Parents' or Guardians' Permission for Your Child to Be in a Research Study

Agreement of a Child to Be in a Research Study

Age 15 to <18

In this form "you" means the child in the study *and* the parent or guardian.

- ✓ If you are the parent or guardian, you are being asked to give permission for your child to be in this study.
- ✓ If you are the child, you are being asked if you agree to be in this study.

In this form "we" means the researchers and staff involved in running this study at the University of Virginia.

In this form "you" means the person (your child) who is being asked to be in this study. As the parent or guardian, you are being asked to give permission for your child to be in this study.

Participant's Name_____**Medical Record #** _____

Principal Investigator: Christine Burt Solorzano, MD
Internal Medicine, School of Medicine
Box 800391
Charlottesville, VA 22908 Telephone: (434) 924-9084

Sponsor: National Institutes of Health (NIH)

What is the purpose of this form?

This form will help you decide if you want to be in the research study. You need to be informed about the study, before you can decide if you want to be in it. You do not have to be in the study if you do not want to. You should have all your questions answered before you give your permission or consent to be in the study.

Please read this form carefully. If you want to be in the study, you will need to sign this form. You will get a copy of this signed form.

Who is funding this study?

This study is being funded by the National Institutes of Health.

Why is this research being done?

Introduction

The purpose of this study is to understand whether insulin changes the effects of high male hormone levels in adolescent girls.

Hormones are substances that are made in the body and sent directly out into the bloodstream to increase or decrease the function of certain organs, glands, or other hormones. Female hormones, such as estrogen and progesterone, help a girl's body develop into a woman's body. Male hormones, such as testosterone, help a boy's body develop into a man's body. All girls and women make low levels of male hormones. Some girls and women produce higher levels of male hormones for unclear reasons.

Many, but not all, girls with high levels of the male hormone testosterone go on to develop polycystic ovary syndrome (PCOS) as adults. Women with PCOS often have irregular menstrual periods, excess facial and body hair, and weight gain. PCOS is also a leading cause of difficulty becoming pregnant. We do not understand why some girls with high hormones develop PCOS and others do not.

In a previous study by our group, some girls with high levels of male hormones had abnormalities in the secretion of another hormone (called LH) that are often seen in women with PCOS. However, another group had normal LH secretion. The girls with the abnormal LH secretion had higher levels of another hormone, called insulin, than the girls with normal LH secretion. Insulin is a hormone that helps control blood sugars and women with PCOS often make high levels of insulin in order to keep their blood sugars normal.

In this study we will use a drug called Metformin (Glucophage). Metformin (Glucophage) is approved by the U.S. Food and Drug administration (FDA) for the treatment of type II diabetes in adults and adolescents, but not for the treatment of the insulin resistance associated with PCOS. However, Metformin is commonly prescribed "off-label" as a treatment for PCOS in girls and women. "Off-label" means that Metformin is prescribed for PCOS even though the drug only has FDA-approval for treatment of diabetes. Metformin (Glucophage) lowers insulin levels and lowers high, but not normal, blood sugar levels. So far, Metformin (Glucophage) has been given to thousands of girls who have elevated male hormone levels, and is thought to be safe and effective in these patients. The use of Metformin is considered to be experimental in this study.

In this study we will also use the drugs progesterone and estradiol (estrace). Estrogen and progesterone are natural hormones. The amount of these hormones used in this study are similar to the amounts that are produced by girls' bodies as they develop. The progesterone syrup that we use is made in the UVa Investigational pharmacy. The progesterone used to make the syrup is FDA approved, but there are no specific data regarding human toxicity and safety of the UVA Health System progesterone syrup. Over 30 girls have taken the progesterone syrup as made by the UVa pharmacy and there have not been any unexpected side effects. Although estradiol and progesterone are not typically given to girls as Estrace and progesterone syrup as is done in this study, they are frequently given in combination as birth control pills in this age group. Birth control pills have been prescribed to numerous adolescent girls as part of the treatment for elevated male

hormone levels and PCOS and are felt to be safe and effective in this population. However, the use of estradiol and progesterone are considered to be experimental in this study.

You are being asked to be in this study, because you are an adolescent girl with elevated male hormone levels.

Up to 60 people will be in this study at UVA.

How long will this study take?

Your participation in this study will require 6 outpatient study visits and 4 overnight admissions over approximately a 4 month period of time. There will be one screening visit that will last no more than one hour. The other outpatient visits should last no longer than 30 minutes. The overnight admissions will last 14-16 hours and take place at the University of Virginia Clinical Research Unit (CRU), alternate UVA hospital unit, or off-site hotel (see below).

What will happen if you are in the study?

All of the procedures performed as part of the study are being done purely to answer research questions.

SCREENING (will take approximately 30-60 minutes to complete):
If you agree to participate, you will sign this consent form before any study related procedures take place. Before you can start the study, there will be a screening period. You will have tests and procedures during this time to make sure you are eligible and it is safe for you to participate. These include the following:

- Review of your medical history
- Physical exam and vital signs (blood pressure, heart rate, etc.)
- Standard blood tests (less than 2 tablespoons of blood) to check: salts, sugars, blood counts, liver function, kidney function, pregnancy test, and a variety of hormones. **We will ask that you not have anything to eat or drink except for water for 8 hours before having this blood work drawn.**
- There are a number of restricted medications which cannot be used during the study. The study personnel will discuss those restriction medications with you.

If these tests show you are eligible, you will be given a 1 month supply of iron to take for up to 30 days. You will receive instructions on the dosage of iron that you will take. How much iron you take will be determined by your weight. Your first study admission can occur anytime within this 30 day period or anytime after this period. You will have the option to pick up this supply of iron from the Clinical Research Unit or have it mailed to your residence. If you are unable to begin the study within 90 days following screening, you will need to come back to have the screening blood tests repeated before taking part in the study.

STUDY Tests and Procedures*:*

If the overnight admission is scheduled to occur greater than one month after the screening visit you will be asked to return for an outpatient blood draw to make sure your red blood cell count is high enough to continue in the study.

In Patient Overnight Admission #1 (Day 0):

- Admission #1 will take place on day 7-11 of your cycle if you are having regular periods and greater than 7 days since your last cycle if your periods are infrequent, as long as your progesterone level is low within 3 days of the scheduled overnight admission. Thus, for girls cycling infrequently, you will be asked to come to the CRU or other clinical unit for a blood draw within 3 days of your scheduled overnight admission to check your progesterone. If your progesterone is found to be too high, then your admission will be cancelled.
- We will ask that you eat at least 150 gm of carbohydrate a day for the 3 days prior to the admission and will give you instructions on how to do this at your screening visit.
- You will be admitted to the CRU, alternate UVA hospital unit, or off-site hotel at 5:00 pm on that day. If the overnight visit occurs at a hotel, your parent or guardian may stay with you but it is not required,. If your parents/guardian are not available to stay with you, two CRU staff members will be at the hotel with you. Whether or not a parent or legal guardian is required to stay during the overnight admission will be discussed when your admission is scheduled.
- During your overnight admission, you will wear an actigraph. It looks like a watch and it is worn on your wrist. The actigraph will help us know when you are awake and when you are asleep.
- An intravenous (IV) line will be placed in your arm. An IV is a small flexible tube that is inserted into a vein using a needle. A medicine, called EMLA cream, may be applied to the skin prior to the IV insertion to try to make it hurt as little as possible. Once the tube is in place, the needle is removed and replaced with a cap that allows blood to be drawn or medication or fluid to be given. This means you will only have the needle stick you in the arm once.
- A urine pregnancy test will be done to make sure you are not pregnant. If you are pregnant you will not be able to continue in the study.
- Starting at 7:00 PM, blood samples will be taken every 10 minutes. With the exception of one blood draw that will be 1 teaspoon, each of the blood draws will be no more than 1/2 of a teaspoon
- You will be given dinner at standard CRU mealtimes (approximately 6:00 pm). You will not be able to eat or drink anything except water from 11:00 pm until 9:00 AM.
- A formal "lights out" will take place at 11:00 pm. At this point the lights and the television will be turned off to allow you to sleep.
- At 6 AM, the nurses will stop taking blood every 10 minutes.

- At 7 AM, the nurses will give you a sugary drink. They will take blood samples (1/2 teaspoon) before you have the drink and 10, 20, 30, 60, 90, and 120 minutes after you drink it.
- After the blood draws are complete at 9:00 AM, you will be served breakfast.
- The nurse will take out the IV and you will be able to go home.
- Before you go home from the admission, you will be given a supply of estrogen (estradiol) pills and progesterone syrup and instructions on when to take them.
- A total of 8 tablespoons of blood will be drawn during this admission.

Start study medication: estrogen, progesterone and iron supplements (Day 1):

- The estrogen pills should be taken by mouth once a day for seven days.
- The progesterone syrup should be taken by mouth three times a day at 7:00 am, 3:00 pm, and 11:00 pm for seven days. If your school schedule makes it difficult to take the syrup at 3:00 pm, please discuss this with the study doctor and we will adjust the dosing schedule. Usually, this will mean that instead of taking the syrup at 3:00 pm, you will take it immediately upon arriving home from school.
- The progesterone needs to be refrigerated and should be shaken well before you take it.
- When you take the progesterone syrup, you should also eat a small snack such as peanut butter crackers and juice or a half of a sandwich and 2% milk. It is important that the snack is eaten as it helps the medicine get absorbed.
- You will also be given iron supplements to help your body rebuild your red blood cells. You will take either one or two pills a day by mouth, depending on how much you weigh. You will receive instructions on how much iron you should take.

Outpatient Blood Draws (Day 3 and 5):

- Three days and then five days after the admission, you will return to the CRU or alternate UVA clinic for an outpatient blood draw at 5:00 pm. This appointment should take no longer than 30 minutes.
- A small amount will be drawn (less than 1/3 teaspoon) to make sure the medication is being absorbed into the blood stream.

In Patient Overnight Admission #2 (Day 7):

- After seven days of taking the estrogen and progesterone, you will return for the second overnight inpatient admission. You will bring your estrogen and progesterone bottles and any unused medicine to the admission and give them to the nurses.
- The second admission will be identical to the first inpatient admission, except that it will end at 7:00 AM. You will not drink the sugary drink and have the additional blood draws during this admission.
- A total of 7 tablespoons of blood will be drawn during this admission.
- At the end of the second admission, you will:
  - stop taking the estradiol and progesterone
  - keep taking the iron supplements

- start taking metformin by mouth. You will start by taking 1 pill (500 mg) at night.

Increase Metformin Dose (Day 14):

- You will increase the metformin dose to 1 pill in the morning and 1 pill at night. We will call you to see how you are feeling and to remind you to increase the dose.

Increase Metformin Dose (Day 21):

- You will increase the metformin dose to 1 pill in the morning and 2 pills at night. We will call you to see how you are feeling and to remind you to increase the dose.

Increase Metformin Dose (Day 28):

- You will increase the metformin dose to 2 pills in the morning and 2 pills at night. We will call you to see how you are feeling and to remind you to increase the dose.

Outpatient blood draw (Between Days 42 and 49):

- During this week, on a day that is convenient for you, you will come to the CRU or clinic for blood work after not eating or drinking anything except water for 8 hours. This appointment should take no longer than 30 minutes.
- A small amount of blood (less than 2 teaspoons) will be drawn to check your salts, sugar, kidney function, liver function, and several hormones.

In Patient Overnight Admission #3 (Day 84):

- Admission # 3 is timed to your cycles, so it may not occur exactly on day 84. After day 77, we will schedule the admission for the first appropriate time in your cycle, which will be will be day 7-11 of your cycle if you are having regular periods or greater than 7 days since your last cycle if your periods are infrequent, as long as your progesterone level is low within 3 days of the scheduled overnight admission. Thus, for girls cycling infrequently, you will be asked to come to the CRU or other clinical unit for a blood draw within 3 days of your scheduled overnight admission to check your progesterone. If your progesterone is found to be too high, then your admission will be cancelled.
- We will ask that you eat at least 150 gm of carbohydrate a day for the 3 days prior to the admission and will give you instructions in how to do this.
- Admission #3 will be exactly the same as Admission #1.
- A total of 8 tablespoons of blood will be drawn during this admission.

Begin Estradiol and Progesterone (Day 85):

- Before you leave, you will be given a supply of estrogen pills (estradiol) and progesterone syrup. These are the same medications and the same doses that you took on days 1-7.
- The estrogen pills should be taken by mouth once a day for seven days.

- The progesterone syrup should be taken by mouth three times a day at 7:00 am, 3:00 pm, and 11:00 pm for seven days. If your school schedule makes it difficult to take the syrup at 3:00 pm, please discuss this with the study doctor and we will adjust the dosing schedule. Usually, this will mean that instead of taking the syrup at 3:00 pm, you will take it immediately upon arriving home from school.
- The progesterone needs to be refrigerated and should be shaken well before you take it.
- When you take the progesterone syrup, you should also eat a small snack such as peanut butter crackers and juice or a half of a sandwich and 2% milk. It is important that the snack is eaten as it helps the medicine get absorbed.

Outpatient Blood Draws (Day 87 and 89):

- Three days and then five days after the Admission #3, you will return to the CRU or clinic for an outpatient blood draw at 5:00 pm. This appointment should take no longer than 30 minutes.
- A small amount will be drawn (less than 1/3 teaspoon) to make sure the medication is being absorbed into the blood stream.

In Patient Overnight Admission #4 (Day 91):

- Admission #4 will be exactly the same as admission #2. You will bring your estrogen, progesterone, and metformin bottles and any unused medicine to the admission and give them to the nurses.
- A total of 7 tablespoons of blood will be drawn during this admission.
- After the admission is complete, you should stop taking the estradiol, progesterone, and metformin. You should continue to take the iron supplements for 1 more month.

FOLLOW UP:

If possible, we would like to follow-up with you 3, 6, and 12 months after the study. This may be done by outpatient visit. If you agree, we would ask you to complete questionnaires that will ask you about general health, progress through puberty, and menstrual periods. We would also like to take a small amount of blood (less than 1 tablespoon) at this time to measure hormone levels. These visits are optional, and each visit would take about 30-45 minutes.

_____ Yes, I agree to participate in the optional follow up visits.

_____ NO, I do not agree to participate in the optional follow up visits.

Study Schedule

Day of Study	Type of Visit	Estradiol	Progesterone	Metformin
Within 3 months of Day 0	Screening visit			
Day 0	In patient Admission #1 Overnight with frequent blood draws Test with sugary drink			
Day 1		x	xx	
Day 2		x	x	
Day 3	Blood draw	x	x	
Day 4		x	x	
Day 5	Blood draw	x	x	
Day 6		x	x	
Day 7	In patient Admission #2 Overnight with frequent blood draws	x	x	
Days 8-41				x
Day 42	Blood draw			x
Days 43-83				x
Day 84	In patient Admission #3 Overnight with frequent blood draws Test with sugary drink			x
Day 85		x	x	x
Day 86		x	x	x
Day 87	Blood draw	x	x	x
Day 88		x	x	x
Day 89	Blood draw	x	x	x
Day 90		x	x	x
Day 91	In patient Admission #4 Overnight with frequent blood draws	x	x	x

Blood Testing

The blood we take will be tested to measure salts, sugar, blood counts, kidney function, liver function, pregnancy tests, and a variety of hormones. A total of 31 tablespoons of blood will be drawn during the study.

After the study is complete, any left over blood/tissue will be thrown away. It will not be stored for any future testing.

If you want to know about the results before the study is done:

During the study your study leader will let you know of any test results that may be important to your health. In addition, as the research moves forward, your study leader will keep you informed of any new findings that may be important for your health or may help you decide if you want to continue in the study. The final results of the research will not be known until all the information from everyone is combined and reviewed. At that time you can ask for more information about the study results.

What are the risks of being in this study?

Likely

- Metformin can cause nausea, diarrhea, bloating, and weakness/fatigue. These symptoms are usually mild and go away if you continue to take the medication. These side effects are less likely to be a problem if you start with a low dose of metformin and gradually increase it, which is what is being done in this study.
- It is expected that you may have some menstrual bleeding 1-5 days after stopping the estrogen and progesterone.
- Iron supplements can cause dark or black bowel movements.

Less Likely

- Estradiol and progesterone can cause nausea, fluid retention/swelling, breast tenderness, and moodiness/irritability.
- The estradiol and progesterone may cause a temporary change in menstrual cycles. If you are already having periods, the timing of your cycles may be somewhat different for the next few cycles. Even if you have not yet started having periods, after you stop taking the estrogen and progesterone, you may have some menstrual bleeding if your own body was ready to start a period within a few months. If you do have a period, you may continue to have periods.
- Iron supplements can cause nausea and constipation.
- Frequent blood draws may result in mildly low red blood cell counts (mild anemia). Mildly low red blood cell counts usually do not cause symptoms in healthy girls, and the body is able to rapidly build red blood cells to bring the counts back to normal within 1-2 months.

Rare but serious

- In rare cases, Metformin can cause lactic acidosis. This is a dangerous build-up of acid in the blood. It is very rare, especially if people have normal kidney, liver, and heart function.

- Frequent blood draws could lead to significantly low red blood cell counts (significant anemia) if precautions were not taken to avoid this. Significantly low red blood cell counts can cause fatigue, lightheadedness, and shortness of breath, particularly with exercise. In order to prevent low red blood cell counts, we will give you iron supplements to make sure that your body has the necessary building blocks to make new red blood cells. We will check the red blood cell levels during the screening and before each overnight admission. If the level is too low, we will not continue the study. We carefully limit the amount of blood drawn to an amount that is safe for someone of your size.
- Long-term (over months to years) use of estrogen has been associated with the formation of blood clots in the deep veins of the body. This risk is similar to the risk of taking birth control pills.
- Long-term (5 years) use estrogen and progesterone in postmenopausal women is associated with a slightly increased risk of heart disease, stroke, and breast cancer. However, there is no evidence that the use of estrogen and progesterone as given in this study would increase these risks in young girls.
- The risk of heart disease, stroke, and breast cancer related to the hormones given in this study is extremely small. The risks are similar to those of taking birth control pills.

Risks of Sharing the Drug

Do not share the study drug with anyone. It is prescribed only for you and could hurt someone else. Keep it out of reach of children and people not able to read or understand the label.

Risks of having your blood drawn:

Having blood drawn may cause:

- ✓ pain (common),
- ✓ a bruise (sometimes),
- ✓ fainting or passing out (not very often), and
- ✓ infection (rare).

If the people doing the study are exposed to your blood or body fluids in a way that could give them a disease, your blood may be tested. The tests might check for:

- ✓ hepatitis,
- ✓ HIV (Human Immunodeficiency Virus), or
- ✓ other infections.

You and the person exposed would be told the test results. However, your name would be kept private. If your test is positive for hepatitis or HIV, we will tell you how to find counseling. You may want help in understanding what the results mean for you.

Risks of taking blood from an IV catheter:
Sometimes the catheter stops working. In order to get the blood we need, we may have to stick you with another needle.

Risk of Heparin Lock Flush:
Heparin works by preventing blood clots from forming in IV catheters when they are not in use. Allergic reactions and side effects are rare. You should not use heparin lock flushes if you are allergic to heparin or pork products. Symptoms of allergic reaction may include, rash, itching or swelling at the IV catheter site severe dizziness or trouble breathing. Side effects though very unlikely may include, unusual bleeding or bruising and mild pain at the I.V. site.

Risk of Saline Lock Flush:
Saline works by preventing blood clots from forming in IV catheters when they are not in use. Saline is a salt solution. There are no known risks to saline lock flush other than mild pain at the injection site.

Risks of EMLA numbing cream:
Common Risks are:

- Temporary redness or paleness of the skin
- Mild itching, burning, or swelling
- Change in skin temperature, which may cause mild discomfort

Rare Risks are:

- Skin discoloration
- Severe allergic reaction
- EMLA overdose (lightheadedness, nervousness, confusion, dizziness, drowsiness, blurred or double vision, vomiting, sensations of heat, cold or numbness, twitching, tremors, convulsions, unconsciousness, respiratory depression, low blood pressure, cardiac arrest).

A caution about giving too much blood:
Because of the amount of blood being taken, you should not give blood for other reasons for 8 weeks. For example, avoid giving blood at a blood bank or in another research study.

Risks of Stopping Hormonal Birth Control:

You may be taking hormonal birth control (pills, patch or injection) and may not want your parents to know. There is a possible risk this information could be shared with parents inadvertently.

If you are sexually active and you would otherwise be taking hormonal birth control, you may be at greater risk for becoming pregnant because you are not allowed to take hormonal birth control medication while you are in this study.

Risks for women:

If you are pregnant, we want you to tell us and we will not include you in the study, because to do so might be harmful to the unborn baby. We also want your child to avoid getting pregnant during this study and expect your child to abstain from sexual activity or use an effective method of birth control. Examples of non-hormonal birth control that can be used in this study include condoms and a diaphragm. If you have questions about birth control, please ask the study leader.

If your child should become pregnant in spite of taking precautions, please immediately contact the investigator whose phone number is listed on this form and he/she will discuss with you and your child the choices which are available for your child's consideration.

Also, your child should be sure you do not get pregnant for 3 months after your participation in the study ends.

Other unexpected risks:

- Subjects should significantly limit their intake of alcohol while taking metformin.
- You may have side effects that we do not expect or know to watch for now. Call the study leader if you have any symptoms or problems.

Could you be helped by being in this study?

We cannot promise that you will be helped by being in this study.You may benefit from being in this study. Metformin is a treatment for excess male hormone, so it is possible that you may benefit from being in this study. Possible benefits include: improvement in acne, excess hair growth, and weight loss. In addition, information researchers get from this study may help others in the future.

What are your other choices if you do not join this study?

You do not have to be in this study to be treated for your illness or condition. You can get the usual treatment even if you choose not to be in this study. The usual treatment for girls with elevated male hormone levels would include birth control pills, metformin, and spironolactone. However, in order to do this study we must delay usual treatment.

If you are an employee of UVa your job will not be affected if you decide not to participate in this study.
If you are a student at UVa, your grades will not be affected if you decide not to participate in this study.

Will you be paid for being in this study?

You will be paid with a $75 Simon Mall gift card for each of the inpatient admissions. In addition you will receive a $100 Simon Mall gift card for completing the medication regimen and outpatient blood draws. Therefore, if you complete the entire study you will receive a total of $400 in gift cards.
You should get your payment for all your visits at the final overnight admission.

The income may be reported to the IRS as income.

However, if you do not finish the study, you will be paid $75 for each overnight admission you have completed. If the study leader says you cannot continue, you will be paid the full amount for the study.

If you owe money to any Virginia state agency, the state can use the money you earn in this study to pay those debts. These state agencies include the UVa Medical Center, VCU Medical Center or a college or university. The money may be withheld to pay back debt for such things as unpaid medical bills, taxes, fines, child support. Even if this happens, the money you earn may be reported to the IRS as taxable income.

By agreeing to be in this study, you are donating your blood samples for research, and giving up any property rights you may have in them. The results of this research using your donated materials may have commercial value. However, you will not receive any payments.

Will being in this study cost you any money?

All the tests and procedures described in this consent are being done solely for research purposes and will be provided to you at NO cost to you or your health insurance. This includes: lab tests, study drugs (metformin, estradiol, progesterone, iron supplements) outpatient visits, and hospital admissions.

You and/or your insurance company must pay for any tests or care given beyond what is required in this study. In addition, you and/or your health insurance may also have to pay for other drugs or treatments that are given to help you control any side effects. You will have to pay for any costs not covered by your health plan. You may be responsible for any co-payments or deductibles. You may wish to ask for an estimate of your financial costs. You may also wish to check with your insurance company before the study starts. Ask what they will cover and if they require you to get their permission before you decide to be in the study. You will be responsible for the cost of travel to come to any study visit and for any parking costs.

What if you are hurt in this study?

If you are hurt as a result of being in this study, there are no plans to pay you for medical expenses, lost wages, disability, or discomfort. The charges for any medical treatment you receive will be billed to your insurance. You will be responsible for any amount your insurance does not cover. You do not give up any legal rights, such as seeking compensation for injury, by signing this form.

What happens if you leave the study early?

You can change your mind about being in the study any time. You can agree to be in the study now and change your mind later. If you decide to stop, please tell us right away. You do not have to be in this study to get services you can normally get at the University of Virginia.

Even if you do not change your mind, the study leader can take you out of the study. Some of the reasons for doing so may include

a) Your study physician is concerned about your health
b) Your disease gets worse
c) The side effects of the treatment are too dangerous for you
d) New information shows the treatment will not work or is not safe for you
e) You do not follow your doctor's instructions
f) The study sponsor closes the study for safety, administrative or other reasons

If you decide to stop being in the study, we will ask you to please notify Dr. Christine Burt Solorzano in writing. We also request that you will return any unused medicine and medicine bottles.
Please send notification to PO Box 800391, Charlottesville, VA 22908.

How will your personal information be shared?

The UVa researchers are asking for your permission to gather, use and share information about you for this study. If you decide not to give your permission, you cannot be in this study, but you can continue to receive regular medical care at UVA.

If you sign this form, we may collect any or all of the following information about you:

- Personal information such as name, address, date of birth,
- Social Security number ONLY IF you are being paid to be in this study
- Your health information. If required for this study, this may include a review of your medical records and test results from before, during and after the study from any of your doctors or health care providers (if required for this study, this may include mental health care records, substance abuse records, and/or HIV/AIDS records).

Who will see your private information?

- The researchers to make sure they can conduct the study appropriately, observe the effects of the study and understand its results
- People or committees that oversee the study to make sure it is conducted correctly
- People who pay for the study, such as the National Institutes of Health, including insurance companies
- Tax reporting offices (if you are paid for being in the study)

- People who evaluate study results, which can include sponsors and other companies that make the drug or device being studied, researchers at other sites conducting the same study, and government agencies that provide oversight such as the Food and Drug Administration (FDA) if the study is regulated by the FDA.

Some of the people outside of UVa who will see your information may not have to follow the same privacy laws that we follow. We ask them to protect your privacy. However, they may release your information to others, and it may no longer be protected by those laws.

The information collected from you might be published in a medical journal. This would be done in a way that protects your privacy. No one will be able to find out from the article that you were in the study.

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

What if you sign the form but then decide you don't want your private information shared?

You can change your mind at any time. Your permission does not end unless you cancel it. To cancel it, please send a letter to the researchers listed on this form. Then you will no longer be in the study. The researchers will still use information about you that was collected before you ended your participation. UVa researchers will do everything possible to protect your privacy.

A copy of this consent form will be put in your medical record. (This is not the same as the record of this research study.) This means that everyone who is allowed to see your records will be able to find out that you are in this study. This is done so your regular doctors will know what drugs or treatment you are getting in the study. If you have other health problems during the study, they will be able to treat you properly.

Please contact the researchers listed below to:

- Obtain more information about the study
- Ask a question about the study procedures or treatments
- Report an illness, injury, or other problem (you may also need to tell your regular doctors)
- Leave the study before it is finished
- Express a concern about the study

Principal Investigator: Christine Burt Solorzano, MD
Internal Medicine, School of Medicine
Box 800391 Charlottesville, VA 22908 Telephone: (434) 924-9084

What if you have a concern about a study?

You may also report a concern about a study or ask questions about your rights as a research subject by contacting the Institutional Review Board listed below.

University of Virginia Institutional Review Board for Health Sciences Research
PO Box 800483
Charlottesville, Virginia 22908 Telephone: 434-924-2620

When you call or write about a concern, please give as much information as you can. Include the name of the study leader, the IRB-HSR Number (at the top of this form), and details about the problem. This will help officials look into your concern. When reporting a concern, you do not have to give your name.

Signatures

What does your signature mean?
Before you sign this form, please ask questions about any part of this study that is not clear to you. Your signature below means that you have received this information and all your questions have been answered. If you sign the form it means that you agree to join the study. You will receive a copy of this document after you have signed it.

Assent from Child (15-17 years of age)
Consent from the parent/guardian MUST be obtained before approaching the child for their assent.

_____	_____	_____
PARTICIPANT (SIGNATURE)	PARTICIPANT (PRINT)	DATE

To be completed for any child age 15 or above.

Person Obtaining Assent of the Child
Consent from the parent/guardian MUST be obtained before approaching the child for their assent.

By signing below you confirm that the study has been explained to the child (less than 18 years of age), all questions have been answered and the child has voluntarily agreed to participate.

_____	_____	_____
PERSON OBTAINING ASSENT (SIGNATURE)	PERSON OBTAINING ASSENT (PRINT)	DATE

Interpreter

By signing below you confirm that the study has been fully explained to the potential subject in a language they understand and have answered all their questions.

_____	_____	_____
INTERPRETER (SIGNATURE)	INTERPRETER (PRINT)	DATE

If an interpreter was used to explain this study to a potential subject who is a child, the interpreter must sign and date the line above.

Parental/ Guardian Permission

By signing below you confirm you have the legal authority to sign for this child.

_____	_____	_____
PARENT/GUARDIAN (SIGNATURE)	PARENT/GUARDIAN (PRINT NAME)	DATE

_____	_____	_____
PARENT/GUARDIAN (SIGNATURE)	PARENT/GUARDIAN (PRINT NAME)	DATE

If you are unable to obtain parental permission from both parents, explain why not:

_____

Person Obtaining Parental Permission

By signing below you confirm that you have fully explained this study to the parent/guardian, allowed them time to read the consent or have the consent read to them, and have answered all their questions.

_____	_____	_____
PERSON OBTAINING PARENTAL PERMISSION (SIGNATURE)	PERSON OBTAINING PARENTAL PERMISSION (PRINT NAME)	DATE

Consent From Impartial Witness

If this consent form is read to the parent(s) because the parent(s) is blind or illiterate, an impartial witness not affiliated with the research or study doctor must be present for the consenting process and sign the following statement. The parent may place an X on the Parent Signature line above.

I agree the information in this informed consent form was presented orally in my presence to the parent(s) and the parent(s) had the opportunity to ask any questions he/she had about the study. I also agree that the parent(s) freely gave their informed consent for their child to participate in this trial.

_____

NAME OF IMPARTIAL WITNESS

_____ _____

SIGNATURE OF IMPARTIAL WITNESS DATE