking Service Client Satisfaction Survey

4.9.3. Follow-up and Outcome Ascertainment Periods

The primary outcome will be obtained by exhaled carbon monoxide level at the final prenatal visit, within 4 weeks of delivery. If the patient has been lost to follow up prior to delivery, every attempt will be made to obtain an exhaled carbon monoxide level at admission for delivery. Patient satisfaction will also be assessed at the final measurement. Each patient will be asked about number of cigarettes smoked per day for the last week at each prenatal visit. Delivery outcomes will be assessed prior to discharge.

5. Statistical Considerations

5.1 Sample Size for Primary Outcome

In order to calculate our sample size, we targeted an alpha of 0.05 and a power of 90%. Based on our clinic population, we estimated the prevalence of smoking ≥10 cigarettes/day among women with substance use disorders who smoke at delivery is 90%. We target a reduction to 50% of women smoking ≥10 cigarettes/day at delivery in the intervention group. With a 20% loss to follow up, the required sample size is 74 women (37 women per group).

Baseline Estimate of Smoking ≥10 cigarettes/day at delivery	Targeted Prevalence of Smoking ≥10 cigarettes/day at delivery	Relative Risk	Number per group	Total Sample Size with 20% Loss to Follow UP
90%	60%	0.67	49	118
	50%	0.55	31	74
	40%	0.44	21	50
80%	60%	0.75	119	286
	50%	0.63	58	140
	40%	0.5	35	84

5.2. Power for Other Outcomes

We will have ample power to detect differences in the secondary outcomes of number of cigarettes smoked at final visit, average exhaled carbon monoxide, and average percent fetal carboxyhemoglobin between groups. Infant outcomes are likely to be underpowered and are considered exploratory. Similarly, patient satisfaction with the Smokerlyzer® device is an exploratory analysis.

5.3. Analysis Plan

Standard baseline characteristics between the two groups will be collected at baseline, including baseline exhaled carbon monoxide. It is assumed that randomization will evenly distribute baseline characteristic differences between the two groups, and thus, we do not anticipate adjusting for these in the primary analysis. Secondary analyses will, though, be analyzed using regression adjustments to account for any possible confounding covariates between the two groups. The primary analysis will be done in an intent-to-treat basis.

The primary analysis will compare the total admission to delivery time in minutes between the two groups. This will be analyzed using a two-sided student's t-test.

6. Future studies

If this small trial demonstrates efficacy in smoking reduction in women with substance use disorders, we will pursue two future avenues of study. 1) Use of the expired maternal carbon monoxide and associated fetal carboxyhemoglobin to encourage smoking cessation in the general pregnancy population. 2) A larger study of women with substance use disorders to detect smaller improvements in smoking cessation and long-lasting smoking cessation post-partum.

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8. Appendix

8.1 Smoking Cessation Resources

Smoking During Pregnancy

Smoking during pregnancy is unhealthy for you and your baby. Smoke from cigarettes, pipes, and cigars contains many chemicals that can cause cancer (*carcinogens*). Cigarettes also contain a stimulant drug (*nicotine*). When you smoke, harmful substances that you breathe in enter your bloodstream and can be passed on to your baby. This can affect your baby's development.

If you are planning to become pregnant or have recently become pregnant, talk with your health care provider about quitting smoking.

How does smoking affect me?

Smoking increases your risk for many long-term (*chronic*) diseases. These diseases include cancer, lung diseases, and heart disease. Smoking during pregnancy increases your risk of:

- Losing the pregnancy (*miscarriage* or *stillbirth*).
- Giving birth too early (*premature birth*).
- Pregnancy outside of the uterus (*tubal pregnancy*).
- Having problems with the organ that provides the baby nourishment and oxygen (*placenta*), including:
  - Attachment of the placenta over the opening of the uterus (*placenta previa*).
  - Detachment of the placenta before the baby's birth (*placental abruption*).

- Having your water break before labor begins (*premature rupture of membranes*).

How does smoking affect my baby?

Before Birth

Smoking during pregnancy:

- Decreases blood flow and oxygen to your baby.
- Increases your baby’s risk of birth defects, such as heart defects.

- Increases your baby's heart rate.
- Slows your baby's growth in the uterus (*intrauterine growth retardation*).

After Birth

Babies born to women who smoked during pregnancy may:

- Have symptoms of nicotine withdrawal.
- Need to stay in the hospital for special care.
- May be too small at birth.
- Have a high risk of:
  - Serious health problems or lifelong disabilities.
  - Sudden infant death syndrome (SIDS).
  - Becoming obese.
  - Developing behavior or learning problems.

What can happen if changes are not made?

When babies are born with a birth defect or illness, they often need to stay in the hospital longer before going home. Hospital stays may also be longer if you had any complications during labor or delivery. Longer hospital stays and more treatments result in higher costs for health care.

Many health issues among babies born to mothers who smoke can have a lifelong impact. This may include the long-term need for certain medicines, therapies, or other treatments.

What are the benefits of not smoking during pregnancy?

You have a much better chance of having a healthy pregnancy and a healthy baby if you do not smoke while you are pregnant. Not smoking also means that you will have a better chance of living a long and healthy life, and your baby will have a better chance of growing into a healthy child and adult.

What actions can be taken?

Quitting smoking can be difficult. Ask your health care provider for help to stop smoking. You may also consider:

- Counseling to help you quit smoking (*smoking cessation counseling*).
- Psychotherapy.
- Acupuncture.
- Hypnosis.
- Telephone QUIT hotlines.

If these methods do not help you, talk with your health care provider about other options. **Do not** take smoking cessation medicines or nicotine supplements unless your health care provider tells you to.

Where to find more information:

Learn more about smoking during pregnancy and quitting smoking from:

- March of Dimes: www.marchofdimes.org/pregnancy/smoking-during-pregnancy.aspx
- U.S. Department of Health and Human Services: women.smokefree.gov
- American Cancer Society: www.cancer.org
- American Heart Association: www.heart.org
- National Cancer Institute: www.cancer.gov

For help to quit smoking:

- National smoking cessation telephone hotline: 1-800-QUIT NOW (784-8669)

Contact a health care provider if:

- You are struggling to quit smoking.
- You are a smoker and you become pregnant or plan to become pregnant.
- You start smoking again after giving birth.

Summary

- Tobacco smoke contains harmful substances that can affect a baby's health and development.
- Smoking increases the risk for serious problems, such as miscarriage, birth defects, or premature birth.
- If you need help to quit smoking, ask your health care provider.

This information is not intended to replace advice given to you by your health care provider. Make sure you discuss any questions you have with your health care provider.

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8.2 Consent Form

CONSENT FORM TO BE PART OF A RESEARCH STUDY

Title of Research: Smoking Reduction In Gravid Women with Substance Use Disorders (SIGS): A Randomized Controlled Trial

UAB IRB Protocol #: IRB-300004487

Principal Investigator: Rubymel Knupp, M.D.

Sponsor: UAB Department of OBGYN

For Children (persons under 18 years of age) participating in this study, the term "You" addresses both the participant ("you") and the parent or legally authorized representative ("your child").

General Information	You are being asked to take part in a research study. This research study is voluntary, meaning you do not have to take part in it. The procedures, risks, and benefits are fully described further in the consent form.
Purpose	The purpose of this study is determine whether patient knowledge of exhaled carbon monoxide levels and the corresponding fetal carboxyhemoglobin levels will decrease the number of cigarettes smoked by women at the end of the pregnancy.
Duration & Visits	You will be in this study from the time of enrollment until up to 5 days after you deliver your baby. Each study participation during your prenatal visits and/or delivery will take 5 minutes.
Overview of Procedures	This is a study that compared two groups to each other. Each group will have different activities and you will be randomized to one of these groups by chance (flip of a coin). This study may include: • Screening interview to determine interest in smoking cessation • An enrollment interview and record the carbon monoxide levels in your breath using the Smokerlyzer device • Resources to quit smoking • Counseling on carbon monoxide levels and its effects • Medical record review for information regarding your pregnancy and your infant • Patient satisfaction survey

	This study will enroll 74 pregnant women who smoke and their infants at UAB.
Risks	There are minimal risks to participating in this study. The risks with this study are those associated with discomfort from using the Smokerlyzer, being assigned to a group that may be less effective than the other and loss of confidentiality.
Benefits	You may or may not benefit directly from taking part in this study.
Alternatives	An alternative to this study is to not participate.

Purpose of the Research Study

We are asking you to take part in a research study. The purpose of this research study is to test whether the knowledge of expired carbon monoxide levels and fetal carboxyhemoglobin levels help women quit smoking in pregnancy. Smokerlyzer® is a small, handheld device that measures the amount of carbon monoxide in your breath. It does not measure any other substances or require any invasive procedures. This device is safe to use for pregnant women. Carbon monoxide is a poisonous gas found in cigarette smoke. You are being invited to participate because you have been identified as being interested in quitting smoking or reducing your smoking. There will be 74 participants enrolled at UAB.

Study Participation & Procedures

If you agree to join the study, and are interested in smoking cessation, you will be randomized (like the flip of a coin) to one of two groups.

In the intervention group, we will measure your expired carbon monoxide levels and inform you of how it affects the oxygen level of your baby. This procedure will be repeated at every prenatal visit. We will also counsel you about what these levels mean in terms of how it affects your pregnancy overall. You will also be asked how many cigarettes you are smoking at each visit. Resources to assist you in quitting smoking will be provided.

In the standard care group, we will measure your expired carbon monoxide level at your first study visit and repeated at every prenatal visit. You will be provided the same resources that can help assist you in quitting smoking as the other group but will not be counselled about your levels. You will also be asked about smoking at each visit.

At your final visit, we will ask you questions about how satisfied you are with the information received about quitting smoking, and about your experiences in trying to quit smoking.

We will review and collect from your medical records information regarding your pregnancy, smoking habits, and we will also collect information about your baby's birth and health.

Products to help you quit smoking are not provided as part of this study (these products are also not typically provided during routine pregnancy care).

Your de-identified private information (private information with all identifiers removed) may be used for future research studies or distributed to another researcher for future research studies without additional informed consent. **This is only when there are no identifiers associated with the data.**

We would like to contact you in the future for research studies related to women's health for which you may be eligible.

Initial your choice below:

___ I agree to be contacted for future research related to women's health.

___ I do not agree to be contacted for future research related to women's health.

Risks and Discomforts

The Smokerlyzer is a non-invasive device used only to measure the level of carbon monoxide in your breath. There may be discomfort with using the Smokerlyzer such as feeling out of breath or having a dry mouth from using the mouth piece.

You will be assigned to a group by chance, which may prove to be less effective or to have more side effects than the other study group or alternatives. If you are assigned to the standard care group, you may be at risk for pregnancy and/or neonatal complications associated with smoking.

Benefits

You may or may not benefit directly from taking part in this study. However, this study may help us better understand how smoking affects pregnant women and their unborn babies as well as how to help other women quit smoking during pregnancy. You will be assigned to a group by chance, which may prove to have more or less benefits than the other study group.

Alternatives

The alternative is to not participate in this study. If you choose not to participate, you will receive routine prenatal care, which includes referral to resources to quit smoking.

Confidentiality and Authorization to Use and Disclose Information for Research Purposes

Federal regulations give you certain rights related to your health information. These include the right to know who will be able to get the information and why they may be able to get it. The study doctor must get your authorization (permission) to use or give out any health information that might identify you.

What protected health information may be used and/or given to others?

All medical information, including but not limited to information and/or records of any diagnosis or treatment of disease or condition, which may include sexually transmitted diseases (e.g., HIV, etc.) or communicable diseases, drug/alcohol dependency, etc.; all personal identifiers, including but not limited to your name, social security number, medical record number, date of birth, dates of service, etc.; any past, present, and future history, examinations, laboratory results, imaging studies and reports and treatments of any kind, including but not limited to drug/alcohol treatment, psychiatric/psychological treatment; financial/billing information, including but not limited to copies of your medical bills; any other information related to or collected for use in the research study, regardless of whether the information was collected for research or non-research (e.g., treatment) purposes; records about any study drug you received or about study devices used; and consent forms from past studies that might be in your medical record.

Your consent form will be placed in your medical record at UAB Health System. This may include either a paper medical record or electronic medical record (EMR). An EMR is an electronic version of a paper medical record of your care within this health system. Your EMR may indicate that you are on a clinical trial and provide the name and contact information for the principal investigator.

If you are receiving care or have received care within this health system (outpatient or inpatient), results of research tests or procedures (i.e. laboratory tests, imaging studies and clinical procedures) may be placed in your existing medical record.

If you have never received care within this health system (outpatient or inpatient), a medical record will be created for you to maintain results of research tests or procedures.

Results of research tests or procedures may be placed in your medical record. All information within your medical record can be viewed by individuals authorized to access the record.

Who may use and give out information about you?

Information about your health may be used and given to others by the study doctor and staff. They might see the research information during and after the study.

Who might get this information?

All Individuals/entities listed in the informed consent document(s), including but not limited to, the physicians, nurses and staff and others performing services related to the research (whether at UAB or elsewhere). Your information may also be given to the sponsor of this research. "Sponsor" includes any persons or companies that are working for or with the sponsor, or are owned by the sponsor, or are providing support to the sponsor (e.g., contract research organization).

Information about you and your health which might identify you may be given to:

- the Office for Human Research Protections (OHRP)
- the U.S. Food and Drug Administration (FDA)
- Department of Health and Human Services (DHHS) agencies
- Governmental agencies in other countries
- Governmental agencies to whom certain diseases (reportable diseases) must be reported
- the University of Alabama at Birmingham - the physicians, nurses and staff working on the research study (whether at UAB or elsewhere); other operating units of UAB, UAB Hospital, UAB Highlands Hospital, University of Alabama Health Services Foundation, Children's of Alabama, Eye Foundation Hospital, and the Jefferson County Department of Health, as necessary for their operations; the UAB IRB and its staff
- the billing offices of UAB and UAB Health Systems affiliates and/or Children's of Alabama and its billing agents

Why will this information be used and/or given to others?

Information about you and your health that might identify you may be given to others to carry out the research study. The sponsor will analyze and evaluate the results of the study. In addition, people from the sponsor and its consultants will be visiting the research site. They will follow how the study is done, and they will be reviewing your information for this purpose.

What if I decide not to give permission to use and give out my health information?

By signing this consent form, you are giving permission to use and give out the health information listed above for the purposes described above. If you refuse to give permission, you will not be able to be in this research.

May I review or copy the information obtained from me or created about me?

You have the right to review and copy your health information. However, if you decide to be in this study and sign this permission form, you will not be allowed to look at or copy your information until after the research is completed.

May I withdraw or revoke (cancel) my permission?

Yes, but this permission will not stop automatically. The use of your personal health information will continue until you cancel your permission.

You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the study doctor. If you withdraw your permission, you will not be able to continue being in this study.

When you withdraw your permission, no new health information which might identify you will be gathered after that date. Information that has already been gathered may still be used and given to others. This would be done if it were necessary for the research to be reliable.

Is my health information protected after it has been given to others?

If you give permission to give your identifiable health information to a person or business, the information may no longer be protected. There is a risk that your information will be released to others. Including others outside of UAB, without your permission.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

Voluntary Participation and Withdrawal

Whether or not you take part in this study is your choice. There will be no penalty if you decide not to be in the study. If you decide not to be in the study, you will not lose any benefits you are otherwise owed.

You are free to withdraw from this research study at any time. Your choice to leave the study will not affect your relationship with this institution. Contact the study doctor if you want to withdraw from the study.

If you are a UAB student or employee, taking part in this research is not a part of your UAB class work or duties. You can refuse to enroll or withdraw after enrolling at any time before the study is over, with no effect on your class standing, grades, or job at UAB. You will not be offered or receive any special consideration if you take part in this research.

Cost of Participation

There will be no cost to you for taking part in this study. The cost of your standard medical care will be billed to you and/or your insurance company in the usual manner.

Payment for Participation

You will receive $10 at the enrollment visit. You will also receive another $20 after your last carbon monoxide level is measured at greater than 36 weeks pregnant or at delivery, whichever comes first. Ask the study staff about the method of payment that will be used for this study (e.g., check, cash, gift card, direct deposit).

Payment for Research-Related Injuries

UAB has not provided for any payment if you are harmed as a result of taking part in this study. If such harm occurs, treatment will be provided. However, this treatment will not be provided free of charge.

New Findings

You will be told by the study doctor or the study staff if new information becomes available that might affect your choice to stay in the study.

Questions

If you have any questions, concerns, or complaints about the research or a research-related injury including available treatments, please contact the study doctor. You may contact Dr. Rubymel Knupp at (205)-934-2565 or after hours by paging her at (205)-934-4966.

If you have questions about your rights as a research participant, or concerns or complaints about the research, you may contact the UAB Office of the IRB (OIRB) at (205) 934-3789 or toll free at 1-855-860-3789. Regular hours for the OIRB are 8:00 a.m. to 5:00 p.m. CT, Monday through Friday.

Legal Rights

You are not waiving any of your legal rights by signing this consent form.

Signatures

Your signature below indicates that you have read (or been read) the information provided above and that you agree to participate in this study. You will receive a copy of this signed consent form.

_____

Signature of Participant Date

_____

Signature of Person Obtaining Consent Date

Waiver of Assent

The assent of _____ (name of child/minor) was waived because of age.

8.3 Study Flyer

PREGNANT & SMOKING?
ENROLL IN THE SIGS TRIAL

(Smoking Reduction In Gravid Substance-Users)

Eligible:

- 16-years-old or greater
- Singleton pregnancy
- Less than 24 weeks gestation
- Interested in quitting smoking
- OBCC patients

Ineligible:

- Multi-fetal gestation
- >24 weeks gestation
- Not interested in smoking cessation
- Fetal anomalies or genetic abnormalities
- Fetal growth restriction

Questions? Page Rubymel Knupp @ 205-934-4966 or talk to your provider about the study

8.4 Smokerlyzer chart interpretation

Smokerlyzer®

bedfont est. 1976

Breath carbon monoxide monitors
Helping people to stop smoking

Adult COppm	Adult %COHb [1]	Maternity COppm	Maternity %FCOHb [2]
30	5.43	20+	5.66
29	5.27	19	5.38
28	5.11	18	5.09
27	4.95	17	4.81
26	4.79	16	4.53
25	4.63	15	4.25
24	4.47	14	3.96
23	4.31	13	3.68
22	4.15	12	3.40
21	3.99	11	3.11
20	3.83	10	2.83
19	3.67	09	2.55
18	3.51	08	2.26
17	3.35	07	1.98
16	3.19	06	1.70
15	3.03	05	1.42
14	2.87	04	1.13
13	2.71	03	0.85
12	2.55	02	0.57
11	2.39	01	0.28
10	2.23		
09	2.07		
08	1.91		
07	1.75		
06	1.59		
05	1.43		
04	1.27		
03	1.11		
02	0.95		
01	0.79		

Having a reading in this zone indicates you may well be a **regular smoker** with higher levels of CO in your blood. Do not despair! Help is at hand and your stop smoking advisor can help you to give up smoking and lower your reading into the target "Green zone".

Having a reading in this zone would indicate a **light smoker** or a **non-smoker** breathing in poor air quality or passive smoke. Your stop smoking advisor will be able to advise on the best course of action to lower this reading to the target "Green zone".

This is where you really need to be!

It means you have less than 2% carbon monoxide (CO) in your blood. Most people have a small amount of CO in their breath, this is due to the air quality around you.

References:

1. COppm- %COHb calculation taken from: Jarvis M et al (1986) "low cost Carbon Monoxide monitors in smoking assessment." Thorax 41 pp 886-887.

2. COppm- %FCOHb calculation taken from: Gomez C. et al (2005) "Expired air carbon monoxide concentration in mothers and their spouses above 5ppm is associated with decreased fetal growth." Preventive Medicine 40 pp 10-15

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Issue 16 - May Part No: LA0291

8.5 Patient Questionnaire

Smoking Reduction In Gravid Women with Substance Use Disorders (SIGS): A Randomized Controlled Trial

Positive and Negative Affect Schedule (PANAS-SF)

Indicate the extent you have felt this way over the past week		Very slightly or not at all	A little	Moderately	Quite a bit	Extremely
PANAS 1	Interested	◯ 1	◯ 2	◯ 3	◯ 4	◯ 5
PANAS 2	Distressed	◯ 1	◯ 2	◯ 3	◯ 4	◯ 5
PANAS 3	Excited	◯ 1	◯ 2	◯ 3	◯ 4	◯ 5
PANAS 4	Upset	◯ 1	◯ 2	◯ 3	◯ 4	◯ 5
PANAS 5	Strong	◯ 1	◯ 2	◯ 3	◯ 4	◯ 5
PANAS 6	Guilty	◯ 1	◯ 2	◯ 3	◯ 4	◯ 5
PANAS 7	Scared	◯ 1	◯ 2	◯ 3	◯ 4	◯ 5
PANAS 8	Hostile	◯ 1	◯ 2	◯ 3	◯ 4	◯ 5
PANAS 9	Enthusiastic	◯ 1	◯ 2	◯ 3	◯ 4	◯ 5
PANAS 10	Proud	◯ 1	◯ 2	◯ 3	◯ 4	◯ 5
PANAS 11	Irritable	◯ 1	◯ 2	◯ 3	◯ 4	◯ 5
PANAS 12	Alert	◯ 1	◯ 2	◯ 3	◯ 4	◯ 5
PANAS 13	Ashamed	◯ 1	◯ 2	◯ 3	◯ 4	◯ 5
PANAS 14	Inspired	◯ 1	◯ 2	◯ 3	◯ 4	◯ 5
PANAS 15	Nervous	◯ 1	◯ 2	◯ 3	◯ 4	◯ 5
PANAS 16	Determined	◯ 1	◯ 2	◯ 3	◯ 4	◯ 5
PANAS 17	Attentive	◯ 1	◯ 2	◯ 3	◯ 4	◯ 5

PANAS 18	Jittery	◯ 1	◯ 2	◯ 3	◯ 4	◯ 5
PANAS 19	Active	◯ 1	◯ 2	◯ 3	◯ 4	◯ 5
PANAS 20	Afraid	◯ 1	◯ 2	◯ 3	◯ 4	◯ 5

8.6 Patient Survey

Smoking Reduction In Gravid Women with Substance Use Disorders (SIGS): A Randomized Controlled Trial Patient Survey*		
Name: _____	MRN: _____	Study ID #:_____

The final part of your participation in the research study is to complete this short survey. This should take a total of 15 minutes of your time.

Please circle the appropriate number for each question:

1. Overall, how satisfied are you with the support you have received to stop smoking?

Very Unsatisfied	Unsatisfied	Unsure	Satisfied	Very Satisfied
1	2	3	4	5

2. Would you recommend using the carbon monoxide reading device (Smokerlyzer) to other smokers who a want to stop smoking?

No	Unsure	Yes
1	2	3

3. In the event that you started smoking again would you use the Smokerlyzer device to help with stopping smoking?

No	Unsure	Yes
1	2	3

4. If you were to become pregnant again and were still smoking, would you participate in the study again?

No	Unsure	Yes
1	2	3

5. Have you smoked since your last prenatal appointment?

No	Unsure	Yes
1	2	3

6. How satisfied are you with how the supportive staff has been?

Very Unsatisfied	Unsatisfied	Unsure	Satisfied	Very Satisfied
1	2	3	4	5

7. How helpful has the information and advice that staff have given to you during your appointment been?

Very Unsatisfied	Unsatisfied	Unsure	Satisfied	Very Satisfied
1	2	3	4	5

8. How helpful has the written information that staff have given to you been?

No	Unsure	Yes
1	2	3

9. Do you find having your carbon monoxide (CO) reading helpful?

No	Unsure	Yes
1	2	3

If there are any changes that you would like to see to the SIGS Trial, or if there was anything they did particularly well, then please write them here: