**Cover Page for ClinicalTrials.gov**

**Document:** Informed Consent

**Document Date:** July 25, 2022

**Official Study Title:** A Pilot Pragmatic RCT of a Hospital-based Precision Pharmacotherapy Smoking Cessation Program

**NCT#:** NCT04897607

**Informed Consent**

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| **Title of Study:** | *A pilot pragmatic RCT of a precision pharmacotherapy hospital-based smoking cessation intervention* |
| **Principal Investigator:** | **Scott Siegel, PhD, MHCDS**<br>**4701 Ogletown-Stanton Road**<br>**Newark, DE 19718** |
| **Contact Phone Number:** | **302-623-4555** |
| **Sponsor:** | **National Institute of General Medical Sciences** |

## Introduction

You have been asked to take part in a clinical research study. Your participation is voluntary and before you agree to participate in this study, you need to know the risks and benefits so you can make an informed decision. This process is known as informed consent. This consent form describes the purpose, procedures, and the possible benefits and risks of the study.

Your researcher will discuss the clinical research study with you. Clinical research studies include only people who choose to take part. Please take your time to make your decision. Discuss it with your family and friends and health care team. Please read this document carefully and if you have any questions, you can ask your researcher for further explanation.

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.

The research study is being conducted to examine the effects of a personalized smoking cessation medication treatment in order to help current smokers quit smoking. You are being asked to take part in this study because you currently smoke at least 5 cigarettes per day, have expressed an interest in quitting, and meet other program criteria. If you choose not to participate, there will be no loss of benefits to which you are otherwise entitled.

The person responsible for this study at Christiana Care is Scott Siegel. Christiana Care is being reimbursed by the sponsor, the National Institute of General Medical Sciences of the National Institutes of Health, for the costs of conducting this study.

## Why is this study being done?

The purpose of this study is to determine the benefits of a personalized treatment approach, compared to a non-personalized treatment approach, for smoking cessation. In other words, this study will help us know if recommending a specific medication to individual smokers will make

it easier to quit smoking than simply offering an option of medications. The specific recommendation for a medication will be based on a test that measures how quickly a smoker breaks down, or metabolizes, nicotine.

**How many people will take part in the study?**
Up to 100 people will take part in this study at Christiana Care Health System.

**What is involved in the study?**
Your participation in this research program will first involve reviewing the study's informed consent/HIPAA form, where you will hear a description of the program. If you are interested in participating after hearing the description and having your questions answered, you will be asked to sign this form and proceed through today's Intake Session. The Intake Session is necessary to make sure it is safe for you to participate. If at the end of today's visit, you are eligible to participate, you will be asked to complete two phone sessions over the next two weeks and one in-person visit about a month later. These visits are described in more detail below.

**If you take part in this study, you will have the following tests and procedures:**
You will need to have the following as part of this study.

Intake Session
This visit will last about 30 minutes and will take place here in the clinic. During this session, you will:

- Complete a paper and pencil assessment of your demographics and smoking history.
- [Women only] A pregnancy screen may be administered. For safety reasons, if you are pregnant, you will not be eligible to participate in this research study.
- In addition, your research assistant will review your potential participation in this study with your medical team and arrange for the blood to be drawn to be used for a nicotine metabolite ratio (NMR) test. This test determines how quickly or slowly your body breaks down, or metabolizes, nicotine.

If you are eligible at the end of this visit, you will receive one of two treatment plans. This study is a randomized clinical study, which means that you will be assigned at random to one of these plans. Which treatment you receive will be based on chance, like flipping a coin. Neither you nor the researcher chooses your assigned treatment group. You have an equal chance of receiving one of the following two treatment plans:

Treatment Plan Option 1: standard smoking cessation counseling + your choice to be provided with an initial supply of nicotine patches or varenicline tablets. You are also free to decline either medication.

Treatment Plan Option 2: standard smoking cessation counseling + a recommendation to take either the nicotine patch or varenicline tablets based on the results of your NMR test. Regardless of the recommendation, it would still remain your choice to be provided with an initial supply of nicotine patches or varenicline. You are also free to decline either medication.

Pre-Quit Telephone Visit
This visit will take place by phone about 7-14 days after your intake visit and will last about 10 minutes. During this session, you will:

- Be informed of your treatment plan option and related information, including the recommended medication if you are assigned to 'treatment plan option 2.'
- Be offered a prescription for a medication of your choosing (nicotine patches or varenicline), which will include instructions on how the medication should be taken. Regardless of condition, you are eligible to receive either medication or choose no medication at all.
- Be offered to coordinate your first appointment with your smoking cessation counselor through the Delaware Quitline, a free phone-based service available to all Delaware residents that is not affiliated with this study.

Follow-Up Call
This session will occur over the phone and will last about 10 minutes. First, we want to check in to see if you have any questions or troubles quitting with smoking cessation services. Next, you will complete a brief assessment of your medication use, quit date or smoking rate if still smoking, and side effects.

In-Person Assessment
This assessment will occur in-person at the clinic at about one month after you were given your study treatment plan. This visit will last about 15 minutes. You will complete a brief assessment of your medication use, quit date or smoking rate if still smoking, and side effects. In addition, you will complete a carbon monoxide (CO) reading by breathing into a machine. Carbon monoxide is a poisonous gas that comprises less than 1% of the air we breathe and is also produced through smoking a cigarette. You will be compensated $25 for completing this visit.

**How long will I be in the study?**
You will be in the study for about 6 weeks.

**What are the risks of the study?**
While on the study, you may be at risk for some side effects. You should discuss these with the researcher. There also may be other side effects that we cannot predict. Side effects may be mild or more serious.

Nicotine Withdrawal Syndrome
Most individuals who quit smoking experience symptoms of withdrawal. These symptoms can occur almost right away and last for 10-14 days. These symptoms include:

- Sadness and mood changes
- Insomnia or changes in sleep
- Constipation
- Decreased heart rate
- Irritability
- Craving for cigarettes
- Anger

- Difficulty concentrating
- Restlessness or nervousness
- Appetite increase and weight gain

A smoking cessation counselor can offer you strategies to help you manage any withdrawal symptoms that you may experience. If you feel that your withdrawal symptoms are not lessening over time or are significantly interfering with your ability to function, you should contact the Principal Investigator, whose contact information is listed on the first page of this form.

Nicotine Patch
The potential side effects of the nicotine patch are described below:

*Most Common Side Effects.* Nausea, vomiting, dizziness, weakness, and rapid heartbeat are side effects that occur rarely, but are most often caused by continuing to smoke while using the patch. You should also be aware of side effects such as difficulty breathing or a severe rash on any part of your body because these could be the symptoms of an allergic reaction. If any of these reactions occur, please speak with your doctor and the Principal Investigator, whose contact information is listed on the first page of this form.

*Skin Reactions.* The most common skin reactions to the patch are skin redness, rash or swelling, itching, bumping or tingling at the patch site. To minimize these reactions, you should move the site of patch placement each day.

*Sleep Disturbances.* When using the patch, some people also report difficulties sleeping or vivid dreams. However, this is rare and can be minimized by removing the patch when you are sleeping and reapplying a new patch in the morning.

*Other Nicotine Patch Risks.* These include risks to children and pets if the nicotine patches are not stored or disposed of properly. Unused and used patches have enough nicotine to poison children and pets. Keep the patches out of the reach of children and pets. Be sure to fold the sticky ends together when disposing of used patches. If a child or pet swallows a nicotine patch, seek professional help or contact a Poison Control Center right away.

Although the nicotine patch delivers nicotine (the addictive ingredient in cigarettes), it is at a lower level than the nicotine delivered when smoking a cigarette. Thus, the level of nicotine in your body from using the nicotine patch is lower than if you were smoking. There is no evidence of addiction to the nicotine patch when used as part of a comprehensive smoking cessation program. Using the nicotine patch is less harmful to your health than cigarette smoking. You should not stop using the patch without discussing your symptoms with your Physician and study staff unless you experience severe or intolerable side effects.

Varenicline
The potential side effects of taking varenicline are described below:

*Most Common Side Effects.* Potential side effects of taking varenicline are nausea, sleep disturbance, constipation, flatulence (gas), or vomiting. These can occur in more than 5% of people taking this medication.

*Allergic Reactions*. There have been rare reports of allergic and skin reactions to varenicline, including swelling of the face, mouth (tongue, lips, and gums), extremities, and neck (throat and larynx). These types of allergic reactions are considered serious and may be life-threatening. However, the risk for these reactions is small (about 1 out of 1000 people taking this medication). If you experience any difficulty breathing, you should stop taking varenicline and seek medical help immediately. At the first appearance of any skin rash, you should also stop using varenicline immediately and contact your health care provider. If you experience any of these symptoms, contact the study staff as soon as possible after seeing your medical provider.

*Mood-related Side Effects*. Rare serious mood-related effects have been reported in a small number of persons taking varenicline. The risk for this type of reaction is about 1 out of 1000 people taking the medication. These include, but are not limited to, depression, agitation, hostility, suicidal thoughts, suicide attempts, and completed suicide. Some reported cases may have been complicated by the symptoms of nicotine withdrawal in patients who stopped smoking. Depressed mood may be a symptom of nicotine withdrawal. Depression, rarely including suicidal thoughts, has been reported in smokers undergoing a smoking cessation attempt without medication. However, some of these symptoms have occurred in patients taking varenicline who continued to smoke. When symptoms were reported, most occurred during treatment with varenicline, while some followed discontinuation of varenicline therapy. All patients being treated with varenicline will be assessed for such symptoms. These events have occurred rarely in patients with and without pre-existing psychiatric disease.

Although patients with serious psychiatric illness such as major depressive disorder, schizophrenia, or bipolar disorder did not participate in the pre-marketing studies of varenicline, recent clinical trials that specifically targeted these patient populations have demonstrated safety of varenicline for use in these populations. These studies did not find significant differences in mood-related side effect rates or any exacerbation of psychiatric symptoms between those taking varenicline versus placebo/sugar pill. Our research staff follow strict procedures to help monitor for the presence of these side effects, including asking you repeatedly during each study session about your reactions to the study medication.

You should stop taking varenicline and contact a healthcare provider immediately if agitation, hostility, depressed mood, or changes in behavior or thinking that are not typical of you are observed, or if you develop suicidal thoughts or behavior. In many cases, resolution of symptoms was reported after discontinuation of varenicline therapy, although in some cases the symptoms persisted; therefore, ongoing monitoring and supportive care should be provided until symptoms resolve.

*Cardiac Side Effects*. Varenicline may be associated with an increased risk for certain cardiac (heart) and vascular (blood vessel) side effects, including chest pain, heart attack, stroke, shortness of breath, calf pain when walking or sudden onset of weakness, numbness or difficulty speaking. One study showed that these risks are rare (~1% or 1 out of 100 people using varenicline) but a later study found no difference between placebo/sugar pill and varenicline in terms of these cardiac risks. Our study staff follow strict procedures to help them monitor for the presence of these side effects, including asking you repeatedly during the study about your reactions to the study medication. For your safety, if you are found to be at risk for experiencing cardiac events, you will be unable to participate in this study.



Patient Initials_____

*Somnambulism.* Cases of somnambulism (sleep walking) have been reported in patients taking varenicline. You should notify research staff as soon as possible if you experience somnambulism.

*Brief Cognitive Side Effects.* Varenicline may cause noticeable drowsiness, dizziness, headache, loss of consciousness, or difficulty concentrating that may impair your ability to perform tasks requiring judgment or motor and cognitive skills such as driving a car and operating machinery. You should proceed with caution in this regard until you are certain that varenicline does not affect your performance.

*Risk of Seizure.* Varenicline may be associated with new or worsening seizures during the first month of treatment. Some patients who reported experiencing a seizure while taking varenicline had no prior history of seizures, whereas others had a history of seizure disorder that was remote or well-controlled. You should not take varenicline if you have an unstable, untreated history of seizures.

*Potential Interaction with Alcohol.* It is possible that varenicline may affect response to alcohol. Some individuals have reported lower alcohol tolerance, aggressive behavior, or impaired memory following consumption of alcohol during varenicline treatment. In these cases, the amount of alcohol consumed was not sufficient to explain the event. It is best to minimize or reduce your alcohol intake (no more than 3 drinks per occasion or within a 24-hour time period) while you are taking varenicline or until you know whether varenicline affects your alcohol tolerance.

Other Risks

*Assessments/Questionnaires and Smoking Cessation Counseling.* Some people can experience anxiety and other types of general distress when they complete questionnaires. This is generally related to your feelings about quitting as well as learning about some of the health risks associated with smoking. These reactions are usually very mild and typically diminish with time. The research staff administering these questionnaires is trained to help you should you experience any concerns.

*Data and Results.* Because we want to protect your confidentiality, we will identify your results with an identification number only (not your name). Only authorized study personnel will be able to link your identification number with your name.

*Threats to Privacy/Confidentiality.* Every attempt will be made by the investigators to maintain all information collected in this study strictly confidential. We will store your information in a secure room with limited access. We will control access to the computer files that hold this information, and all computers will be password protected. When the results of the study are published, no names or identifying information will be used. Social harms may result when sensitive and personal information is inappropriately disclosed. Inappropriate disclosure of study data about subjects' beliefs, attitudes, behavior (including smoking), and health may result in damage to their economic status. These harms can include loss of employment, health insurance, life insurance, housing, and ability to travel.

*Reproductive Risks [Females Only].* Because of the effects of varenicline and the nicotine patch, there could be serious harm to unborn children or children who are breast-feeding. These effects could also harm the mother. It is also possible that harmful side effects that are not yet known could happen to both the mother and unborn or breast-feeding child. If you are currently pregnant, it is

important that you inform the research coordinator because you will not be able participate in the study. If you are able to become pregnant, you will be given a pregnancy screen before entry into the study. You are asked to use a medically accepted method of birth control while you participate in the study. Examples of effective methods include barrier contraceptives (condoms or diaphragm) with spermicide, intrauterine devices (IUDs), hormonal contraceptives, oral contraceptive pills, surgical sterilization, and abstinence. Only methods that use condoms provide protection against sexually transmitted infections. You should not become pregnant while you using varenicline or the nicotine patch. If you do become pregnant, you must tell the investigator and consult an obstetrician or maternal-fetal specialist.

**Are there benefits to taking part in the study?**

If you agree to take part in this study, it is possible that you may not benefit. The researchers hope the information learned from this study will benefit future patients who are interested in quitting smoking

The study drug may help you quit smoking, but there is no guarantee that being in this study will help you. By participating in this research study, you will have the opportunity to participate in a smoking cessation program. Therefore, you will have the opportunity to quit smoking completely or reduce your amount of smoking.

**Can I stop being in the study?**

You can stop being in the study at any time. The researcher may decide to take you off this study at any time if the Principal Investigator determines it is necessary for your health and safety; you have not followed the study instructions; or the sponsor, Principal Investigator, or the Food & Drug Administration (FDA) decides to stop the study.

If you agree to participate in the study, you still have the right to withdraw at a later time. In addition, at the time you withdraw you have the right to refuse to allow future information about you to be collected and used for the research study. If you decide to withdraw from the study, you will be asked to tell a member of the research staff and sign a written notice (called an Acknowledgement of Withdrawal form). Withdrawal will not interfere with your future care.

**What other choices are there if I do not take part in this study?**

You do not have to take part in this research study in order to receive treatment. Your participation is voluntary. You may refuse to take part, or stop participating at any time without penalty, or jeopardizing your continued medical care at Christiana Care, or lose benefits you would otherwise be entitled to. If you do not wish to enroll in this program and still wish to seek help with quitting smoking, we can provide you with information on other treatment options offered at ChristianaCare and within the local community.

**Instead of being in this study, you have these options:**

The alternative to participation is to decide not to enroll in this program. If you do not wish to enroll in this program and still wish to seek help with quitting smoking, we can provide you with information on other treatment options offered at ChristianaCare and within the local community.

**What about Confidentiality?**

We need to collect information about you to conduct this study. Your personal health information is

health information about you that could be used to identify you. This information may include demographics (such as your age, sex, height, weight), information about your health now and in the past, and other facts about you collected for the purposes of this research study. The information that will be collected will be the minimum needed to meet the goals of this research study and will be used only for the study described in this consent. If you decide not to allow this use of your information, you may not take part or continue to take part in the research study, since the researcher needs this information to meet the study goals.

We try to keep your personal health information private and confidential. However, we cannot guarantee absolute confidentiality. Your personal information may be disclosed if required by law and it may be disclosed to others as described in this section.

Individuals and organizations that may look at and/or copy your research records to conduct this research, assure quality of the data and analyze the data, as it pertains to this study, include:

- Members of the research team at ChristianaCare
- Medical staff who are directly or indirectly involved in your care related to this research
- People who oversee or evaluate research and care activities at ChristianaCare, including the Christiana Care Institutional Review Board (IRB), a committee that reviews research projects to help ensure that the rights of research participants are protected
- People from agencies and organizations that provide oversight of research, such as the Department of Health and Human Services (DHHS), Office for Human Research Protections (OHRP), and the Food & Drug Administration (FDA).

By signing this document, you are authorizing ChristianaCare to use and release your health information for this research. Some of these groups listed above may not be required to protect your information. If permitted by law, they may be allowed to share it with others without your permission.

It is also possible that important information will be shared with your primary caregiver or other health care professionals as needed for your safety.

If information from this study is presented or published at scientific meetings or in journals, your name and other identifying information will not be used.

You have the right to see any medical information about yourself. However, during the research study you will not have access to all of the health information that is created or collected during the study. You do not have the right to review and/or copy records kept by the sponsor or other researchers associated with the study.
It may be necessary to contact you at a future date regarding new information about the treatment you have received. For this reason, we ask that you notify the institution where you received treatment on this study of any changes in your address. If you move, please provide your new address to the principal investigator or study staff at 4701 Ogletown-Stanton Road, Newark, DE 19718.

**What are the costs?**
Taking part in this study may lead to added costs to you or your insurance company. Routine

medical care for your condition (care you would have received whether or not you were in this study) will be charged to you or your insurance company and you are still responsible for any deductibles or applicable co-pays. We will provide an initial supply of medication (4 weeks) at no cost while enrolled in the study. If you choose to continue with medication after the completion of the study, this could result in out-of-pocket costs.

In the case of injury or illness resulting from this study, emergency medical treatment is available but will be provided at the usual charge. No funds will be offered to compensate you in the event of injury. However, by signing this document, you are not giving up any rights you have to pursue legal remedies for injury resulting from participation in this study.

**Will I get paid for being in this study?**

You will receive $25 for your intake visit and $25 for the in-person assessment visit about 4 weeks after your assignment to a study treatment plan, for up to a total of $50 for your participation. These funds are provided to help support you with time and travel associated with your participation. You will not receive payment for any visits you do not complete.

In accordance with IRS regulations, any payment may be reportable as income on your taxes.

You will be issued a ClinCard, which is a specially designed debit card for clinical research onto which your funds will be loaded as appropriate. When a visit is completed, funds will be approved and loaded onto your card. The above scheduled funds will be loaded and available on your card within 2 business days. Please keep this card in a secure place as you will be issued one card for the duration of your participation. If your card is lost, please contact your research coordinator for a replacement card. If stolen, call (866) 952-3795 for assistance marking the card as "stolen" and opening a case with MasterCard.

You will have the option to receive updates related to payment via text message and email message if you provide your contact information below (Standard text messaging rates will apply). You are not required to provide your cell phone or email address to be enrolled in the study or to receive payment. If you choose to receive messages and decide at a later date that you want to stop these messages, you will have the ability to opt-out.

I agree to receive text and/or email messages _____
Initials and date

Cell phone # for texts_____Email address: _____

I do not agree to receive text and/or email messages _____
Initials and date

**What are my rights as a participant?**

Taking part in this study is voluntary. You may choose not to take part or may leave the study at any time. Leaving the study will not result in any penalty or loss of benefits to which you are entitled. If you decide not to take part in the study, you will continue to receive the usual medical care appropriate for your condition. However, if you are thinking about stopping, we encourage you to talk to the researcher and your regular doctor first. They will tell you how to stop safely. We will tell you about new information that may affect your health, welfare, or willingness to stay in this

study. If you decide to withdraw from the study, you will be asked to tell a member of the research staff and sign a written notice (called an Acknowledgement of Withdrawal Form).

**Who do I call if I have questions or problems?**

For questions about the study or a research-related injury, contact the researcher Scott Siegel at 302-733-4730.

For questions about your rights as a research participant, contact the Christiana Care Institutional Review Board at (302) 623-4555.

**Signature**

You have read the information provided above. You voluntarily agree to take part in this study. You will be given a copy of this form.

_____ _____

Signature of Research Subject Date

_____

Printed Name of Research Subject

_____ _____

Signature of Person Obtaining Consent Date

_____

Printed Name of Person Obtaining Consent