Facilitating the Implementation of Population-wide Genomic Screening across Diverse Populations and Settings (FOCUS): A Protocol for an Implementation Mapping Study to Identify Best Practices for Implementing Population-wide Genomic Screening Programs

Caitlin Allen, Jarrod Marable, Kimberly Foss, Cason Whitcomb, Ceborah Cragun, Adam Buchanan, Miranda Hallquist, Nathaniel Baker, Rebecca Bosch, Derek Craig, Maria Fernandez, Chanita Hughes-Halbert

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Caitlin Allen[1] PhD, MPH; Jarrod Marable[1] BSc; Kimberly Foss[2] CGC; Cason Whitcomb[2] BSc; Ceborah Cragun[3] PhD, CGC, MS; Adam Buchanan[4] MS, MPH, CGC; Miranda Hallquist[4] LGC; Nathaniel Baker[1] MS; Rebecca Bosch[2] MPH; Derek Craig[5] PhD; Maria Fernandez[5] PhD; Chanita Hughes-Halbert[6] PhD

[1] MUSC Hollings Cancer Center Charleston US
[2] University of North Carolina Hospitals Chapel Hill US
[3] University of South Florida Tampa US
[4] Geisinger Health System Danville US
[5] The University of Texas Health Science Center at Houston Houston US
[6] University of Southern California Los Angeles US

Corresponding Author:
Caitlin Allen PhD, MPH

MUSC Hollings Cancer Center
86 Jonathan Lucas St
Charleston
US

Abstract

Background: Population genomic screening (PGS) offers great promise in identifying the 1-2% of the population that carries a pathogenic variant that puts them at elevated risk for serious, yet manageable genetic conditions such as Hereditary Breast and Ovarian Cancer Syndrome, Lynch Syndrome, and Familial Hypercholesterolemia.1-5 Rapidly decreasing sequencing costs, endorsement of PGS by national bodies, and attention to precision medicine applications have accelerated the spread of PGS programs.6,7

To date, no clear guidelines or strategies exist to support the equitable implementation of PGS. Contextual factors, including program-level procedures, organizational structure, and characteristics of the patient population, influence implementation of these large-scale PGS initiatives. Research by our team and others has identified factors impacting the implementation of PGS, including engagement of key stakeholders and champions, implementation of PGS as a research program or clinical service, and availability of genetic counseling services.8-11 Given the anticipated growth of PGS programs, practice-based research is needed to better understand these and other factors to inform equitable implementation of PGS programs.11

In its report, the Genomics and Population Health Action Collaborative emphasized the importance of engaging diverse populations in PGS, including racial and ethnic minority groups, people living in rural communities, and those with lower education or income.12-14 Diverse populations are at risk of being left behind in the implementation of PGS if efforts are not oriented to explicitly address health equity in genomics.15 Current PGS implementation inequities limit the ability for genomics-based research and genetics services to capture genetic diversity from a broad range of populations to support the development of effective precision prevention strategies and therapies for individuals of all backgrounds.13,14,16,17 Implementation science contains tools to integrate health equity and genomic medicine to ensure implementation of PGS does not exacerbate inequities.

To help facilitate growth of PGS programs and enhance recruitment and retention of representative populations into genomic initiatives, we propose to identify best practices for PGS implementation and develop and test a freely available, online, multicomponent implementation guide (FOCUS toolkit). Our project's specific aims are as follows: 1) Describe differences in processes, barriers, and facilitators to equitable implementation across sites at various stages of PGS implementation, 2) Develop

and package implementation strategies into the FOCUS toolkit to support the equitable implementation of PGS programs, 3) Evaluate the impact of the FOCUS toolkit on improving implementation of PGS in diverse populations and settings using a hybrid stepped wedge cluster randomized trial. This project will establish a gold standard approach for equitably integrating PGS and offer the field generalizable methods and knowledge about PGS implementation. In this paper we describe the planned approach for achieving these aims and highlight how this approach is intended to advance the goal of implementing equitable PGS programs that improve population health.

Objective: With a focus on health equity and stakeholder engagement, the FOCUS toolkit will establish a standardized approach to scaling PGS programs across diverse populations and settings, ensuring genomics benefits are accessible to all.

Methods: Overall Study Design and Conceptual Model
We will use an implementation mapping (IM) approach to complete the FOCUS project (Figure 1).Once an organization has made the decision to implement an evidence-based intervention (e.g., PGS), use of IM supports the integration of this program in real-world settings.18 IM is a structured framework involving five steps that incorporates theory, empirical evidence, and diverse perspectives with the target population to iteratively guide decision making at each step.18 We incorporate a health equity focus in genomic medicine as described by the NHGRI in 2019 throughout all components of the IM process, the global applicability of genomic knowledge, fair and even access to genomic services such as testing and counseling, and unbiased implementation of genomic medicine.15

Consolidated Framework for Implementation Research integrated with the Health Equity Implementation Framework (CFIR/HE)
The Consolidated Framework for Implementation Research (CFIR) integrated with health equity (HE) helps create a robust approach for advancing equitable implementation. CFIR/HE includes multilevel determinants of implementation and factors that inform differences in individuals' access to health services, including key factors at the patient, provider, and system levels.19,20 When combined with CFIR, the HE framework, which focuses on identifying and addressing structural and systemic barriers that perpetuate health disparities, supports a nuanced understanding of determinants of implementation. The CFIR/HE framework will be used to guide Task 1 of IM.

Reach, Effectiveness, Adoption, Implementation, Maintenance framework for Health Equity (RE-AIM/HE)
The RE-AIM/HE framework emphasizes the five dimensions of reach, effectiveness, adoption, implementation, and maintenance to evaluate implementation across diverse settings. Integration of HE adds and explicit focus on identifying and addressing health disparities by incorporating structural, cultural, and systematic factors that influence equitable implementation, which can help inform the evaluation and impact of new programs such as PGS across diverse populations and settings.21,22 The RE-AIM/HE framework will be used to guide Task 5 of IM.

PGS Sites
We will work with two distinct sets of PGS sites: FOCUS Design Sites and FOCUS Test Sites. The FOCUS Design Sites will be part of Aim 1, which will involve identification and synthesis of evidence about the implementation processes, barriers, and facilitators for PGS implementation. We will include 10 diverse organizations that can speak to experiences across implementation stages: exploration, preparation, implementation, sustinment.23 We will also work with FOCUS Test Sites to rigorously evaluate the FOCUS toolkit for improving the implementation of PGS. These sites will also be at various stages of implementation. We plan to include 12 organizations as FOCUS Test Sites.23,24

Implementation Mapping (IM) Advisory Panel
Stakeholder engagement is a critical part of implementation mapping (IM) to ensure an equity-focused approach to the project and will support all aspects of this work. Thus, we have organized an Advisory Panel of 13 individuals consisting of public health agency members, community members, patient groups, a private population screening company, primary care, and clinical stakeholders that will be engaged throughout each Aim. The group will meet on a quarterly basis and support the study team in prioritizing, designing, and conducting research throughout the duration of the project.

Study Aim 1: Describe differences in processes, barriers, and facilitators to equitable implementation across sites at various stages of PGS implementation
The first Aim of the FOCUS study is aligned with IM Task 1. We will conduct a qualitative needs assessment among ten PGS programs (i.e. FOCUS Design Sites) at various implementation stages (exploration, preparation, implementation, and sustainment) guided by CFIR/HE.19,20 Emerging Sites are defined as institutions in the planning and development stages of PGS program implementation. Implementing Sites are defined as institutions that have begun conducting screenings and are building out their programs. Sustaining Sites are defined as sites that have been implementing their PGS program for over a year. These 10 sites will be enrolling either clinical or research PGS cohorts.22,25 The CFIR/HE framework will be used to create an interview guide to identify barriers and facilitators of implementing PGS.

The needs assessment will be conducted via interview(s) of implementation team members (ITM), PGS patients (PAT), and laboratory sites. Participants will be assigned a study identification number and all identifying data elements (e.g., name, dates) will be removed. The questions asked during the interviews have been adapted from CFIR and agreed upon by the FOCUS study team and the IM Advisory Panel. Interview questions will be specific to the participants (e.g., IMP, PAT, laboratory sites).

As interviews are completed, we will begin extracting qualitative data from the transcripts and audio/visual recordings, via Microsoft Teams for analysis. We will use rapid qualitative data analysis methods to code interviews for each site.26,27 We will complete Transcript Summaries for each interview that match interview question responses to CFIR/HE domains and sub-domains. These Transcript Summaries will be utilized in two subsequent qualitative data analysis steps – Process Mapping and Data Matrix Heat Mapping - that have been described by Salvati et al.28 Briefly, process maps will visually detail the PGS implementation process and workflow described by each team member during their interview. Upon completion of all interviews at the respective site, we will conduct member checking among these interviewees to reconcile discrepancies or omissions in the process maps. This will allow us to create a final aggregate process map for each site.

Site-level data matrix heat maps will be generated through an iterative process that involves mapping interview data to each of the CFIR/HE factors within a spreadsheet and then color coding each construct to represent the extent to which it serves as a facilitator or barrier for PGS implementation at that site. Site-level heat maps will then be consolidated and combined to allow for cross-site comparisons and the identification of patterns of factors that are similar and different across sites.

Study Aim 2: Develop and package implementation strategies into the FOCUS toolkit to support the equitable implementation of PGS programs

The second Aim of the FOCUS study is to develop the FOCUS toolkit consisting of equity-focused implementation strategies, materials, and protocols for implementing and improving PGS programs. This Aim will cover IM Tasks 2-4.

First, we will identify outcomes and objectives by working with the IM Advisory Panel to prioritize the facilitators, barriers, and inefficiencies identified in IM Task 1 by importance, health equity relevance, and changeability. This will allow us to identify outcomes (i.e., what needs to be added or changed to improve PGS implementation) and objectives (i.e., how we will address the identified outcomes) (IM Task 2).

We will work with the IM Advisory Panel during Aim 2 to select evidence-based strategies to address the facilitators, barriers, and inefficiencies of PGS implementation (e.g., information chunking, guided practice, etc.). Using the CFIR-ERIC matching tool (IM Task 3),29 which aligns ERIC strategies with CFIR factors identified in Task 1. This will allow us to identify appropriate implementation strategies for each priority implementation need,30 including the need for equity in access to and quality of PGS. The study team will host a feedback session with the IM Advisory Panel on these potential methods and strategies at the conclusion of Task 3 and integrate feedback from the panel based on this session.

Ultimately we will draft implementation strategy protocols and develop materials to package our implementation strategies into the online FOCUS Toolkit for PGS (IM Task 4). Once the FOCUS toolkit draft has been developed, we will host a feedback session with the IM Advisory panel to capture and integrate recommendations. Finally, we will use a human centered design approach to prototype and refine the FOCUS toolkit with our FOCUS design sites.731 Engaging program champions and implementation team members from the eight FOCUS design sites, we will conduct a live rapid prototyping and iterating session (non-statistical approaches) to refine our proposed protocols and materials. Validated measures will be used to assess acceptability, appropriateness, and feasibility of using the FOCUS toolkit.32,33 Through these live sessions we will collect feedback until we have reached consensus among the IM Advisory Panel of the planned FOCUS toolkit materials. We will prioritize strategies that were common across PGS sites and that aim to achieve equity in PGS participation and implementation.

Study Aim 3: Evaluate the impact of the FOCUS toolkit on improving implementation of PGS in diverse populations and settings using a hybrid stepped wedge cluster randomized trial

The final Aim of the FOCUS study is to evaluate the impact of the FOCUS toolkit on Reach, Effectiveness, Implementation, Adoption, Maintenance (RE-AIM), and HE outcomes for PGS in 12 FOCUS Test Sites with diverse populations and settings. The Stepped-Wedge Cluster Randomized Trial design to evaluate the utility of the FOCUS toolkit for improving outcomes among the 12 FOCSU test sites).21 This approach will allow us to assess improvements in RE-AIM/HE outcomes among sites at varying stages of implementation: exploration, preparation, implementation, and sustainment. Because sites in the exploration phase will not have begun implementing PGS prior to using the FOCUS toolkit (no baseline/pre-FOCUS toolkit data about the PGS program), they will be randomized 1:1 to either control (no FOCUS toolkit) or intervention (FOCUS toolkit) conditions using a parallel design. The eight existing sites will be actively implementing or sustaining their PGS programs (have baseline/pre-FOCUS toolkit data) and will be randomized 1:1 to one of four possible time steps every three months for a

21-month implementation period (steps at 3, 6, 9, and 12 months) (Figure 2). This hybrid stepped wedge cluster randomized trial design is a pragmatic approach that will allow us to simultaneously assess RE-AIM/HE outcomes across a representative and generalizable sample of PGS sites with varying amounts of baseline program implementation data and assessment of correlates of post-toolkit use outcomes.34-36

Quantitative data about RE-AIM/HE outcomes will be collected using three tools: 1) PGS Program Data Collection Form, 2) Stakeholder Surveys, and 3) Toolkit Tracking Data (Table 1). The PGS Program Data Collection Form will be completed monthly by each site using a REDCap (Research Electronic Data Capture) form designed by the study team. The form will assess metrics related to the implementation outcomes of Reach, Effectiveness, and Adoption. Reach, or how well the PGS site recruits the intended audience, will be measured by the total number of people recruited to participate in the PGS program.37 Effectiveness will be assessed based on how well the PGS program is achieving its intended public health outcome of identifying individuals with pathogenic variants in genes associated with Tier 1 conditions. Our primary measure of Effectiveness is the proportion of eligible individuals tested. We will also evaluate rate of positive findings (number of positive results returned/number tested). Adoption will be assessed based on the number of providers who participate in the PGS program at each site out of the total number of providers eligible to participate at the site. The Stakeholder Surveys will be distributed to implementation stakeholders at each site prior to beginning to use the PGS toolkit, three months after starting to use the toolkit, and at the conclusion of using the toolkit. These will capture data to assess RE-AIM/HE outcomes of Implementation and Maintenance. Implementation assessment will include acceptability, appropriateness, and feasibility of PGS. These will be captured using the Acceptability of Intervention Measure, Intervention Appropriateness Measure, and Feasibility of Intervention Measure, where the Intervention is defined as PGS.33 To assess Maintenance, we will ask stakeholders to complete the Program Sustainability Assessment Tool to rate the PGS program on the presence of elements associated with long-term sustainability. We will also capture fidelity to the FOCUS toolkit through the Toolkit Tracking Data, which will include website metrics of 1) FOCUS test sites' registered users and 2) the number of times the FOCUS toolkit was opened and number of pages or components of the toolkit are visited.

Our primary research question is: Does the use of the FOCUS toolkit improve PGS implementation and effectiveness. RE-AIM/HE outcomes among the eight existing sites (i.e., implementation and sustainment sites) that are actively implementing or sustaining PGS using generalized mixed effects regression models (GLMM).38 The primary temporal variable for the analysis of RE-AIM/HE outcomes is the time step; all participants enrolled during a given time step will be retained in that step regardless of study completion date. Statistical analysis will be based on the principle of intention to treat. The step at which a participant was enrolled in the PGS program will be used as the treatment indicator. At the participant level, a mixed effects logistic regression model will be used to estimate the impact of sites' use of the FOCUS toolkit strategies on the likelihood of participants returning for sample collection. Fixed effects of study time will be included in the model to adjust for secular temporal events throughout the study and random site effects included to account for correlation of participants within site over time. Participant-level baseline data will be assessed for association with study outcomes and when significant, included in adjusted models. Between-site sample size imbalance may impact the study power and estimation bias, thus initial models will be fit using Fay and Graubard bias corrected sandwich variance estimator.39,40 Period-specific recruitment totals will be assessed at the site level utilizing a gaussian distribution with an identity link. We will use GLMM to assess the impact of the FOCUS toolkit among the four emerging sites that are part of the parallel design (FOCUS toolkit use vs no FOCUS toolkit use). In addition to addressing primary study outcomes, models including post-intervention data from all sites will be assessed to determine if newly emerging PGS sites differ across outcomes as compared to existing sites. Generalized linear mixed effects regression will be assessed with an indicator of site implementation stage to assess post-intervention RE-AIM/HE outcomes.

All RE-AIM/HE outcomes will also be assessed qualitatively through in-depth Stakeholder Interviews conducted with five implementation stakeholders (e.g., program champion (n=1), genetic counselor (n=1), organizational leadership (n=1), and implementation teams (n=2)) per site (n=60) at the conclusion of the implementation period. Reach will include questions to understand whether all populations are equitably reached, who is not reached, and how the FOCUS toolkit supports better reach among diverse populations. Effectiveness will focus on whether program impact is equitable across groups, whether sample collection and findings are different across sociodemographics. Adoption will be assessed by asking about the uptake of PGS among clinicians and other key stakeholders within their setting. Implementation will be assessed by asking how PGS has been implemented, facilitators and barriers to implementation, and ways that the FOCUS toolkit helped the site overcome these barriers. To assess Maintenance, we will ask stakeholders about the ways they plan to sustain the PGS program long-term and plans for institutionalization of the FOCUS toolkit.41

A summary will be created immediately following each interview. These summaries will allow for high-level analysis during data collection, facilitate initial codebook development and reduce the number of new codes requiring re-coding during data analysis. Coding will be conducted using an a priori codebook guided by the RE-AIM/HE and CFIR (for contextual factors that are described as impacting RE-AIM/HE outcomes. After initial review of this codebook, new codes will be added to the other

relevant sections of the transcript text not fitting a priori codes. A team-based approach will be used to refine the codebook with discrepancies resolved by the study team. All coding will occur in MaxQDA and completed by two coders. Qualitative and quantitative results will be reviewed together, and triangulation of data will occur using a rapid analytic coding matrix.42-44 This will allow us to better understand how the PGS programs have changed over time and to what extent the FOCUS toolkit was adapted and/or used in accordance with the protocol.

Results: n/a

Conclusions: n/a

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Megan Roberts
University of North Carolina
Chapel Hill, NC USA

Jarrod Marable
Medical University of South Carolina
Charleston, SC USA

Kimberly Foss
University of North Carolina
Chapel Hill, NC USA

Cason Whitcomb
University of North Carolina
Chapel Hill, NC USA

Deborah Cragun
University of South Florida
Tampa, FL

Adam Buchanan
Geisinger Health System
Danville, PA USA

Miranda Hallquist
Geisinger Health System
Danville, PA USA

Nathaniel Baker
Medical University of South Carolina
Charleston, SC USA

Becca Bosch
University of North Carolina
Chapel Hill, NC USA

Derek Craig
University of Texas Houston
Houston, TX USA

Maria Fernandez
University of Texas Houston
Houston, TX USA

Chanita Hughes-Halbert
University of Southern California
Los Angeles, CA USA

Caitlin Allen (contact, allencat@musc.edu)
Medical University of South Carolina

Charleston, SC USA

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Contributions to the Literature:

- This study addresses a critical gap in implementation science by developing and testing an equity-centered implementation toolkit to guide best practices for implementing population-wide genomic screening (PGS).
- By examining barriers and facilitators across diverse sites, this work identifies key contextual factors, such as organizational structures and processes, that influence equitable PGS implementation.
- The FOCUS project highlights the importance of stakeholder engagement in designing implementation strategies to ensure genomics benefits reach underrepresented populations.
- Through its hybrid stepped-wedge cluster randomized trial, the study advances methods for evaluating the scalability and sustainability of PGS programs.
- The findings contribute actionable insights to support the equitable adoption and maintenance of PGS initiatives in diverse healthcare settings across the US.

Abstract

Background: Population-wide genomic screening (PGS) for genetic conditions such as Hereditary Breast and Ovarian Cancer Syndrome, Lynch Syndrome, and Familial Hypercholesterolemia presents opportunities to reduce morbidity and mortality among the 1-2% of the population at elevated risk for these serious, preventable diseases. With decreasing sequencing costs and growing support from national bodies, there are increasing numbers of PGS programs in the US. However, guidelines and strategies to support implementation are limited, especially regarding equitable access to PGS. Contextual factors, such as organizational structures and processes impact PGS implementation, often failing to benefit underrepresented populations. To address these challenges, we are completing the FOCUS project, which will develop and test a freely available, equity-centered online implementation toolkit to guide best practices for implementing PGS. **Methods:** The FOCUS project aims to 1) examine barriers and facilitators of equitable PGS implementation at sites at various stages of implementation, 2) develop implementation strategies with input from a diverse advisory panel and package them into the FOCUS toolkit, and 3) evaluate the toolkit's impact on improving PGS reach, effectiveness, adoption, and maintenance using a hybrid stepped-wedge cluster randomized trial design. **Discussion:** With a focus on health equity and stakeholder engagement, the FOCUS toolkit will establish a standardized approach to scaling PGS programs across diverse populations and settings, ensuring genomics benefits are accessible to all.

Keywords: population genomic screening, health equity, implementation science

Background

Population genomic screening (PGS) offers great promise in identifying the 1-2% of the population that carries a pathogenic variant that puts them at elevated risk for serious, yet manageable genetic conditions such as Hereditary Breast and Ovarian Cancer Syndrome, Lynch Syndrome, and Familial Hypercholesterolemia.[1-5] Rapidly decreasing sequencing costs, endorsement of PGS by national bodies, and attention to precision medicine applications have accelerated the spread of PGS programs.[6,7]

To date, no clear guidelines or strategies exist to support the equitable implementation of PGS. Contextual factors, including program-level procedures, organizational structure, and characteristics of the patient population, influence implementation of these large-scale PGS initiatives. Research by our team and others has identified factors impacting the implementation of PGS, including engagement of key stakeholders and champions, implementation of PGS as a research program or clinical service, and availability of genetic counseling services.[8-11] Given the anticipated growth of PGS programs, practice-based research is needed to better understand these and other factors to inform equitable implementation of PGS programs.[11]

In its report, the Genomics and Population Health Action Collaborative emphasized the importance of engaging diverse populations in PGS, including racial and ethnic minority groups, people living in rural communities, and those with lower education or income.[12-14] Diverse populations are at risk of being left behind in the implementation of PGS if efforts are not oriented to explicitly address health equity in genomics.[15] Current PGS implementation inequities limit the ability for genomics-based research and genetics services to capture genetic diversity from a broad range of populations to support the development of effective precision prevention strategies and therapies for individuals of all backgrounds.[13,14,16,17] Implementation science contains tools to integrate health equity and genomic medicine to ensure implementation of PGS does not exacerbate inequities.

To help facilitate growth of PGS programs and enhance recruitment and retention of representative populations into genomic initiatives, we propose to identify best practices for PGS implementation and develop and test a freely available, online, multicomponent implementation guide (FOCUS toolkit). Our project's specific aims are as follows: 1) Describe differences in processes, barriers, and facilitators to equitable implementation across sites at various stages of PGS implementation, 2) Develop and package implementation strategies into the FOCUS toolkit to support the equitable implementation of PGS programs, 3) Evaluate the impact of the FOCUS toolkit on improving implementation of PGS in diverse populations and settings using a hybrid stepped wedge cluster randomized trial. This project will establish a gold standard approach for equitably integrating PGS and offer the field generalizable methods and knowledge about PGS implementation. In this paper we describe the planned approach for achieving these aims and highlight how this approach is intended to advance the goal of implementing equitable PGS programs that improve population health.

Methods

Overall Study Design and Conceptual Model

We will use an implementation mapping (IM) approach to complete the FOCUS project (Figure 1).Once an organization has made the decision to implement an evidence-based intervention (e.g., PGS), use of IM supports the integration of this program in real-world settings.[18] IM is a structured framework involving five steps that incorporates theory, empirical evidence, and diverse perspectives with the target population to iteratively guide decision making at each step.[18] We incorporate a health equity focus in genomic medicine as described by the NHGRI in 2019 throughout all components of the IM process, *the global applicability of genomic knowledge, fair and even access to genomic services such as testing and counseling, and unbiased implementation of genomic medicine.*[15]

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The RE-AIM/HE framework emphasizes the five dimensions of reach, effectiveness, adoption, implementation, and maintenance to evaluate implementation across diverse settings. Integration of HE adds and explicit focus on identifying and addressing health disparities by incorporating structural, cultural, and systematic factors that influence equitable implementation, which can help inform the evaluation and impact of new programs such as PGS across diverse populations and settings.[21,22] The RE-AIM/HE framework will be used to guide Task 5 of IM.

PGS Sites

We will work with two distinct sets of PGS sites: FOCUS Design Sites and FOCUS Test Sites. The FOCUS Design Sites will be part of Aim 1, which will involve identification and synthesis of evidence about the implementation processes, barriers, and facilitators for PGS implementation. We will include 10 diverse organizations that can speak to experiences across implementation stages: exploration, preparation, implementation, sustinment.[23] We will also work with FOCUS Test Sites to rigorously evaluate the FOCUS toolkit for improving the implementation of PGS. These sites will also be at various stages of implementation. We plan to include 12 organizations as FOCUS Test Sites.[23,24]

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Study Aim 1: Describe differences in processes, barriers, and facilitators to equitable implementation across sites at various stages of PGS implementation

The first Aim of the FOCUS study is aligned with IM Task 1. We will conduct a qualitative needs assessment among ten PGS programs (i.e. FOCUS Design Sites) at various implementation stages (exploration, preparation, implementation, and sustainment) guided by CFIR/HE.[19,20] Emerging Sites are defined as institutions in the planning and development stages of PGS program implementation. Implementing Sites are defined as institutions that have begun conducting screenings and are building out their programs. Sustaining Sites are defined as sites that have been implementing their PGS program for over a year. These 10 sites will be enrolling either clinical or research PGS cohorts.[22,25] The CFIR/HE framework will be used to create an interview guide to identify barriers and facilitators of implementing PGS.

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subsequent qualitative data analysis steps – Process Mapping and Data Matrix Heat Mapping - that have been described by Salvati et al.[28] Briefly, process maps will visually detail the PGS implementation process and workflow described by each team member during their interview. Upon completion of all interviews at the respective site, we will conduct member checking among these interviewees to reconcile discrepancies or omissions in the process maps. This will allow us to create a final aggregate process map for each site.

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Study Aim 2: Develop and package implementation strategies into the FOCUS toolkit to support the equitable implementation of PGS programs

The second Aim of the FOCUS study is to develop the FOCUS toolkit consisting of equity-focused implementation strategies, materials, and protocols for implementing and improving PGS programs. This Aim will cover IM Tasks 2-4.

First, we will identify outcomes and objectives by working with the IM Advisory Panel to prioritize the facilitators, barriers, and inefficiencies identified in IM Task 1 by importance, health equity relevance, and changeability. This will allow us to identify outcomes (i.e., what needs to be added or changed to improve PGS implementation) and objectives (i.e., how we will address the identified outcomes) (IM Task 2).

We will work with the IM Advisory Panel during Aim 2 to select evidence-based strategies to address the facilitators, barriers, and inefficiencies of PGS implementation (e.g., information chunking, guided practice, etc.). Using the CFIR-ERIC matching tool (IM Task 3),[29] which aligns ERIC strategies with CFIR factors identified in Task 1. This will allow us to identify appropriate implementation strategies for each priority implementation need,[30] including the need for equity in access to and quality of PGS. The study team will host a feedback session with the IM Advisory Panel on these potential methods and strategies at the conclusion of Task 3 and integrate feedback from the panel based on this session.

Ultimately we will draft implementation strategy protocols and develop materials to package our implementation strategies into the online FOCUS Toolkit for PGS (IM Task 4). Once the FOCUS toolkit draft has been developed, we will host a feedback session with the IM Advisory panel to capture and integrate recommendations. Finally, we will use a human centered design approach to prototype and refine the FOCUS toolkit with our FOCUS design sites.[731] Engaging program champions and implementation team members from the eight FOCUS design sites, we will conduct a live rapid prototyping and iterating session (non-statistical approaches) to refine our proposed protocols and materials. Validated measures will be used to assess acceptability, appropriateness, and feasibility of using the FOCUS toolkit.[32,33] Through these live sessions we will collect feedback until we have reached consensus among the IM Advisory Panel of the planned FOCUS toolkit materials. We will prioritize strategies that were common across PGS sites and that aim to achieve equity in PGS participation and implementation.

Study Aim 3: Evaluate the impact of the FOCUS toolkit on improving implementation of PGS in diverse populations and settings using a hybrid stepped wedge cluster randomized trial

The final Aim of the FOCUS study is to evaluate the impact of the FOCUS toolkit on Reach, Effectiveness, Implementation, Adoption, Maintenance (RE-AIM), and HE outcomes for PGS in 12 FOCUS Test Sites with diverse populations and settings. The Stepped-Wedge Cluster Randomized Trial design to evaluate the utility of the FOCUS toolkit for improving outcomes among the 12 FOCSU test sites).[21] This approach will allow us to assess improvements in RE-AIM/HE outcomes among sites at varying stages of implementation: exploration, preparation, implementation, and sustainment. Because sites in the exploration phase will not have begun implementing PGS prior to using the FOCUS toolkit (no baseline/pre-FOCUS toolkit data about the PGS program), they will be randomized 1:1 to either control (no FOCUS toolkit) or intervention (FOCUS

toolkit) conditions using a parallel design. The eight existing sites will be actively implementing or sustaining their PGS programs (have baseline/pre-FOCUS toolkit data) and will be randomized 1:1 to one of four possible time steps every three months for a 21-month implementation period (steps at 3, 6, 9, and 12 months) (**Figure 2**). This hybrid stepped wedge cluster randomized trial design is a pragmatic approach that will allow us to simultaneously assess RE-AIM/HE outcomes across a representative and generalizable sample of PGS sites with varying amounts of baseline program implementation data and assessment of correlates of post-toolkit use outcomes.[34-36]

Quantitative data about RE-AIM/HE outcomes will be collected using three tools: 1) PGS Program Data Collection Form, 2) Stakeholder Surveys, and 3) Toolkit Tracking Data (**Table 1**). The PGS Program Data Collection Form will be completed monthly by each site using a REDCap (Research Electronic Data Capture) form designed by the study team. The form will assess metrics related to the implementation outcomes of Reach, Effectiveness, and Adoption. *Reach*, or how well the PGS site recruits the intended audience, will be measured by the total number of people recruited to participate in the PGS program.[37] *Effectiveness* will be assessed based on how well the PGS program is achieving its intended public health outcome of identifying individuals with pathogenic variants in genes associated with Tier 1 conditions. Our primary measure of Effectiveness is the proportion of eligible individuals tested. We will also evaluate rate of positive findings (number of positive results returned/number tested). *Adoption* will be assessed based on the number of providers who participate in the PGS program at each site out of the total number of providers eligible to participate at the site. The Stakeholder Surveys will be distributed to implementation stakeholders at each site prior to beginning to use the PGS toolkit, three months after starting to use the toolkit, and at the conclusion of using the toolkit. These will capture data to assess RE-AIM/HE outcomes of Implementation and Maintenance. *Implementation* assessment will include acceptability, appropriateness, and feasibility of PGS. These will be captured using the Acceptability of Intervention Measure, Intervention Appropriateness Measure, and Feasibility of Intervention Measure, where the Intervention is defined as PGS.[33] To assess *Maintenance*, we will ask stakeholders to complete the Program Sustainability Assessment Tool to rate the PGS program on the presence of elements associated with long-term sustainability. We will also capture fidelity to the FOCUS toolkit through the Toolkit Tracking Data, which will include website metrics of 1) FOCUS test sites' registered users and 2) the number of times the FOCUS toolkit was opened and number of pages or components of the toolkit are visited.

Our primary research question is: *Does the use of the FOCUS toolkit improve PGS implementation and effectiveness.* RE-AIM/HE outcomes among the eight existing sites (i.e., implementation and sustainment sites) that are actively implementing or sustaining PGS using generalized mixed effects regression models (GLMM).[38] The primary temporal variable for the analysis of RE-AIM/HE outcomes is the time step; all participants enrolled during a given time step will be retained in that step regardless of study completion date. Statistical analysis will be based on the principle of intention to treat. The step at which a participant was enrolled in the PGS program will be used as the treatment indicator. At the participant level, a mixed effects logistic regression model will be used to estimate the impact of sites' use of the FOCUS toolkit strategies on the likelihood of participants returning for sample collection. Fixed effects of study time will be included in the model to adjust for secular temporal events throughout the study and random site effects included to account for correlation of participants within site over time. Participant-level baseline data will be assessed for association with study outcomes and when significant, included in adjusted models. Between-site sample size imbalance may impact the study power and estimation bias, thus initial models will be fit using Fay and Graubard bias corrected sandwich variance estimator.[39,40] Period-specific recruitment totals will be assessed at the site level utilizing a gaussian distribution with an identity link. We will use GLMM to assess the impact of the FOCUS toolkit among the four emerging sites that are part of the parallel design (FOCUS toolkit use vs no FOCUS toolkit use). In addition to addressing primary study outcomes, models including post-intervention data from all sites will be assessed to determine if newly emerging PGS sites differ across outcomes as compared to existing sites. Generalized linear mixed effects regression will be assessed with an indicator of site implementation stage to assess post-intervention RE-AIM/HE outcomes.

All RE-AIM/HE outcomes will also be assessed qualitatively through in-depth Stakeholder Interviews conducted with five implementation stakeholders (e.g., program champion (n=1), genetic counselor (n=1),

organizational leadership (n=1), and implementation teams (n=2)) per site (n=60) at the conclusion of the implementation period. ***Reach*** will include questions to understand whether all populations are equitably reached, who is not reached, and how the FOCUS toolkit supports better reach among diverse populations. ***Effectiveness*** will focus on whether program impact is equitable across groups, whether sample collection and findings are different across sociodemographics. ***Adoption*** will be assessed by asking about the uptake of PGS among clinicians and other key stakeholders within their setting. ***Implementation*** will be assessed by asking how PGS has been implemented, facilitators and barriers to implementation, and ways that the FOCUS toolkit helped the site overcome these barriers. To assess ***Maintenance***, we will ask stakeholders about the ways they plan to sustain the PGS program long-term and plans for institutionalization of the FOCUS toolkit.[41]

A summary will be created immediately following each interview. These summaries will allow for high-level analysis during data collection, facilitate initial codebook development and reduce the number of new codes requiring re-coding during data analysis. Coding will be conducted using an *a priori* codebook guided by the RE-AIM/HE and CFIR (for contextual factors that are described as impacting RE-AIM/HE outcomes. After initial review of this codebook, new codes will be added to the other relevant sections of the transcript text not fitting *a priori* codes. A team-based approach will be used to refine the codebook with discrepancies resolved by the study team. All coding will occur in MaxQDA and completed by two coders. Qualitative and quantitative results will be reviewed together, and triangulation of data will occur using a rapid analytic coding matrix.[42-44] This will allow us to better understand how the PGS programs have changed over time and to what extent the FOCUS toolkit was adapted and/or used in accordance with the protocol.

Discussion

The FOCUS project will be the first to systematically identify facilitators and barriers to PGS implementation across a range of settings and stages of implementation. Further, the FOCUS toolkit will offer implementation strategies to address the identified barriers and leverage facilitators to support equitable PGS implementation. The diversity of PGS programs and comprehensive approach to data collection allows for findings to be broadly applicable and generalizable, recognizes contextual differences, collects data about strategies used in the real-world, and is directly aligned with calls to develop a strategic PGS implementation agenda.[45] This approach can support widespread integration of PGS into routine practice by reducing evidence-based knowledge gaps about barriers and facilitators that impact PGS implementation.

There are several limitations to consider, which include potential dropout of FOCUS design sites and difficulty in recruiting diverse stakeholders and participants from each site. We have identified a Program Champion at each FOCUS design site and offered incentives for qualitative interviews. We will continue outreach until we reach saturation of qualitative themes among PGS programs or until all associated stakeholders from each program have been approached. In addition, testing the toolkit with FOCUS test sites could be challenging. We will include sites at various stages of implementation (emerging, implementing, and sustaining). Given the timing, we will need to identify emerging sites closer to the start of Aim 3 to ensure they are still in the emerging phase. As such we will not identify these sites a priori; however, the literature has demonstrated a steep annual increase in the number of PGS programs in the US, with triple the number of programs in the US since 2017.[2,6,46] Thus, it will be feasible to identify at least four emerging sites to participate. We will use our professional and research networks to identify and invite these sites to participate.

The FOCUS project will be foundational for the field by capturing what has been collectively learned to date about implementation of PGS and providing a flexible multicomponent implementation guide (FOCUS toolkit) to support the success of these programs with a special focus on advancing health equity in PGS. We will fill an unmet need to understand the best practices associated with implementation of PGS and the toolkit that we produce will help develop, implement, and optimize PGS programs in the face of an evolving landscape. Findings from this research are critical to enhance the rapid expansion of PGS programs in the US, as it will provide generalizable methods for effective implementation of PGS to ultimately improve health outcomes through more comprehensive and equitable identification of individuals with inherited cancer and cardiovascular conditions.

Declarations

Ethics Approval and Consent to Participate:
This project was approved by the Medical University of South Carolina IRB as Exempt Research on 8/2/2023 (Pro00130721).

Consent for Publication:
All authors have reviewed the manuscript and consent for publication.

Availability of Data and Materials:
Not Applicable

Competing Interests:
Authors report no competing interests.

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Authors' Contributions:
Conceptualization and Study Design (CA, MR, KF), Methods (CA, MR, KF, CW, DC, AB, MH, NB, AE, MF, CH), Data Collection (CA, MR, JM, KF, CW), Formal Analysis (CA, MR, JM, KF, CW, NB), Writing Original Draft (CA, MR, JM), Writing Review and Editing (CA, MR, KF, CW, DC, AB, MH, NB, AE, MF, CH).

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Authors' Information:
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References

1. Evans JP, Khoury MJ. The arrival of genomic medicine to the clinic is only the beginning of the journey. *Genetics in medicine : official journal of the American College of Medical Genetics.* 2013;15(4):268-269.
2. Evans JP, Berg JS, Olshan AF, Magnuson T, Rimer BK. We screen newborns, don't we?: realizing the promise of public health genomics. *Genetics in medicine : official journal of the American College of Medical Genetics.* 2013;15(5):332-334.
3. Genomics and Population Health Action Collaborative. National Academies. https://www.nationalacademies.org/our-work/genomics-and-population-health-action-collaborative. Accessed 18MAY, 2022.
4. Manickam K, Buchanan AH, Schwartz MLB, et al. Exome Sequencing-Based Screening for BRCA1/2 Expected Pathogenic Variants Among Adult Biobank Participants. *JAMA Netw Open.* 2018;1(5):e182140.
5. Gabai-Kapara E, Lahad A, Kaufman B, et al. Population-based screening for breast and ovarian cancer risk due to BRCA1 and BRCA2. *Proc Natl Acad Sci U S A.* 2014;111(39):14205-14210.
6. Williams MS. Population Screening in Health Systems. *Annual Review of Genomics and Human Genetics.* 2022;23.
7. Foss KS, O'Daniel JM, Berg JS, et al. The Rise of Population Genomic Screening: Characteristics of Current Programs and the Need for Evidence Regarding Optimal Implementation. *Journal of personalized medicine.*

2022;12(5).
8. Khoury MJ, Feero WG, Chambers DA, et al. A collaborative translational research framework for evaluating and implementing the appropriate use of human genome sequencing to improve health. *PLoS Med.* 2018;15(8):e1002631.
9. Murray MF, J. P. Evans, M. Angrist, K. Chan, W. Uhlmann, D. L. Doyle, S. M. Fullerton, T. Ganiats, J. Hagenkord, S. Imhof, S. H. Rim, L. Ortmann, N. Aziz, W. D. Dotson, E. Matloff, K. Young, K. Kaphingst, A. Bradbury, J. Scott, C. Wang, A. Zauber, M. Levine, B. Korf, D. Leonard, C. Wicklund, G. Isham, and M. J. Khoury. A Proposed Approach for Implementing Genomics-Based Screening Programs for Healthy Adults. *NAM Perspectives DIscussion Paper.* 2018.
10. Roberts MC. Using a Participatory Approach to Develop Research Priorities for Future Leaders in Precision Public Health. *Research Square.* 2022(1).
11. Shen EC, Srinivasan S, Passero LE, et al. Barriers and facilitators for population genetic screening in healthy populations: a systematic review. 2022.
12. Khoury MJ, Bowen S, Dotson WD, et al. Health equity in the implementation of genomics and precision medicine: A public health imperative. *Genetics in medicine : official journal of the American College of Medical Genetics.* 2022.
13. Landry LG, Ali N, Williams DR, Rehm HL, Bonham VL. Lack Of Diversity In Genomic Databases Is A Barrier To Translating Precision Medicine Research Into Practice. *Health Aff (Millwood).* 2018;37(5):780-785.
14. Popejoy AB, Fullerton SM. Genomics is failing on diversity. *Nature.* 2016;538(7624):161-164.
15. Jooma S, Hahn MJ, Hindorff LA, Bonham VL. Defining and Achieving Health Equity in Genomic Medicine. *Ethnicity & disease.* 2019;29(Suppl 1):173-178.
16. Sirugo G, Williams SM, Tishkoff SA. The Missing Diversity in Human Genetic Studies. *Cell.* 2019;177(1):26-31.
17. Halbert CH, Harrison BW. Genetic counseling among minority populations in the era of precision medicine. *American journal of medical genetics Part C, Seminars in medical genetics.* 2018;178(1):68-74.
18. Fernandez ME, Ten Hoor GA, van Lieshout S, et al. Implementation Mapping: Using Intervention Mapping to Develop Implementation Strategies. *Frontiers in public health.* 2019;7:158-158.
19. Damschroder LJ, Reardon CM, Opra Widerquist MA, Lowery J. Conceptualizing outcomes for use with the Consolidated Framework for Implementation Research (CFIR): the CFIR Outcomes Addendum. *Implementation science : IS.* 2022;17(1):7.
20. Damschroder LJ, Reardon CM, Widerquist MAO, Lowery J. The updated Consolidated Framework for Implementation Research based on user feedback. *Implementation science : IS.* 2022;17(1):75.
21. Shelton RC, Chambers DA, Glasgow RE. An Extension of RE-AIM to Enhance Sustainability: Addressing Dynamic Context and Promoting Health Equity Over Time. *Frontiers in public health.* 2020;8:134.
22. Woodward EN, Matthieu MM, Uchendu US, Rogal S, Kirchner JE. The health equity implementation framework: proposal and preliminary study of

hepatitis C virus treatment. *Implementation science : IS.* 2019;14(1):26.
23. Walugembe DR, Sibbald S, Le Ber MJ, Kothari A. Sustainability of public health interventions: where are the gaps? *Health Res Policy Syst.* 2019;17(1):8.
24. Glasgow RE, Vogt TM, Boles SM. Evaluating the public health impact of health promotion interventions: the RE-AIM framework. *American journal of public health.* 1999;89(9):1322-1327.
25. Woodward EN, Singh RS, Ndebele-Ngwenya P, Melgar Castillo A, Dickson KS, Kirchner JE. A more practical guide to incorporating health equity domains in implementation determinant frameworks. *Implement Sci Commun.* 2021;2(1):61.
26. Gale RC, Wu J, Erhardt T, et al. Comparison of rapid vs in-depth qualitative analytic methods from a process evaluation of academic detailing in the Veterans Health Administration. *Implementation science : IS.* 2019;14(1):11.
27. Nevedal AL, Reardon CM, Opra Widerquist MA, et al. Rapid versus traditional qualitative analysis using the Consolidated Framework for Implementation Research (CFIR). *Implementation science : IS.* 2021;16(1):67.
28. Salvati ZM, Rahm AK, Williams MS, et al. A picture is worth a thousand words: advancing the use of visualization tools in implementation science through process mapping and matrix heat mapping. *Implement Sci Commun.* 2023;4(1):43.
29. Powell BJ, Waltz TJ, Chinman MJ, et al. A refined compilation of implementation strategies: results from the Expert Recommendations for Implementing Change (ERIC) project. *Implementation science : IS.* 2015;10:21.
30. Waltz TJ, Powell BJ, Fernández ME, Abadie B, Damschroder LJ. Choosing implementation strategies to address contextual barriers: diversity in recommendations and future directions. *Implementation Science.* 2019;14(1):42.
31. Chen E, Neta G, Roberts MC. Complementary approaches to problem solving in healthcare and public health: implementation science and human-centered design. *Transl Behav Med.* 2021;11(5):1115-1121.
32. Proctor E, Silmere H, Raghavan R, et al. Outcomes for Implementation Research: Conceptual Distinctions, Measurement Challenges, and Research Agenda. *Administration and Policy in Mental Health.* 2011;38(2):65-76.
33. Weiner BJ, Lewis CC, Stanick C, et al. Psychometric assessment of three newly developed implementation outcome measures. *Implementation Science.* 2017;12(1):108.
34. Nguyen AM, Cleland CM, Dickinson LM, et al. Considerations Before Selecting a Stepped-Wedge Cluster Randomized Trial Design for a Practice Improvement Study. *Ann Fam Med.* 2022;20(3):255-261.
35. Brown CA, Lilford RJ. The stepped wedge trial design: a systematic review. *BMC medical research methodology.* 2006;6:54.
36. Zhan Z, van den Heuvel ER, Doornbos PM, et al. Strengths and weaknesses of a stepped wedge cluster randomized design: its application in a colorectal cancer follow-up study. *Journal of clinical epidemiology.*

2014;67(4):454-461.
37. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support. *Journal of biomedical informatics.* 2009;42(2):377-381.
38. Hussey MA, Hughes JP. Design and analysis of stepped wedge cluster randomized trials. *Contemporary clinical trials.* 2007;28(2):182-191.
39. Fay MP, Graubard BI. Small-sample adjustments for Wald-type tests using sandwich estimators. *Biometrics.* 2001;57(4):1198-1206.
40. Thompson JA, Hemming K, Forbes A, Fielding K, Hayes R. Comparison of small-sample standard-error corrections for generalised estimating equations in stepped wedge cluster randomised trials with a binary outcome: A simulation study. *Stat Methods Med Res.* 2021;30(2):425-439.
41. Holtrop JS, Rabin BA, Glasgow RE. Qualitative approaches to use of the RE-AIM framework: rationale and methods. *BMC Health Serv Res.* 2018;18(1):177.
42. Heale R, Forbes D. Understanding triangulation in research. *Evidence Based Nursing.* 2013;16(4):98.
43. Moon MD. Triangulation: A method to increase validity, reliability, and legitimation in clinical research. *J Emerg Nurs.* 2019;45(1):103-105.
44. O'Cathain A, Murphy E, Nicholl J. Three techniques for integrating data in mixed methods studies. *Bmj.* 2010;341:c4587.
45. Ginsburg G, Penny M, Feero WG, Miller M, Addie S, Beachy SH. The National Academies' Roundtable on Genomics and Precision Health: Where we have been and where we are heading. *Am J Hum Genet.* 2021;108(10):1817-1822.
46. Green RF, Ari M, Kolor K, et al. Evaluating the role of public health in implementation of genomics-related recommendations: a case study of hereditary cancers using the CDC Science Impact Framework. *Genetics in medicine : official journal of the American College of Medical Genetics.* 2019;21(1):28-37.

Figure 1. Overview of FOCUS Study

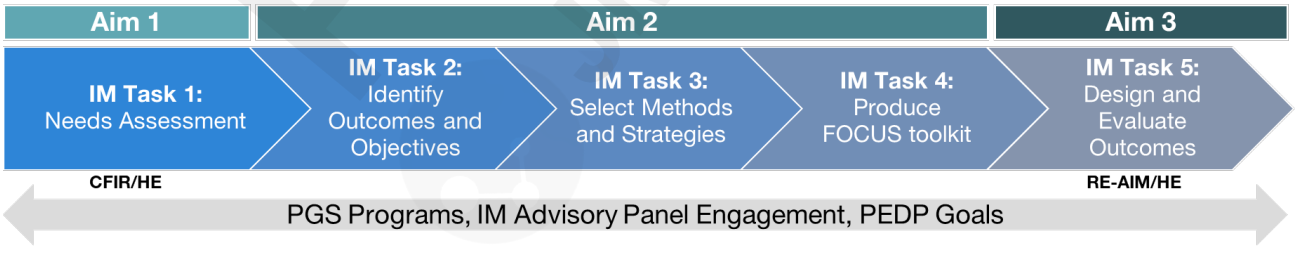

Figure 2: Hybrid Stepped Wedge Cluster Randomized Trial with Data Collection Summary

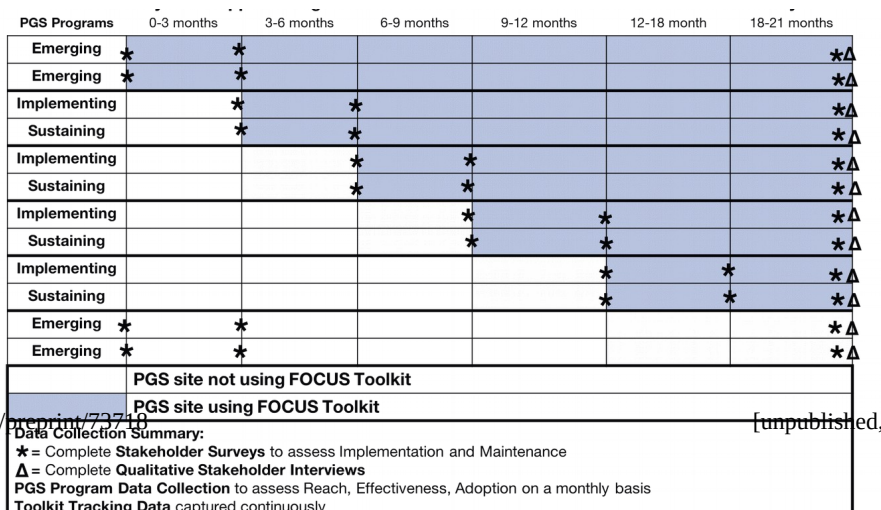

Table 1: Aim 3 Outcome Metrics				
Outcome Metric	***Measure and Description***	***Data Source***	***Level***	***Health Equity Analysis***
Reach	# of participants	EHR or site administrative records	Individual	Are there differences in reach across sociodemographics?
Effectiveness	Positive findings: proportion of pathogenic variant and likely pathogenic variant results returned	EHR or site administrative records	Individual	Are there differences in effectiveness across sociodemographics?
Adoption	Number of providers participating in PGS program vs. number of providers that are available at the institution	Administrative records	Site	Are there differences in adoption across sites?
Implementation	Acceptability, appropriateness, and feasibility	REDCap survey[45]	Site	Are there differences in PGS implementation across sites?
Maintenance	Intention to sustain PGS	REDCap survey[46]	Site	Are there differences in intention to sustain across sites?