Population-based Research Optimizing Screening Through Personalized Regimens: The PROSPR Initiative

Governance Document

Version 3.0

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Section 1: Overview

1.1 Introduction

The Population-based Research Optimizing Screening through Personalized Regimens initiative (PROSPR) provides a unique and valuable opportunity to better understand and improve breast, cervical, and colorectal cancer screening in US clinical practice. The initiative began in September, 2011, with funding of seven research centers (three breast, one cervical, and three colorectal cancer centers) and a statistical coordinating center (SCC). In 2013 three new cervical sites were funded. These 11 entities comprise the PROSPR Research Network. PROSPR is funded under a cooperative agreement mechanism, and as such, the National Cancer Institute (NCI) is closely involved in administrative and scientific activities.

Each PROSPR research center (PRC) is responsible for the following activities:

- To submit multi-level screening process data to the PROSPR central data repository (CDR);
- To conduct three independent cancer screening research projects as proposed in each PRC's response to the PROSPR Funding Opportunity Announcement (FOA);
- To propose and participate in collaborative projects, known as "trans-PROSPR projects," that address aspects of the screening process, including characterization of the process and opportunities for optimization.

The primary responsibility of the SCC is to create and house the CDR. This includes development of systems to allow for consistent and efficient submission of data by the PRCs.

1.2 Background

Most US medical and cancer research organizations recommend some form of screening for breast, cervical, and colorectal cancer. The screening process for these cancers, however, is not without challenges. Common challenges include high rates of false positives, access to screening in low-resource communities, financial barriers, rapid changes in technology, dissemination of technology not yet known to be of benefit, and extrapolation of efficacy findings to populations in which modalities have not been tested.

The screening process includes invitation, screening, results reporting, diagnostic evaluation, diagnosis, and referral for first course of treatment. Given its multi-step nature, there are numerous points at which the process can fail. Patients, physicians, facilities, and healthcare payers are participants in this process, and the challenges they face must be carefully considered when addressing successes and failures.

PROSPR will examine the breast, cervical, and colorectal cancer screening processes in the US, identify shortcomings, and explore possible solutions. PROSPR's objective is to make the screening process more consistent with the Institute of Medicine's (IOM) aims for the twenty-first century's health care system, that is, effective, patient-centered, timely, efficient, and equitable.

1.3 Specific Aims

PROSPR's specific aims are:

- To populate the Central Data Repository (CDR) with data involved in the US screening processes for breast, cervical, and colorectal cancer.
- To conduct comparative effectiveness research to better understand the failures and successes associated with, and manners in which to optimize, the US screening process for breast, cervical, and colorectal cancer screening.
- To conduct comparative effectiveness research to explore and identify potential risk-based screening strategies for breast, cervical, and colorectal cancer screening in the US.

1.4 Additional Information

The PRC and SCC FOAs provide additional information. They can be found at:

http://grants.nih.gov/grants/guide/rfa-files/RFA-CA-11-003.html (PRC FOA)

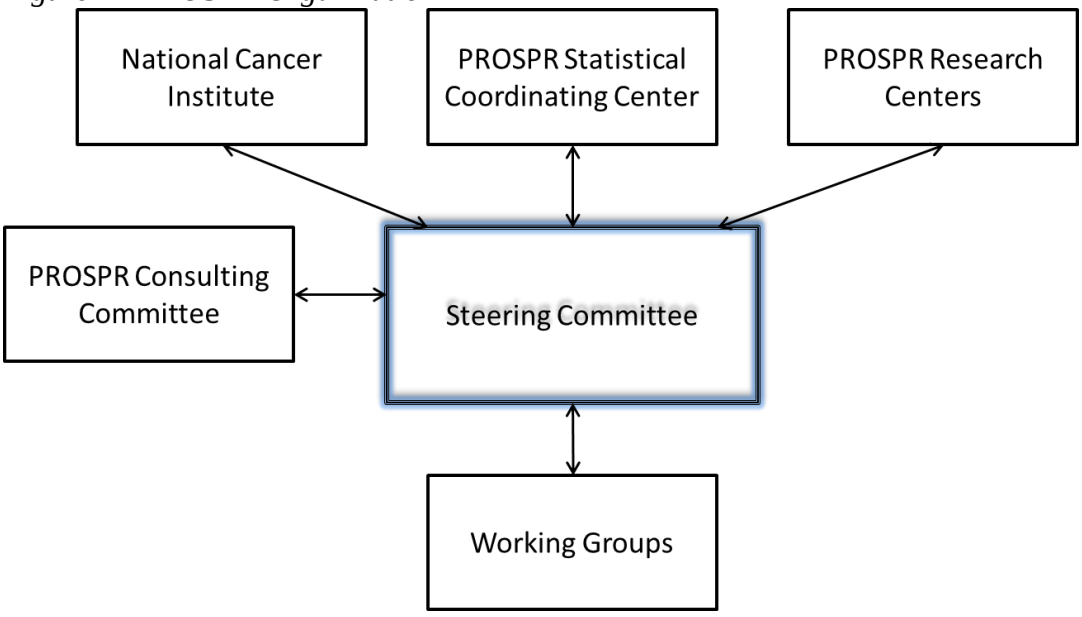
http://grants.nih.gov/grants/guide/rfa-files/RFA-CA-11-004.html (SCC FOA)

Section 2: Organization

2.1 Introduction

PROSPR's organizational structure includes the National Cancer Institute (NCI), seven PROSPR Research Centers (PRC), a Statistical Coordinating Center (SCC), a Steering Committee (SC), a PROSPR Consulting Committee (PCC) and various working groups. An overview of the PROSPR initiative organization is shown in *Figure 1 - PROSPR Organization* and detailed descriptions of these groups are provided below.

Figure 1 - PROSPR Organization



2.2 National Cancer Institute (NCI)

PROSPR is funded by the National Cancer Institute through a cooperative agreement mechanism. Therefore, the NCI has substantial scientific and administrative involvement. The NCI supports and stimulates PROSPR activities through involvement or scientific collaboration with the PROSPR SCC and PRCs. The NCI is a partner in these activities, and will not assume direction, prime responsibility, or a dominant role in activities unless the role is documented and agreed upon by the relevant PROSPR grantees.

The NCI PROSPR Program team has three components:

Project Scientists: Project scientists are responsible for discussions involving science. They discuss and evaluate changes in scientific plans that are proposed by grantees due to budget cuts or other reasons. The Lead Project Scientist oversees scientific issues relevant to PROSPR as a whole. Organ-site Project Scientists focus on scientific issues for one specific organ site.

Program Directors: Program Directors are the link between the NCI Office of Grants Administration and the Project Scientists. They are knowledgeable about the science of the grant as well as administrative and funding policy issues. Program Directors participate in conversations between the Project Scientist and grantee when the grantee proposes modifications to the science that affect the budget. Each institution funded under PROSPR has a Program Director assigned to its award.

Advisors: Advisors are typically senior-level federal staff. They can be consulted about PROSPR issues that involve scientific or funding policy.

2.2.1 Responsibilities of NCI Project Scientists

The NCI Project Scientists have the following responsibilities:

- To monitor the operations and assess the progress of the SCC and PRCs;
- To provide input and suggestions on PRC individual research projects;
- To participate in the development, conduct, coordination, and evaluation of trans-PROSPR projects;
- To collaborate with individual investigators on research projects if desired or requested;
- To co-author manuscripts on research efforts when appropriate;
- To monitor and assess common or similar PROSPR research efforts to identify duplication;
- To attend the twice-yearly PROSPR scientific meeting;
- To participate in yearly PRC site visits, either in-person or by telephone/webinar;
- To serve as a member of the PROSPR Steering Committee;
- To facilitate interactions between the grantees and NIH and NCI programs to provide opportunities to leverage existing resource and infrastructures as well as to disseminate PROSPR results effectively;
- To oversee activities of the PROSPR Consulting Committee.

2.2.2 Responsibilities of NCI Program Directors

The NCI Program Directors' responsibilities include:

- To keep abreast of PROSPR activities, including scientific progress; administrative issues, and fiscal matters;
- To review grantee progress reports and discuss them with NCI project scientists;

- To complete forms required by Office of Grants Administration (OGA);
- To act as the liaison between OGA, grantees, and NCI project scientists on fiscal issues;
- To communicate administrative and funding issues to grantees;
- To answer questions from grantees on administrative and funding issues;
- To monitor and assess the adherence of grantees to research plans, data sharing, and intellectual property plans**.**

2.3 PROSPR Research Centers (PRC)

In September, 2011 three breast cancer, three colorectal cancer, and one cervical cancer screening PRCs were funded for five years. In 2013 three new cervical sites were funded.

2.3.1 Responsibilities

The PRCs' responsibilities include:

- To work with the SCC to coordinate processes for submission of data to the CDR;
- To compile data based on shared common data elements from each of their research centers;
- To submit data to the CDR according to agreed upon policies;
- To provide representation on the PROSPR Steering Committee;
- To complete the individual research projects proposed in their PROSPR application;
- To participate in trans-PROSPR projects;
- To participate in PROSPR working groups;
- To provide representation at the bi-annual PROSPR scientific meeting;
- To prepare for and participate in yearly PRC site visits made by the SCC and NCI;
- To participate in internal evaluations as outlined below in section 3.2;
- To participate in activities relating to the PROSPR Consulting Committee;
- To submit an annual progress report to NCI that documents progress for the previous year.

2.4 PROSPR Statistical Coordinating Center (SCC)

The Statistical Coordinating Center is responsible for the creation and maintenance of the CDR. The SCC also is responsible for certain administrative and scientific activities.

2.4.1 Responsibilities

The SCC will have the primary responsibility:

- To house and maintain the CDR;
- To promote and coordinate cross-PROSPR scientific collaboration;
- To provide leadership for organizing the common data collection to describe the screening process and its outcomes;
- To provide logistical infrastructure for data collection, including a data dictionary, and to collect data from the PRC's at specified intervals;
- To provide summaries, analysis, and interpretation of pooled data;
- To develop new statistical methods to address aspects of the screening process
- To facilitate analyses on trans-network projects and provide statistical consultation to PRCs (if requested)
- Provide consultation on statistical issues to PRC's if requested
- To provide logistical infrastructure for information diffusion for PROSPR;
- To organize PROSPR in-person Scientific Meetings and all PROSPR conference calls and provide logistical support;
- To release data and protocols according to the approved plans for timely sharing of research resources and data generated through the award, as agreed upon by the PROSPR Steering Committee;
- To accept and implement all scientific, practical, and policy decisions approved by the PROSPR Steering Committee to the extent consistent with applicable grant regulations;
- To prepare for and participate in yearly PRC site visits made by the SCC and NCI;
- To participate in internal evaluations as outlined below in section 3.2;
- To participate in activities relating to the PROSPR Consulting Committee;
- To submit an annual progress report to NCI that documents progress for the previous year including Inclusion Enrollment Tables for the pooled data resource.

2.5 Steering Committee

The PROSPR Steering Committee (SC) is the governing body of the PROSPR initiative.

2.5.1 Membership

The SC will consist of the following members:

- Two representatives from each PROSPR Research Center Organ Group (the Center PD/PI (Project Director/Principal Investigator) or a lead PD/PI and a designated investigator) who will collectively have one vote (20 members with a total of 10 votes);
- Two representatives of the PROSPR Statistical Coordinating Center (the Center PDs/PIs or a lead PD/PI an a designated senior investigator) who will collectively have one vote;
- Three NCI Project Scientists will participate in the PROSPR Steering Committee for the NCI who will collectively have one vote.

2.5.2 Responsibilities

The Steering Committee will meet by telephone at least once a month, and in person at the bi-annual PROSPR scientific meetings. Agendas for these meetings usually will be created by the Executive Committee (see Section 2.5.3.1) with input from others. Individuals associated with PROSPR who are not members of the Steering Committee may attend Steering Committee meetings if the Steering Committee is amenable to their attendance. They may not vote, however.

The Steering Committee, in conjunction with NCI, will establish the PROSPR Consulting Committee, an external review board. (Please see Section 3.3.1 for the composition of the PROSPR Consulting Committee and its responsibilities.) The Steering Committee will meet with the PROSPR Consulting Committee twice a year: once in-person (at one of the twice-yearly scientific meetings) and once by telephone/webinar. The Steering Committee will present to the PROSPR Consulting Committee at the in-person meeting on topics requested by the PCC. The Steering Committee will respond to other requests made by the PCC throughout the year.

Other duties of the Steering Committee include:

- To oversee PROSPR organization and operations;
- To review and evaluate progress on meeting PROSPR's research goals;
- To develop prototype working group structures and operating principles that will promote the exchange of ideas and experiences, and the accomplishment of tasks and goals;

- To establish specific Working Groups and sub-committees as needed, including groups charged with advisory roles, research roles, and operations roles, as well as development of trans-PROSPR project proposals;

- To oversee (jointly with Working Groups) the PROSPR-wide requests for trans-PROSPR Network projects and develop processes to evaluate these requests;

- To develop formats for working group and trans-PROSPR progress reports;

- To oversee and evaluate working groups and trans-PROSPR projects to ensure adherence with operating principles;

- To decide whether languishing trans-PROSPR projects should be modified or terminated;

- To review and vote on PRC requests to limit data use (see Section 4.2.5.3);

- To resolve conflicts that arise between PROSPR parties.

2.5.3 The Steering Committee Chair

The Steering Committee will select a chair from one of the PRCs. Steering Committee members will volunteer to serve as chair. Steering Committee members will confirm the election of a chair by a majority vote prior to the annual in-person spring meeting. The term of office for the PRC chair is one year beginning after each spring scientific meeting, with an option to renew for an additional one-year term, upon Steering Committee approval.

2.5.3.1 Responsibilities of the Chair and the Executive Committee

The chair will meet at least monthly with a representative from the SCC and NCI to develop an agenda for the next Steering Committee meeting and review minutes of all Steering Committee meeting. The chair will preside at Steering Committee meetings.

The Steering Committee Chair plus the SCC PI (or designee) plus the NCI Lead Project Scientist are the PROSPR Executive Committee (EC). The Executive Committee is responsible for the coordination of PROPSR including:

- To develop agendas for SC meetings;

- To review the SC minutes before sending out to the entire SC for approval;

- To develop tentative plans for in person meetings prior to appointment of a dedicated committee for a specific meeting;

- To coordinate and plan site visit schedules;

- To suggest PROSPR working groups or working group member leaders and sub-committees;

- To discuss IRB, Data Use Agreements, and other legal concerns;
- To monitor progress in data submission from the PRCs;
- To provide oversight of the activities of the SCC.

The Executive Committee is charged with monitoring progress of PROSPR, but does not make decisions. All matters requiring decisions to be made are referred to the Steering Committee.

2.5.4 Voting Rules

In matters requiring a vote, each PROPSR entity will cast one vote. NCI has one vote, the SCC has one vote, and each PRC has one vote (in the case of a PRC representing both Cervical and Colorectal, each organ within the PRC has one vote), for a total of 12 voter. A quorum, defined as at least eight voting entities, is required for voting to occur. A majority of the voting entities must approve of an action for it to be passed. Any decision must comply with NCI fiscal and other policies.

Changes to the governance document must be approved by no fewer than eight affirmative votes.

2.6 Working Groups and Subcommittees

2.6.1 Membership

Working groups and subcommittees are convened by the Steering Committee. It is anticipated that members of the PROSPR initiative will volunteer to serve on working groups, but in some instances the Steering Committee may request that certain persons participate. Composition of a working group or subcommittee will depend on the purpose of the group. Working groups and subcommittees should include representatives with interest in the activities or who may be affected by decisions of the working group or subcommittee. Investigators not associated with PROSPR may participate in working groups if the Steering Committee and PROSPR members of that working group are amenable to their inclusion.

Trans-PROSPR projects are considered to be a special type of working group.

2.6.2 Responsibilities

Working groups are committees assembled by the Steering Committee to address specific research areas. Subcommittees are convened to implement administrative tasks required for the conduct of PROSPR. Working groups and subcommittees may be temporary or standing.

Recommendations for working groups may be made to the Steering Committee.. Working Group responsibilities are:

- To submit a report or communicate to the SC on progress or completion as required by working group procedures;

- To develop mission statements as required by working group procedures and submit them to the SC;

- To request data as per the working group procedures, which must be approved by the SC.

Examples of possible Working Groups are: methodology working group, modeling working group, biomarker working group.

The Steering Committee is responsible for establishing these WGs or sub-committees. The SCC is responsible for providing technical and logistical support.

2.6.3 Chair

Each working group will choose from among its members a chair. This individual must be formally affiliated with the PROSPR initiative, that is, a PRC PI, a PRC investigator, a SCC member, or an NCI Project Scientist. The term of office for the working group chair is one year with option to renew.

The chair will preside at meetings, coordinate scheduling of meetings, and arrange for preparation, distribution, and posting of minutes of meetings. The chair also will report its activities and progress to the Steering Committee.

Final minutes should be submitted to the SCC for posting on the PROSPR website and distribution to working group members. If requested, the SCC will forward minutes to the Steering Committee as well.

Section 3: Evaluation

3.1 Introduction

PROSPR will be evaluated through both an internal and external review. The purpose of the internal evaluation is for awardees to reflect on their accomplishments and goals for their individual site and the PROSPR network as a whole. The external evaluation will monitor and assess the progress of the PROSPR Network towards meeting the overall goals of the Initiative. Members of the Steering Committee are required to participate in both evaluations.

3.2 Internal Evaluation

The purpose of the internal evaluation is to monitor and assess the progress of individual PROSPR Research Centers, the SCC, and the PROSPR Network as a whole towards meeting the goals of the PROSPR Initiative. Also, the internal evaluation will be used to identify necessary improvements and set future objectives. The internal evaluation will be an analysis of how the PROSPR Network works together, an analysis of PRC-data deliverables and cross-PROSPR projects. The internal evaluation will be conducted in two parts: completion of a survey by each PROSPR Research Centers as well as the SCC, and discussion of survey results by all PROSPR entities. The internal evaluation will be a cooperative effort of the PROSPR Steering Committee, individual Research Centers, and NCI Program Staff. Details for the evaluation process are described in the Operations Manual.

3.2.1 Process for Internal Evaluation

The PROSPR Statistical Coordinating Center will develop and administer an annual survey for the internal evaluation. A working group will be formed in order to assist with the development of the survey. Survey questions will be focused on the accomplishments and goals of each PROSPR Research Center; interactions with other PROSPR Research Centers, the Statistical Coordinating Center and the National Cancer Institute; efforts to improve performance; and objectives for the next year.

The survey will be completed by one Principal Investigator from each PROSPR Research Center. The Principal Investigator is encouraged to complete the survey with co-investigators and other key personnel. Additionally, the Statistical Coordinating Center will complete a self-evaluation prior to the next PROSPR Scientific Meeting. The Statistical Coordinating Center will analyze and disseminate the results of the survey to the SC prior to the upcoming PROSPR Scientific Meeting. PRC SC representatives are responsible for further dissemination of the survey results to their overall PRC site members.

At the next PROSPR Scientific Meeting, the results of the individual PROSPR Research Center evaluations and the Statistical Coordinating Center self-evaluation will be discussed as a group.

All PROSPR key personnel will be invited to attend this evaluation session. The group will discuss the accomplishments from the past year, identify goals that were met as well as goals not met and efforts to meet those goals, and set goals for the next year.

3.2.2 Process for Submission of Confidential Comments

Individuals will be able to submit anonymous comments for the purposes of the internal evaluation and in general through the PROSPR website. The secured section of the PROSPR website will have a submission form for comments that will not contain any identifying information. The SCC will receive these comments and bring them to the attention of the PROSPR Steering Committee, which will discuss any comments.

3.3 External Evaluation

The PROSPR Initiative will be subject to external evaluation, which will be facilitated by the NCI Program Staff. In consultation with the NCI, the PROSPR Steering Committee will form a PROSPR Consulting Committee (PCC) that will conduct the external review and provide recommendations to the PROSPR Steering Committee and the PROSPR awardees. All PROSPR awardees will be expected to contribute materials and respond to requests required for the external evaluation. The purpose of the evaluation process is to monitor and assess the progress of the PROSPR Network toward achieving its goals. This component includes evaluating the quality and innovation of the research conducted by the PROSPR awardees.

3.3.1 The PROSPR Consulting Committee (PCC)

Candidates for the PCC will be identified through discussions among the SC. The PCC will have no more than nine members, which may include: a CDC representative, an NCI representative, an AHRQ representative (known as "agencies"); a breast cancer screening expert, a cervical cancer screening expert, a colorectal cancer screening expert, a comparative effectiveness research expert, an oncologist with expertise in health services delivery and comparative effectiveness research, and an expert in screening evaluation. Candidates must be approved by the Steering Committee. Appointments will be revisited and, if applicable, renewed annually.

The PROSPR Consulting Committee will be charged with the following activities:

- To review the overall progress of the PROSPR and making appropriate recommendations to strengthen activities in certain areas at least once a year;
- To participate in the semi-annual PROSPR Investigator Meeting;
- To provide additional consultations, responding to inquiries (via e-mail and telephone) as needed; and
- To provide links to investigators not funded by PROSPR but conducting, or interested in conducting, related research.

3.3.1.1 Process for Appointing Members to the PROSPR Consulting Committee

The individuals chosen to represent the agencies will be suggested by NCI and approved by the Steering Committee. Four additional individuals to serve on the PROSPR Consulting Committee also will be chosen by the PROSPR Steering Committee. A subcommittee comprised of one representative from the National Cancer Institute, the PROSPR Statistical Coordinating Center, and a PROSPR Research Center Principal Investigator will be formed to develop a list of candidates for the PROSPR Consulting Committee. This subcommittee will make their recommendations to the Steering Committee, and may suggest additional candidates. The Steering Committee will vote to select candidates, including alternates, and then approve all the members of the PROSPR Consulting Committee.

The National Cancer Institute will send invitations to potential members of the PROSPR Consulting Committee who will then be appointed to the PROSPR Consulting Committee upon acceptance.

4 Publications and Presentations

4.1 Introduction

Given the nature of PROSPR, it is expected that numerous collaborative efforts, including those that result in publications and presentations, will exist. In all cases, authorship for collaborative efforts is reserved for those persons who make significant and substantial contributions to activities that lead to the manuscript or its preparation. PROSPR members are eligible to be authors, as are persons not affiliated with a PROSPR entity if they are involved in these collaborative efforts. For additional information, refer to the PROSPR Publication Policies and Procedures Document which can be found on the PROSPR Secure Site (prosprnetwork.org).

PROSPR collaborative publication procedures strive to achieve the following:

- To ensure equitable distribution of authorship within and across sites;
- To maximize the scientific productivity of PROSPR and accomplish its objectives;
- To engage junior investigators who may eventually assume key PROSPR roles;
- To provide an opportunity for non-PROSPR members to utilize PROSPR data in collaboration with PROSPR investigators;
- To ensure that the content of manuscripts do not significantly overlap;
- To ensure that similar or compatible approaches are used across manuscripts;
- To identify potential discrepancies between manuscripts;
- To provide a standardized and rigorous internal review to ensure that published research meets PROSPR standards for quality;
- To allow for the tracking of PROSPR publications;
- To ensure that the PROSPR initiative and NCI funding are appropriately acknowledged in the manuscript.

Adherence to PROSPR publication procedures is required for all publications resulting from collaboration between two or more PROSPR entities, be they data-oriented or conceptual in nature. In addition, manuscripts that intend to represent PROSPR as a whole, even if not arising from collaboration across PROSPR entities, are required to follow the publication procedures. Manuscripts resulting from a PRC's three individual research projects or exclusively from their own data are not required to adhere to PROSPR publication procedures.

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4.1.1.1 Data Use

The intent is to produce a complete common use data set to be used by PROSPR researchers. All data use must be compliant with the data use agreements between the PRCs and the SCC. Most analyses will include data from all PRC's able to supply the data of interest. In rare cases use of the data from a particular PRC may violate the data use agreement or may interfere with the timing of an individual PRC publication. In this case the PRC can withdraw its data from the overall publication by providing an explanation to the Steering Committee. The data would be retained at the SCC, but not used in that publication. While this option may never be invoked, we consider it essential to protect the PRC's and such withdrawal cannot be overruled by the Steering Committee.

It is a given that PRCs will have the opportunity to complete projects and publish analyses proposed in their original application or as part of supplementary proposals. When there is significant overlap between PRC and transnetwork projects, PRCs are expected to execute their work in a timely way so that transnetwork projects are not hindered.

Use of PROSPR data by outside investigators:

All use of the data by either internal or external investigators must be approved by the Steering Committee. However, separate rules apply to use of data by investigators outside of PROSPR if the data are to be analyzed outside the SCC. In particular, certain data belong to a protected class of variables which cannot be provided to outside investigators without the consent of the Steering Committee and each individual PRC providing data. Such consent would be restricted to a specific analysis under a data use agreement. These would include specific dates (birthdate, screening date, diagnosis date, etc.) as well as all higher level variables such as provider ID (even masked), provider-level variables, clinic ID, and clinic-level variables. Even the individual PRC identifier may not be provided. This is not a complete list and such a list will be compiled as the database develops. Outside investigators wishing to use such variables can request that the SCC perform the analyses given approval of the Steering Committee and PRC's contributing data to the analysis.