Title:	Toward the Implementation of Genomics in Substance Use Disorder Treatment
Protocol ID#	201704049
NCT#	NCT04768114
Date:	11/06/2023

Genomics Implementation in SUD

PI: Alex Ramsey
IRB ID #: 201704049

Project Details

1. Demographics

1.1 Project Title:
Toward the Implementation of Genomics in Substance Use Disorder Treatment

1.2 Short Title (required):
Genomics Implementation in SUD

1.3 Project is primarily:
Biomedical

1.3.a Does this study require review under ICH-GCP?
No

1.4 Type of Study:
Other Interventional

1.4.a Is your research study one in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes (NIH clinical trial definition).
Yes

1.5 Select how you plan to obtain consent:
- Sign a consent document or a consent letter
- Letter or information sheet with no signature
- Script for use either in person or over the phone with no signature

2. Source(s) of Support

2.1 Source(s) of Support

Type/Source	Grant Title	Name of PI on Grant	Status	WUSTL Awardee Institution
Federal Agency NIH, National Institutes of Health	Washington University Career Development Program in Drug Abuse and Addiction	Laura Bierut	AWARDED	Yes
Federal Agency NIH, National Institutes of Health	Mechanisms of Behavior Change in a Genetics-Informed Smoking Cessation Intervention	Alex Ramsey	AWARDED	Yes

Attachment Name	Category	Version	Date Attached
K12_submitted_grant_HRPO.pdf	Grant from funding source or private foundation/association	1	05/05/17
K12_final combined.pdf	Grant from funding source or private foundation/association	1	05/05/17

3. Research Team

3.1 Principal Investigator

Name	E-mail	Title
Alex Ramsey	aramsey@wustl.edu	Assoc Prof of Psychiatry

3.2 Team Members

Research Team Members

Role	Name	Role Desc	Student	Email	Title	School

PI	Alex Ramsey, BS, PhD, MA, BS, MA, PHD		No	aramsey@wustl.edu	Assoc Prof of Psychiatry	School of Medicine
	Laura Bierut, MD			laura@wustl.edu	Alumni Endowed Prof of Psychiatry	School of Medicine
	Yoonhoo Chang, BS		No	yoonhoochang@wustl.edu	DBBS Graduate Research Asst	School of Medicine
	Jingling Chen, BS		No	chenjingling@wustl.edu	Statistical Data Analyst	School of Medicine
	Li-Shiun Chen, ScD, MD, MPH			li-shiun@wustl.edu	Prof of Psychiatry	School of Medicine
	Sherri Fisher, MS		No	sherri@wustl.edu	Clinical Research Specialist	School of Medicine
	Louis Fox, BS		No	foxl@wustl.edu	Research Statistician	School of Medicine
	Anastasia Hanonick, BA, Psychology		No	hanonick@wustl.edu	Professional Rater II	School of Medicine
	Elizabeth Laurentius, BS, Psychology		No	laurentius@wustl.edu	Professional Rater II	School of Medicine
	Giang Pham, MPH		No	g.pham@wustl.edu	Statistical Data Analyst	School of Medicine
	Enola Proctor, PHD			ekp@wustl.edu	Research Professor	Brown School
	Thuelfaqar Rammaha, MS		No	r.thue@wustl.edu	Clinical Research Coordinator II	School of Medicine
	Patricia Salyer, M.Ed., MA		No	salyerp@wustl.edu	Clinical Research Supervisor	School of Medicine
	Elizabeth Sekarski, BS, Psychology		No	esekarski@wustl.edu	Professional Rater II	School of Medicine
	Kristen Sextro, BA		No	sextro@wustl.edu	Clinical Research Coordinator I	School of Medicine
	Nina Smock, BA		No	smockn@wustl.edu	Clinical Research Specialist	School of Medicine
	Alia Thomas, High School		No	a.a.thomas@wustl.edu		ARTS AND SCIENCES
	Lauren Waight, BA		No	lwaight@wustl.edu	Professional Rater II	School of Medicine
	Erika Waters, MPH, PHD		No	waterse@wustl.edu	Prof of Surgery (Public Health Sciences)	School of Medicine
LA	Jessica Bourdon, PHD	Jessica Bourdon is the Director of Research Administration at Wellbridge Addiction Treatment and Research. She completed her post-doctorate at Washington University and has played a key role in this research for several years. She	No	jbourdon@wellbridge.org		

		will be responsible for consenting and conducting focus groups for Aim 2 of the study with patients and clinicians at Wellbridge. These focus groups will be conducted at Wellbridge. She will also be involved in assisting with publications resulting from this work. Jessica will transfer the data collected from the focus groups through WUSTL Box where it will be securely stored.				
LA	Genevieve Slavens, AA	Genevieve will be trained to conduct recruitment calls and administer a brief phone follow-up. After training, she will complete calls and phone follow-ups under supervision of a member of the research team.	No	gslavens@email.wustl.edu		

Team Member Financial Interest

Name	Financial Interests
Alex Ramsey, BS, PhD, MA, BS, MA, PHD	none
Laura Bierut, MD	none
Yoonhoo Chang, BS	none
Jingling Chen, BS	none
Li-Shiun Chen, ScD, MD, MPH	none
Sherri Fisher, MS	none
Louis Fox, BS	none
Anastasia Hanonick, BA, Psychology	none
Elizabeth Laurentius, BS, Psychology	none
Giang Pham, MPH	none
Enola Proctor, PHD	none
Thuelfaqar Rammaha, MS	none
Patricia Salyer, M.Ed., MA	none
Elizabeth Sekarski, BS, Psychology	none
Kristen Sextro, BA	none
Nina Smock, BA	none
Alia Thomas, High School	none
Lauren Waight, BA	none
Erika Waters, MPH, PHD	none
Jessica Bourdon, PHD	none
Genevieve Slavens, AA	none

4. Other Institutional Reviews/Requirements

4.1 Do any of the objectives of this study involve the diagnosis, prevention, screening, evaluation, treatment or support of cancer patients?
Yes

4.2 Are more than 30% of the patients involved in this study likely to have an active cancer diagnosis?
No

4.2.a Is this application for treating a single patient without the goal of publication?
No

4.3 Will any subject be asked to undergo a radiation therapy procedure (including external beam therapy, brachytherapy, or radiopharmaceutical therapy)?
No

4.4 Does your study involve the administration of non therapeutic radiopharmaceuticals (radioactive drugs) for research purposes?
No

4.5 Will any participant be asked to undergo any of the following:

- a standard radiology procedure involving ionizing radiation (includes X-rays, fluoroscopy, DEXA, CT)
  OR
- a standard nuclear medicine examination with FDA-approved radioactive drugs (including bone scans, radionuclide ventriculogram (RVG or MUGA), myocardial perfusion imaging, FDG-PET)
- **DO NOT include a nuclear medicine examination performed with the investigational radioactive drug(s) listed above in Question 4.4.**
- DO NOT include MRI or ultrasound

No

4.6 Will the study involve any of the following activity **PROSPECTIVELY** at WUSM or any BJC hospitals, even if subjects or their insurance will not be billed for the item or service, and regardless of the study funding source (including studies with departmental or no funding)?

- Procedures, tests, examinations, hospitalizations, use of Pathology, Laboratory, Cardiology, or Radiology services, use of clinic facilities or clinical equipment, or any patient care services, including services conducted in the Clinical Research Unit; or
- Physician services or services provided by non-physicians who are credentialed to bill (ARNPs, Physician Assistants, etc.)

No

4.7 Does this study involve administration of recombinant or synthetic nucleic acids (gene therapy or mRNA vaccines) or microorganisms?
No

4.8 Does this study involve the use of human embryonic stem cells or human induced pluripotent stem cells?
No

4.9 Does this study involve research in which a human embryo or embryos are destroyed, discarded, or knowingly subjected to risk of injury or death greater than that allowed for research on fetuses in utero?
No

4.12 Will a Certificate of confidentiality be used for this research?
Yes, certificate automatically issued by funding agency

4.13 Does this project need to be registered on ClinicalTrials.gov?
No

4.14 Title that should appear in Epic (and will be visible in the patient medical record):
Genetics & Smoking Study

4.15 Select one person from the study team that should appear in Epic as the contact person for this study:
Alex Ramsey

4.17 Would you like to submit a request for the Epic team to consider your study for the use of BPA (Best Practice Advisory) in Epic?
No

4.18 Would you like to submit a request for the Epic team to build your questionnaires in Epic for the purposes of recruitment?
Yes

4.19 Will any external monitors require access to this study in Epic?
No

4.21 Mark all that apply to your study:

Mark any service(s) you'd like to use:

- Participant Recruitment Services available through Recruitment Enhancement Core (REC)
- Participant Recruitment Services available through Community Based Recruitment and Retention (REACH)

1. Protocol

1.1 Is there a separate, written protocol that will be submitted in addition to this form? (Note: a grant application is not considered to be a protocol)
No

1.2 Select up to three key words below that best describe this research study:

- Genetics and Genomics
- Psychiatry
- Public Health

1.3 Provide a short summary/abstract of the purpose and procedures of the study proposed in this IRB application.

- DO NOT include information on studies not proposed in this application.
- Use LAY terminology only. This must be easily understandable by IRB community members and nonscientists.
- DO NOT cut and paste technical abstracts from source of support applications that may not be understood by a general audience.

The overall goal of this project is to conduct early-stage implementation research to (1) establish the feasibility of returning genomic results to patients and providers in clinical and community settings and (2) pilot test novel implementation strategies for integrating genomic applications for smoking cessation treatment in clinical care. The use of personal genomic results to inform treatment has great potential to advance precision medicine efforts, and emerging genomic discoveries, such as the ability to predict smoking-related disease risk and treatment responsiveness, may soon be primed for implementation into community and routine care settings. Pre-implementation research is thus urgently needed to identify and address anticipated barriers at the patient (concerns of genomic profiling) and physician (resistance to change) levels that might thwart implementation and, as a result, the public health impact of genomic advances in community and clinical care settings. Through both quantitative and qualitative interviews to address these potential barriers, we will further advance the field toward appropriate implementation of genomic applications in routine settings.

This study has two parts (Aim 1 and Aim 2). Aim 1: Examine the acceptability and effect of personalized genomic results on smoking behaviors in different subgroups of adult smokers. As an important pre-implementation step, we will examine the extent to which smokers in the community (1) agree to genetic testing, (2) recall details of their personalized genomic results, and (3) change their smoking behaviors following review of their results. We will give particular attention to potential differences in outcomes between subgroups, including African Americans and European Americans. Aim 2: Pilot test implementation strategies for integrating genomics of smoking cessation treatment in clinical care. The purpose of this aim is to pilot test two strategies--patient-mediated and provider-focused return of results prior to clinical encounters--and begin to track implementation outcomes of incorporating patients' personal genomic information into smoking cessation treatment plans. We will collect data for Aim 1 first. Once the initial evaluation of Aim 1 results is performed we will submit a modification to add Aim 2 to the study, or alternatively, once the initial evaluation of Aim 1 results is performed we will submit a separate application to conduct Aim 2.

As a next step for Aim 1 in the context of COVID-19, we will conduct a fully-remote, pilot randomized controlled trial via telehealth to (1) test the preliminary effects of the genetically-guided RiskProfile compared to brief cessation counseling, and (2) assess the feasibility and acceptability of genetically-guided smoking cessation via telehealth.

For Aim 1, we will also re-consent participants by phone using the attached verbal script to complete a brief 10-15 minute phone follow-up approximately 18 months after their intervention to see if changes in attitude and behavior as a result of receiving their personalized genetic results profile have persisted.

1.4 Specify your research question(s), study aims or hypotheses:
Aim 1: Examine the acceptability and effect of personalized genomic results on smoking behaviors, also referred to as the RiskProfile, in different subgroups of adult smokers. As an important pre-implementation step, we will examine the extent to which smokers in the community (1) agree to genetic testing, (2) recall details of their personalized genomic results, and (3) change their smoking behaviors following review of their results. We will give particular attention to potential differences in outcomes between subgroups, including African Americans and European Americans. We will also examine potential mechanisms of behavior change, including health-related cognitions and engagement, that may explain the observed outcomes (acceptability and effect of the RiskProfile).

Aim 2: Adapt the RiskProfile and evaluate feasibility and acceptability for use in real-world community settings. In this mixed methods approach, we will aim to conduct an iterative process of data collection and adaption to determine the feasibility of delivering the RiskProfile in a real-world setting. There are two data sources that will inform the adaptation of the RiskProfile: 1) adapting for internal validity, using evidence from Aim 1 on potential mechanisms that may identify elements that need to enhance potency of the intervention, and 2) adapting for

external validity, using focus group feedback from a sample representing patient and provider viewpoints on necessary modifications to the RiskProfile for use in a community health agency setting.

Feasibility of delivering the adapted RiskProfile will be determined by conducting a small-scale feasibility trial among current smokers using structured interviews and quantitative metrics to examine the extent to which the RiskProfile is translatable to real-world community settings. We hypothesize that successful completion of this aim will generate feasibility and acceptability data that will support standardized use of the RiskProfile by community-based providers in real-world settings.

1.5 Background and significance and/or Preliminary studies related to this project:

C. SIGNIFICANCE

C1. Substance use disorders, including tobacco use disorders, are a major public health problem. Tobacco use remains the largest cause of preventable death in the United States, contributing to chronic obstructive pulmonary disease, myocardial infarction, at least 14 types of cancer, and numerous other medical illnesses.55–57 Harmful effects of smoking cost the United States more than $200 billion each year in health and productivity-related costs and will eventually kill half of those who regularly use tobacco.58 There are several evidence-based pharmacotherapies for smoking cessation—including varenicline, nicotine-replacement therapies, and bupropion—and 70% of smokers currently want to quit.59–61 Nevertheless, sustained patient engagement and adherence to treatment are low,61,62 and only about 5% of smokers are able to successfully quit smoking,61 suggesting the need for improved personalized smoking cessation treatment protocols.63

C2. Genomic data predict heaviness of smoking, risk of smoking-related diseases, and effect of smoking cessation pharmacotherapy. Similar to genomic advancements in other fields, genomic information may be instrumental to recovery of tobacco use disorder and other substance use disorders (SUD).58,62–65 In fact, genomic data have been shown to predict smoking heaviness, smoking-related disease risk, likelihood of smoking cessation, and responsiveness to smoking cessation treatments.26–35 For instance, smokers with high-risk genomic variants in the CHRNA5 nicotinic receptor gene were far less likely to successfully abstain from smoking than those with low-risk genotypes. Additionally, while smokers with high-risk genotypes responded to pharmacologic cessation treatments with a two-fold increase in abstinence, those with low-risk genotypes did not benefit from pharmacotherapy.26,27 Effective translation of these genomic findings may be critical to engaging high-risk patients and informing the most appropriate treatment approaches for smoking cessation.58,62,63 Within the SUD field, given that the science of genomic discovery is farthest along with respect to tobacco use disorder, the current research project focuses on the role of genomic medicine for smoking cessation.

C3. Genomic advancements will increasingly provide opportunities to personalize care for SUD. The Precision Medicine Initiative has sparked a new era of medicine in which data on genomics and patient preferences are being used to better engage individuals, inform decision-making, and personalize treatment for a wide range of diseases.37,42–46 This proposal aims to prepare the SUD field for the phenomenon referred to as "the unstoppable march of genomics into clinical practices."66 The integration of genomic medicine into practice is still in its infancy, and countless scientific discoveries will continue to advance and refine our understanding of the role of genomic data in clinical care.23 However, the unprecedented potential of genomic data to engage populations and inform SUD treatment demands timely conduct of "early stage" implementation studies such as the one currently proposed.58,62 Assessing the feasibility of returning genomic results for SUD in multiple contexts (community, clinical) and pilot testing potential implementation strategies will generate long-range, translatable findings that will greatly benefit the field as genomic medicine continues to advance.

C4. Implementation science offers valuable approaches for bringing genomic medicine to clinical care. Despite the potential of genomic medicine to radically improve patient engagement and treatment for SUD, there has been a notable lack of implementation research on the use of rapidly-emerging genomic discoveries for improved clinical care.47,58,62,64 Implementation research has traditionally focused on long-established and well-validated interventions. However, the often-cited 17-year delay in translating research to practice54,67–69 necessitates an aim to better understand the process of implementing new classes of rapidly-emerging innovations (e.g., genomics)—an approach essential to narrowing the vast translational gap.54,70,71 The NIH-funded Implementing Genomics in Practice consortium has begun to demonstrate the useful role of implementation science in preparing the medical field to integrate genomics into clinical diagnosis and treatment.49 The use of implementation science theory (e.g., Consolidated Framework for Implementation Research),49,72,73 implementation outcomes such as adoption (actual utilization) and acceptability (favorable attitudes) of evidence-based innovations,74,75 and implementation strategies (e.g., clinical decision support systems)76,77 have proven valuable in increasing the readiness of the field to implement genomics to improve clinical care of other chronic diseases. This value may translate to the field of SUD as well; however, the proposed research is needed given the unique challenges of implementing new innovations in the SUD field.78

Preliminary Findings. Prior research led by Dr. Laura Bierut's team at WU and replicated by others has demonstrated that variation in the nicotinic cholinergic receptor subunit gene CHRNA5 (particularly rs16969968) and nicotine metabolism predict risk of tobacco use disorder and developing smoking-related diseases including lung cancer and chronic obstructive pulmonary disease.30–33,37,38,90–92 Studies indicate that variants in the CHRNA5 gene also predict delayed smoking cessation26 and more favorable response to pharmacological treatment and success of pharmacotherapy for smoking cessation.27,34,35,93–95 While the evidence base in genomics for smoking cessation and SUD continues to develop, these findings constitute important discoveries that are not yet being incorporated into clinical care or public health programs. Dr. Bierut's team also found that by returning genetic results to smokers, smoking cessation attempts increased from 21% at baseline to 53% after 4 to 8 weeks96 and, importantly, did not lead to "false reassurance" or increased risk of smoking in former or non-smokers.97 Large strides in implementing genomics have been made in other fields, including oncology, and these efforts have resulted in a growing bank of instruments and other research materials. These resources provide a much-needed foundation by which other fields, including SUD, can begin to study the integration of genomic discoveries in clinical care and other settings. The current research aims are built on this existing infrastructure which enhances the feasibility of the study. However, this study explores new research questions within the unique and different field of a behavioral disorder, thereby contributing to the rapidly developing science of implementing genomic findings into diverse settings.

1.6 Literature cited/references (if attaching a grant enter N/A):

N/A

1.7 Describe EACH of your participant populations

- Include description of any control group(s)
- Specify the Inclusion/Exclusion criteria for EACH group

AIM 1:
For the Aim 1 lab-based study, participants will include adults who are current smokers of tobacco. Participants will primarily be located in the Greater St. Louis Area; however, in the event of recruitment challenges, participants may be geographically dispersed throughout the United States. Subjects cannot have a condition that prevents them from providing informed consent or effectively participating in the protocol (e.g., language difficulty, central nervous system damage, or extremely poor health).

For the Aim 1 campus-based study, participants will include adult pedestrians in various parts of WUSM and Danforth campuses. Participants may include healthcare professionals, academicians, students, patients, or other members of the public. Subjects cannot have a condition that prevents them from providing informed consent or effectively participating in the protocol (e.g., language difficulty, central nervous system damage, or extremely poor health). As part of this study, will also enroll participants who work at the National Council on Alcoholism and Drug Abuse – St. Louis Area (NCADA). These participants will predominantly consist of substance abuse counselors.

AIM 2:
For Aim 2, participants will include adults who are current tobacco smokers and clinicians and peer support specialists in a partnering community health agency (Wellbridge Addiction Treatment and Research). Two focus groups will be conducted: one with current smokers who are inpatient at Wellbridge (n=20) and one with clinicians and peer support specialists (n=10) at Wellbridge. Each group will be engaged in qualitative interviews to address the feasibility and acceptability of the content and format of the adapted RiskProfile. These focus groups will be led by a member of the research team.

To test the feasibility of delivering the RiskProfile in a real-world community setting, a second group of current smokers (n=25) and peer support specialists (n=10) will be invited to participate in a small-scale feasibility trial that will involve current smokers getting genetic testing while they are inpatient at Wellbridge and then receiving their their RiskProfile via Zoom after they are discharged. The RiskProfile will be delivered by their peer support specialist under the supervision of the research team.

Inclusion/exclusion criteria for individuals in the patient focus group are below.
Inclusion criteria: Past 30-day use of combustible cigarettes, patient in rehabilitation within addiction treatment center
Exclusion criteria: Primarily vaping, in detoxification unit of addiction treatment center, participation in a previous focus group for this study (if re-admitted)

Inclusion/exclusion criteria for current smokers in the feasibility trial are below.
Inclusion criteria: Past 30-day use of combustible cigarettes, patient in rehabilitation within addiction treatment center
Exclusion criteria: Primarily vaping, in detoxification unit of addiction treatment center

Individuals in the clinician focus group or in the clinician group in the feasibility trial must be currently employed clinicians or peer support specialists at Wellbridge Addiction Treatment and Research.

1.8 Check all materials/methods that will be used in recruiting participants:

- Ads/Brochures/Posters/News Release/Fliers
- Email or letters
- Other Research Study - COGA subjects (IRB ID 201105402) and GISC subjects (IRB ID 201305128)
- Existing Registry/database - Research Participant Registry (RPR) and ResearchMatch through Volunteer for Health - Recruitment methods through VFH include posting ads on Centerwatch (www.centerwatch.com), RPR Fan Page listing on Facebook, and an RPR database query for referrals who have self-identified as current smokers. The RPR database is a HIPAA approved, secure database of consented potential participants that have expressed interest in getting contacted about currently enrolling Washington University clinical trials.
- Word of Mouth/Snowball sampling
- Medical Records or Other PHI
- Epic - MyChart
- Other Methods/Source - ResearchMatch.org will be utilized as a recruitment tool for this protocol. ResearchMatch.org is a national electronic, web-based recruitment tool that was created through the Clinical & Translational Science Awards Consortium in 2009.

Attachment Name	Category	Version	Date Attached
Red Poster (2).rtf	Recruitment Materials: Ads/Brochures/Posters/News Release/Fliers	5	07/09/21
Ramsey 201704049 - Centerwatch_TS edits.rtf	Recruitment Materials: Ads/Brochures/Posters/News Release/Fliers	1	07/05/19
mailed recruitment letter.rtf	Recruitment: Email or letters	1	06/20/19
Feasibility Clinician Recruitment Flyer.pdf	Recruitment Materials: Ads/Brochures/Posters/News Release/Fliers	1	07/14/23
Ramsey 201704049-Facebook_TS edits.rtf	Recruitment Materials: Ads/Brochures/Posters/News Release/Fliers	1	07/05/19

Wellbridge Clinician Flyer Final.pdf	Recruitment Materials: Ads/Brochures/Posters/News Release/Fliers	1	10/07/22
Wellbridge Inpatient Flyer_FINAL.pdf	Recruitment Materials: Ads/Brochures/Posters/News Release/Fliers	1	10/07/22
Grey Poster (1).rtf	Recruitment Materials: Ads/Brochures/Posters/News Release/Fliers	5	07/09/21
GENIMP_V5 recruitment letter_4-6-2023.docx	Recruitment: Email or letters	1	04/07/23
Feasibility Patient Recruitment Flyer.pdf	Recruitment Materials: Ads/Brochures/Posters/News Release/Fliers	1	07/14/23
ResearchMatch Contact Message.docx	Recruitment: Email or letters	2	08/28/20
Study name and description for MyChart.docx	Recruitment: Email or letters	2	08/28/20
201704049 VHF Recruitment Flyer_12-21-21.rtf	Recruitment Materials: Ads/Brochures/Posters/News Release/Fliers	3	12/23/21
email correspondence_v5.rtf	Recruitment: Email or letters	9	06/28/21
Recruitment Letter_for recruiting from GISC_v2.rtf	Recruitment: Email or letters	3	08/16/19
V5 follow-up Flyer4.pdf	Recruitment Materials: Ads/Brochures/Posters/News Release/Fliers	1	08/23/23

1.8.b List the individual data elements you will access from the medical records (or other source of PHI) to identify potential participants for recruitment and, if applicable, any individual data elements that you will include on a screening log prior to consent.
We will be recruiting participants from COGA and GISC who smoke and will need to obtain identifiable health information for recruitment purposes. To identify potential participants for recruitment, we will access and use self-reported past month smoking and breath carbon monoxide levels from their previous records.

We will also filter results by age and current smoking status from Epic/MyChart, RPR, and ResearchMatch to identify potential participants for recruitment.

1.8.c What is the plan for individual identifiers obtained to identify participants and, if applicable, those identifiers maintained on a screening log prior to consent?
Identifiers for both those who enroll and those who do not enroll will be retained beyond the period of recruitment and enrollment of participants

- Data analysis/verification
- Long term follow-up
- Linking to other data

1.8.d Does the research team agree that the requested information will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the study, or for other research for which the use or disclosure of the requested information would be permitted by the HIPAA Privacy Rule?
Yes

1.10 Describe where the consent discussion will occur (check all that apply):

- Private room or area
- By phone
- Online

1.11 Participants and/or their legally authorized representative will have (check all that apply to the consent process and explain process in Question 1.12 below):

- As much time as they desire to consider enrolling in the study, including:
    - An opportunity to thoroughly review the consent materials with knowledgeable members of the research team, and with family and/or friends as appropriate
    - Sufficient time to have all of their questions answered

1.12 Provide a description of the enrollment and consent process in sequential order and address EACH of the bulleted points below:

- Describe each study population separately including control population
- Describe when recruitment and consent materials are used
- Indicate how much time individuals will have to consider participation
- If eConsent will be used to obtain an electronic signature, describe how the eConsent will be presented to participants, how their questions will be answered and how the participant will receive a copy of the final, signed

consent
- Describe the steps that will be taken by the research team to minimize the possibility of coercion or undue influence during the consent process

For Aim 1, participants will include approximately 250 adults who are current smokers from the Greater St. Louis Area. The research team will recruit subjects from the existing COGA study (IRB ID 201105402) and GISC study (IRB ID 201305128), including only those who are current smokers, and will also Epic/MyChart and work with Volunteer for Health (VFH) to identify and enroll individuals who are current smokers and at least 18 years of age. Participants can search for and volunteer to be enrolled in this study or may be identified as potentially eligible for this study. Through word-of-mouth, participants may also provide us with contact information for others who may be interested in participating. Once identified, the principal investigator will send the postal mail recruitment letter or email recruitment letter to potential participants who can then contact the research team to find out more about the study and set up an in-person or electronic consent (e-Consent) and screening visit or phone call, as desired. Informed consent will be obtained from all subjects by a trained research assistant. E-Consent will be conducted in REDCap, and we will email to the participant a link to the e-Consent to complete. Participants will be able to download or print a copy of the consent from REDCap. Participants will have the option to receive a signed copy of their consent emailed to them by the research team via REDCap. During the in-person consent visit or e-Consent, participants will be provided with a copy of the consent form for review and given the opportunity to ask questions prior to agreeing to participate. Participants will be assured that they can choose not to participate or can discontinue participation at any time without losing any benefits for which they would otherwise qualify. Participants for this study will also be invited to consent to be enrolled in the ICTS Genomic Database Protocol (IRB# 201902019). This protocol allows their genetic data, research data and electronic health care data to be placed in the ICTS Genomic Database for future research. Details for the ICTS Genomic Database Protocol are provided in the ICTS Genomic Database IRB.

For the brief V5 follow-up, we will reach out to participants by email, mail, and phone to re-engage participants in completing the phone call visit. Participants will be consented by phone using the Genimp phone consent (attached for review). A member of the research team will review the consent with the participant, answer any questions they have, and ask for their verbal consent to participate in the visit.

As a developmental activity prior to the above research study, two research team members will use a brief script to engage with a convenience sample of individuals walking through various areas of campus, as well as in brief interactions with staff members (e.g., substance abuse counselors) who work at the National Council on Alcoholism and Drug Abuse – St. Louis Area (NCADA). Interactions with NCADA staff may instead take place in meeting rooms at NCADA or at Washington University. We will request that individuals spend 30-60 seconds giving feedback on the design and formatting of a sample template of the personalized genomic results profile, or report card (see attachments). The goal is to maximize clarity, simplicity, appeal, and usefulness of the report card for future participants. We will conduct this activity by setting up a table for people to walk up to, as well as a more mobile, free-range approach of walking around to solicit feedback from other individuals on campus. Participants of this brief activity may include healthcare professionals, academicians, students, patients, or other members of the public. This activity will take place intermittently at various times for up to 6 hours per week for up to 3 weeks, until saturation of design-related themes is reached. The brief script will be used to request participation, and if individuals decline or do not show interest in participating, they will simply be thanked for their consideration.

Participants will include a group of current smokers (n=20) and a group of clinicians and peer support specialists (n=10) in a partnering community health agency (Wellbridge Addiction Treatment and Research). The current smokers will be adults who are inpatient at Wellbridge for substance abuse treatment and the clinicians will be substance abuse counselors who work at Wellbridge. The peer support specialists will include former Wellbridge clients who have successfully maintained their sobriety and now assist with treatment of new patients. A member of the research team will recruit participants for the study by posting flyers (attached for review) at Wellbridge Treatment Center. One poster will be targeted for recruitment of patients who are current smokers and the other will be targeted for clinicians. Individuals interested in participating will be instructed to contact the research team to sign up. The research team member will make it clear that participation in the study is completely optional and is not a requirement of the treatment program and that they can stop their participation at any time. For potential participants who are patients, a member of the research team will verify that they are a current smoker at this time. For potential participants who are patients, a member of the research team will ask them a couple screening questions to verify that they are a current tobacco smoker at this time. Potential participants will be given as much time as they need to decide about participation. Individuals who are interested in participating will then be scheduled for a focus group by a member of the research team.

Prior to the focus group, a member of the research team will provide participants with an information sheet (attached) that describes the main points of the study and what participation involves. Participants will then have the opportunity to ask the research team member any questions they have prior to participating.

For the Aim 2 small scale feasibility trial, current smokers (N=25) and counselors or peer support specialists (n=10) will be recruited and enrolled from the Wellbridge Treatment Center using the procedures described above. Individuals who are interested in participating will be asked to contact a member for the research team. Prior to participation in the small scale feasibility trial, a research team will obtain consent from current smokers at Wellbridge Treatment center using a paper copy of the consent. During the consent process, current smokers will be provided with a copy of the consent form for review and given the opportunity to ask questions prior to agreeing to participate. Current smokers will be assured that they can choose not to participate or can discontinue participation at any time without losing any benefits for which they would otherwise qualify and that their participation in the study is completely voluntary. A signed copy of the consent will be provided to current smokers. Counselors and peer support specialists will be provided with a copy of the clinician consent form to review and given the opportunity to ask questions before being asked to sign.

1.13 Provide a detailed description in sequential order of the study procedures following the consent process - DO NOT cut and paste from the Consent Document.

Describe study populations separately if they will be participating in different procedures

DESCRIBE:

- Control populations, if applicable
- Any randomization, if applicable
- What participants will be asked to do/what happens in the study (in sequential order)
- The time period over which procedures will occur
- Long-term follow-up and how it occurs

For Aim 1, via in-person or remote (phone or Zoom) interviews, we will ask baseline questions about smoking behaviors and genetic knowledge and then offer genetic testing to the participant. As an objective measure of acceptability, we will track the proportion of eligible participants who decline the genetic testing; this will inform how many individuals must be targeted to achieve desired samples in future research. This interview will take approximately 20 minutes. During the in-person visit, participants will contribute DNA via saliva sample; during remote visits, participants will contribute DNA via saliva sample using a 23andMe kit that was mailed to them. We will give each participant a tube to collect each saliva sample. Participants will spit into the tube until there is enough saliva in the tube. This typically takes 1 to 5 minutes. The research team (for in-person visits) or the participant (for remote visits) will send the saliva samples to 23andMe for genetic testing and analysis in a CLIA certified laboratory. Saliva samples sent to 23andMe will be registered via an on-line account created by the participant on the 23andMe website using their personal email address. Participants must provide first and last name, sex and date of birth to register their saliva sample. During the in-person or remote visit, participants will register their sample with 23andMe, including ancestry and health information, and will authorize the research team to receive their results but will not automatically agree to other research through 23andMe. A member of the research team will assist participants in creating an online account through the 23andMe website. Participants can choose whether or not they want 23andMe to store their saliva sample. A member of the research team will show participants this option on the 23andMe website while helping them to register their sample. We will ask participants to log into their 23andMe account and give permission for the research team to download their genetic data and use it for research purposes. We will use these data to create a personalized genetic profile (RiskProfile) specific to participants' smoking-related genetic risk and likely responsiveness to medication. The data used for genomic profiles that we will create are part of the standard data generated by 23andMe. We will then randomize participants to one of two groups--Intervention (receive RiskProfile) or Control (receive brief cessation counseling and then receive RiskProfile at end of study)--and ask participants to return for a separate in-person or remote visit to receive their personalized genetic profile or brief cessation counseling and respond to the interview questions during that in-person or remote visit. The personalized genetic profile will be referred to as a genetics-informed "RiskProfile" and was refined through the developmental/design-oriented study with multiple stakeholder groups. Depending on the specific genetic profile of the participant, the RiskProfile will slightly differ; for example, for some, it will say "at very high risk", for some, it will say "at high risk", and for some, it will say "at risk". This will enable us to receive important feedback about the return of results procedure within the context of recently receiving personalized genetic results profile. These participants will then be asked to participate in a 30-day follow-up and then a 6-month follow-up, both comprising a 20-minute interview by phone or Zoom to examine changes in attitude and behavior as a result of receiving their personalized genetic results profile. Control group participants will receive their RiskProfile during the 6-month follow-up assessment. For the remote study, each participant's unique RiskProfile will be stored in the participant's unique folder on WUSTL Box platform and viewable to that participant and the research team only. Participants will also be asked to do a brief 10-15 minute phone follow-up approximately 18 months after their intervention to see if changes in attitude and behavior as a result of receiving their personalized genetic results profile have persisted.

Interviews will be audio recorded, and both audio and video recorded for Zoom interviews, for purposes of quality monitoring and assurance and to serve as a backup in case of technical difficulties (e.g., data entry software crash) during the interview that would risk data loss.

For the developmental activity to gather design-related feedback on the report card template, we will ask participants to review the report card and then share ideas on the clarity, simplicity, appeal, and usefulness of the sample report card, as well as how the design or formatting could be improved. Finally, we will ask a non-identifying question about whether the individual is a professional in the medical field and, if so, their general role in this field.

These campus-based interactions and interactions with NCADA staff (e.g., substance abuse counselors) will not be audio recorded.

Description of 23andMe and 23andMe Service: 23andMe, Inc. is a leading personal genetics company. Founded in 2006, the mission of the company is to help people access, understand and benefit from the human genome. The 23andMe® Service is a genetic service available directly to customers. The 23andMe Service includes personalized genetic reports that meet FDA standards for being scientifically and clinically valid and access to proprietary interactive tools to share, compare and discover with family and friends. The service is not intended to diagnose any disease. As noted in the 23andMe Privacy Statement (www.23andme.com/about/privacy/), 23andMe employs software, hardware and physical security measures to protect the computers where customer data is stored, as well as robust authentication methods to access their systems. 23andMe customers' personal information and genetic data are stored in physically separate computing environments, which is in line with the industry standards for security.

AIM 2:
For Aim 2, we will engage current smokers (n=20) and clinicians and peer support specialists (n=10) in a partnering community health agency (Wellbridge) to adapt the RiskProfile for use in real-world community-based settings. Focus groups and participatory design activities will be used to guide the adaptation of the existing RiskProfile. We will conduct two focus groups with current smokers and counselors each to garner additional feedback on the RiskProfile intervention. Focus groups will attend to the feasibility and acceptability of the content and format of the version of the intervention in which participants engaged, including aspects of the intervention messaging that require clarification or that may lead to unintended consequences (e.g., negative behavioral or psychological reactions). All relevant intervention materials, including a sample RiskProfile, the standardized verbal script, and procedural manual, will be

reviewed by design participants for their relevance and fit within the community setting. Additionally, participants will be presented a de-identified recording of the RiskProfile being delivered to gather their feedback on the process. Finally, focus group participants will be presented an experimental version of the RiskProfile "PrecisionTx" for feedback. This version provides a hypothetical specific recommendation of medication based on genetic/metabolic factors. We will seek feedback on the concept of including specific recommendations of medication as part of the genetically-informed tool. The attached "GENIMP Aim 2_Focus Group Guide" will be used as a guide for the focus groups.

Focus groups will be conducted using elements of design thinking (e.g., human-centered design) which emphasizes (1) developing empathy for target end-users (i.e., current smokers not yet ready to quit), (2) radical collaboration with input from a diverse set of perspectives, and (3) rapid prototyping by iteratively generating and vetting ideas of refinements to the tool in collaboration with participants (i.e., both current smokers and substance abuse counselors). Although the primary mode of delivery to be explored will be in-person sessions with substance abuse counselors, we will also explore the potential feasibility of more scalable intervention delivery platforms, including postal mail and web-based tools to deliver the intervention content. We will also examine perceptions of communication framing strategies among current smokers with relatively high and low genetic risks for smoking-related diseases.

A second group of current smokers (n=25) and counselors and peer support specialists (n=10) will be engaged in a small-scale feasibility trial of the genetic testing and intervention delivery protocol. Using the same study procedures in Aim 1 to guide participants to create a 23andMe account and provide their saliva sample via genetic testing, the second group of current smokers will undergo genetic testing while they are inpatient at Wellbridge and then be invited to receive their RiskProfile at the next counseling session via Zoom or in-person at Wellbridge, which will be delivered by a counselor or peer support specialist at Wellbridge, once their genetic data is ready.

Using structured assessments (attached for approval), we will assess the acceptability and feasibility of the RiskProfile using quantitative and qualitative metrics for both patients and clinicians. We will use modified versions of the Aim 1 assessments, the Acceptability of Intervention Measure (AIM), and the Feasibility of Intervention Measure (FIM). The AIM (4 items measuring approval, appeal, and favorability of the RiskProfile) and FIM (4 items measuring usability, intuitiveness, and comprehensibility) is measured on a 5- point scale (Completely disagree=1.0; Completely agree=5.0).

1.14 Will participants be randomized?
Yes

1.15 Will any of the following be used to collect information from the participant or others?

- Screening questions or screening/eligibility questionnaires
- Surveys
- Questionnaires
- Stimuli
- Any other written assessments

Yes

Attachment Name	Category	Version	Date Attached
Aim 2_V1 Assessment_07142023.docx	Subject Data Collection Instruments	1	07/14/23
Aim 2_Clinician V2 Assessment.docx	Subject Data Collection Instruments	1	07/14/23
Eligibility Screener for Focus Groups.docx	Subject Data Collection Instruments	1	10/07/22
V5 Assessment_7-10-23.docx	Subject Data Collection Instruments	4	07/11/23
V1 Assessments_08052021.docx	Subject Data Collection Instruments	15	08/05/21
Aim 2_V2 Assessment_071423.docx	Subject Data Collection Instruments	1	07/14/23
Open Ended Interview Questions_082620.docx	Subject Data Collection Instruments	7	08/28/20
Eligibility Script for GENIMP2_011421 (1).docx	Subject Data Collection Instruments	4	01/14/21
V4 Assessments_7-10-2023.docx	Subject Data Collection Instruments	12	07/11/23
Locator Form.docx	Subject Data Collection Instruments	1	06/25/19
Script for Report Card Design Feedback_071919.docx	Subject Data Collection Instruments	5	07/22/19
GENIMP Aim 2_Focus Group Guide Final.docx	Subject Data Collection Instruments	1	10/07/22
V2 Assessments_7-10-23.docx	Subject Data Collection Instruments	17	07/11/23
V3 Assessments_7-10-23.docx	Subject Data Collection Instruments	17	07/11/23

1.16 Does this project involve creating any audio, video, or photographs?
Yes

1.17 Does the study include any form of deception (e.g., providing participants with false information, misleading information, or withholding information about certain study procedures)?
Examples:

- Procedure includes a cover story that provides a plausible but inaccurate account of the purposes of the research.
- Participants will be provided with false information regarding the particular behaviors of interest in the research.
- Procedures include a confederate pretending to be another participant in the study.
- Participants will be told that the research includes completion of a particular task, when in fact, that task will not be administered.
- Study is designed to introduce a new procedure (or task) that participants are not initially told about.

No

1.18 Indicate any payments or reimbursements to participants (check all that apply)

- Cash
- Check
- Gift or Debit Card
- Forte Debit Card

1.19 Does this study have a plan to have an individual or committee review combined data from all participants on a periodic basis (such as summary or aggregate safety and/or efficacy data)?
No

1.20 What have you done to minimize any risks?

- No forseeable risks

1.21 What are the potential benefits related to this project for:

- the participant (if any)
- benefits to society (if any)

Participants (adults who smoke) will have the direct benefit of receiving their individual genomic results profiles which could potentially improve their health behaviors (e.g., reduce tobacco use) and effectiveness of their treatment plans. Participants will receive genetic testing by 23andMe at no cost to them. From 23andMe they will receive genetic ancestry results and health results including carrier status reports, trait reports, and wellness reports.

The potential benefits to society are significant if the proposed research increases understanding of the best approaches to integrating genomic findings for substance use disorders into diverse settings. It is possible that the results of this study could be used to improve smoking and substance use disorder prevention and treatment strategies.

1.22 Provide a summary of the analysis methods you will use, including, if applicable, the data points or outcomes you will analyze.
For Aim 1, we will assess the acceptability of using genomic results (i.e., % agreeing to genetic testing, sharing results with others, recalling personal genomic results) and test whether smoking behaviors (frequency, heaviness) change more following delivery of the RiskProfile intervention than following brief cessation counseling. We expect higher rates of smoking cessation and reduction the Intervention group, particularly for those who accepted and recall their genomic results and whose health-related cognitions were altered (e.g., increased perceptions of disease risk, cessation benefits, value of cessation medications, self-efficacy). We will also examine whether the acceptability and recall of their genomic data for smoking cessation differ by age, sex, race, education level, or initial smoking behaviors. Given prior research on disparities in use of genomic results, we anticipate that acceptability and recall of results, or other mechanisms of behavior change, may be lower in African Americans, men, and heavier smokers. We will conduct multiple linear regression analyses to determine the extent to which race, initial smoking heaviness, or level of genetic risk predict acceptability and recall of genomic results, and whether receiving the RiskProfile predicts smoking cessation or reduction.

For Aim 2, we will identify key themes that will guide the adaption and improvement of the RiskProfile to deliver the tool in real-world settings. Adapting the RiskProfile will include data points consisting of refining the content, format, and delivery mode.

1.23 Provide the rationale or power analysis to support the number of participants proposed to complete this study.
Prior samples of a similar size and nature have allowed for adequate generalizability and power to detect relationships between variables of interest, including the ability to detect moderating relationships through interaction analyses. The current study is expected to mirror this prior experience, yielding adequate validity and range of responses. However, this study stands on its own as a pilot project, and any challenges related to power analysis do not negate the usefulness of this small-scale project to demonstrate proof of concept, establish the feasibility of returning genomic results to patients and physicians in a clinical setting, and provide the necessary rationale to test these implementation approaches with larger samples in future research.

1.25 Will any data from this project be stored for use in future research studies?
Yes - contribution for future use is optional

1.26 Does this project involve the collection or use of biological samples or genetic data?

Yes

1.26.a Will genetic/genomic research occur as part of this study?
Yes

1.26.b Do you plan to return any genetic/genomic results of testing generated as part of this study to participants (including either primary or incidental findings)?
Yes

1.26.c Attach a return of results plan.

Attachment Name	Category	Version	Date Attached
Return of Results Plan_082620.docx	Return of Results Plan	7	08/28/20

1.26.d Will biologic samples or genetic data be stored for future research?
No

1.26.f Will participants be able to request at a later time that the biological samples or genetic data be destroyed?
No

1.27 Are you requesting institutional certification to contribute human data or samples to a repository or database for broad sharing (public or restricted access)?
No

2. Participants

2.1 Will there be any adult participants?
Yes

2.1.a How many adult participants do you expect to consent or enroll under a waiver for this project?
600

2.1.b What is the age of the youngest adult participant?
18.0

2.1.c What is the age of the oldest adult participant?
No age limit

2.2 Will there be any minor participants?
No

2.3 Will there be any emancipated minor participants?
No

2.7 Do you plan to recruit/enroll non-English speaking people?
No

2.8 Do you propose to enroll any of the following in this study as participants?

- Employee of the PI or employee of a research team member
- Individual supervised by PI or supervised by member of research team
- Individual subordinate to the PI or subordinate to any member of the research team
- Student or trainee under the direction of the PI or under the direction of a member of the research team

No

2.9 Is this project about pregnant women?
No

2.10 Will this project involve fetuses?
No

2.11 Does this project involve the use of fetal tissue from any source?
No

2.12 Does this project recruit adult participants who may be incompetent or have limited decision-making capacity on initial enrollment into the study?
No

2.13 Does this project involve prisoners as participants?
No

3. Performance Sites

3.1 Indicate type of site(s) where research will occur (check all that apply):
- Hospital
- Academic Institution

3.2 Where will project procedures take place (check all that apply)?
- School of Medicine
- Danforth Campus
- Barnes Jewish Hospital (BJH)
- Barnes Jewish West County
- Barnes Jewish St. Peters
- Boone Hospital Center
- Christian Hospital NE
- Goldfarb School of Nursing
- St. Louis Children's Hospital
- U.S. off-campus - Meetings with National Council on Alcoholism and Drug Abuse – St. Louis Area (NCADA) staff to get feedback on the report card template may take place at the NCADA office off-campus, for convenience of study participants. Focus groups will take place at Wellbridge Addiction Treatment and Research to get feedback on the RiskProfile (letter of support attached).

3.3 Is this project also being conducted by other researchers at their own sites (e.g. a multi-site collaborative project)?
No

4. Drugs/Devices

4.1 Does this project involve:

	Yes	No
Drug(s) (including radioisotopes)	○	◉
Use of contrast agent(s)	○	◉
Other substance injected, ingested, or applied to the body	○	◉
Testing a Device (Including companion devices, software, mobile health devices, assays, not FDA approved or outside approved indications, etc.)	○	◉
Combination product (as determined by the FDA - must have FDA documentation identifying this as a combination product)	○	◉

4.2 Does this project involve a drug washout (asking participant to stop taking any drugs the participant is currently taking)?
No

4.3 Will any participants receive a placebo in place of standard therapy?
No

5. Privacy & Confidentiality

5.1 Indicate your plans to protect the privacy interests of the participants during the conduct of the study (check all that apply):
- Only the minimum necessary private information is collected for the purposes of the study
- Any procedures or interventions conducted as part of the study will be conducted in private setting to the extent possible
- Recruitment/consent will occur in a private setting
- Participants will be able to ask questions in a private setting

5.2 Are you collecting or using the Social Security Number of any participants for any purpose?
Yes

5.2.a Provide the intended usage of SSN:
- To provide compensation to participants

5.3 Project uses paper or hard copy consents, surveys, data collection forms, research subject binders, or other hard copy materials (check all that apply):
Yes
- All materials are stored in secured environment
- Access is limited to research team members only

5.4 Project collects, stores and/or transmits electronic data on mobile devices, desktop computers, servers including cloud servers, email, or any other information in electronic form (check all that apply):
Yes

- Data are encrypted
- Data in Redcap
- Data in Survey Monkey
- Data in Qualtrics (Use of Qualtrics is not allowed when collecting Protected Health Information (PHI) or Personally Identifiable Information (PII) (Information Security Requirements).
- Password protected
- Access is limited to research team only

5.5 Project collects or uses biologic specimens (check all that apply):
Yes

- Transported securely/shipped with tracking mechanism
- Stored in secured environment
- Coded and the identifiers or key is stored separately from the data

5.6 Identify any additional protections in place for data and or samples (check all that apply):

- Formal research staff training process