PRINCIPAL INVESTIGATOR (MCCLAY, JAMES, C.):

PCORnet® Phase 4 CRN: TECHNICAL PROPOSAL

TECHNICAL STRATEGY *Do not exceed 16 pages.*

A. Executive Network Summary: The Greater Plains Collaborative[1] (GPC) is a network of fourteen leading medical centers providing care in fourteen states (CA, CO, IA, ID, IL, KS, MN, MT, MO, NE, TX, UT, WI, WY) committed to a shared vision of improving health through ongoing learning, adoption of evidence-based practices, and active research dissemination. James McClay, MD, Elizabeth Chrischilles, PhD, and Bradly Taylor, MBA, will lead the GPC from the University of Missouri (MU), University of Iowa (UIowa) and the Medical College of Wisconsin (MCW), respectively, and other partners are: Allina Healthcare (Allina); Intermountain Healthcare (IHC); Marshfield Clinic (MCRI); University of California Los Angeles (UCLA); the University of Kansas Medical Center (KUMC); University of Nebraska Medical Center and Children's Nebraska (UNMC); Washington University (WashU); University of Texas Health Science Center at Houston (UTHSCH); University of Texas Southwestern Medical Center (UTSW); University of Utah (UUtah); and University of California Davis Health (UCD) as a new partner.

The GPC combines flexible, scalable data infrastructure supporting traditional and contemporary (e.g. machine learning, deep learning) analytics[2], robust engagement[3] for prospective pragmatic trial recruitment[4,5], and a large clinical population to advance national representativeness of PCORnet® for definitive studies. GPC sites encompass[6] acute and ambulatory care settings across the lifespan and a broad geographic region including urban and rural diverse populations, with investigators and teams experienced in engaging these populations. Phase 4 GPC activities focus on improving research readiness, cultivating investigators attuned to patient centered research, and maintaining required and GPC aligned infrastructure to support of PCORnet® core principles[7]:

1) *Ensuring Meaningful Engagement of Patient and Stakeholders*: As shown in Figure 1 (Criterion 1) and further described in Criterion 2, our governance and operational functions (a) nourish long-term relationships with PCORnet for stakeholder-engaged governance and (b) foster focused, shorter-term engagement for specific projects to impact research at the earliest phases of feasibility and research question refinement. We will build upon our successful programmatic engagement and highlight: (a) continued transparency in communication with each site's engagement leaders and external investigators via our Front Porch website[8], (b) aligning the External Stakeholder Advisors cultivated in Phase 3 with our Health System Leaders plus patients, families, caregivers, and other community health partners , (c) continuing annual Learning Engagement Conferences (LEC)[9] which have served as a venue for culture building, engaged policy development, and research sharing, and (d) using the Rapid Patient and Community Engagement (Rapid PACE)[10] platform for investigators using the GPC to engage patients via one-hour facilitated project discussion sessions with patient participants who provide their insights, questions, and recommendations across all stages of the research process from design, to implementation, and dissemination.

2) *Centrally Accessible Distributed Research Model*: GPC follows a distributed model where protected health information is held at the sites but consolidates limited data at the network level to support data linkage and efficient self-service query tools and analysis environments. Individual GPC sites' response time to central PCORnet queries (4.8 days; over 297 total queries responses since Phase 3 started) continues to be on par with the overall PCORnet average. As part of the Phase 3 PCORnet Query Fulfillment[14] Coordinating Center, UIowa acted as a PCORnet query development center while MU tailored NIH initiatives[11-13] self-service query tools[16] to allow PCORnet investigators to search the GPC's PCORnet Common Data Models (CDM) in minutes, not days.

3) *Commitment to Sharing Resources and Tools*: GPC is transparent in sharing resources and communications at the PCORnet level[17,18] and via the GPC website Front Porch[19], open Google Docs[20] meeting agendas and minutes, and liberal use of GitHub[21] for open source code repositories, a GPC Commons wiki[22], and issue tracking. As part of the Engagement Core for PCORnet, Jeff Ordway (patient partner co-investigator) co-created a toolkit of PCORnet engagement resources as a framework to assist all partners in implementation of engagement strategies and Criterion 5 provides added detail.

4) *Advancing the PCORnet Common Data Model with Quality and Consistency*: GPC sites continue to have their CDMs ``Approved for Research'' and GPC leverages established studies for discovery of data gaps and resolutions by having our GPC data scientist and doctoral students catalog and periodically re-execute quality assurance programs that are shared with our sites, healthcare systems, and shared nationally[23,24]. Additionally, we have started leveraging quality assessment tools developed by the OHDSI[25] consortium and data quality assessment methods developed by PEDSnet. In Phase 4, we use our GROUSE linked claims environment to assess data completeness by comparing our sites' CDMs against the linked encounter activities billed to Medicare/Medicaid as well as registry data on a quarterly basis. We will continue to enrich site-level capability by standardizing tumor registry data and organizing clinical notes[26,27] in the PCORnet CDM.

5) *Streamlining Research Conduct*: All GPC sites have implemented and comply with PCORnet standardized mechanisms such as SmartIRB for research institutional review board[28] oversight and leverage this capability with funding opportunities through PCORI and other agencies. All sites have signed confidentiality and data sharing agreements and GPC rapidly distributes Front Door requests to sites for participation. GPC has developed transparent pricing in alignment with national guidance and also supports sending data to external investigators leveraging our external institution collaborator agreement[29]. In Phase 3 GPC developed streamlined patient partner bank card payment methods[30] which reduced onerous administrative processes for patients as many institutions either classify patient partners as either business or human subjects in clinical trials. Phase 4 adds the Research Readiness Coordinator role to catalyze capability.

6) *Advancing Complete and Comprehensive Data through Linkages*: GPC record linkage strategies optimize CRN level and site level data completeness. The GPC Reusable Observable Unified Study Environment (GROUSE)[31] is a unique de-identified data resource linking Medicare and Medicaid claims, environmental exposures, and social determinants of health with electronic health records and registries from all GPC sites. GROUSE is used for continued characterization of data quality, the GPC's three PCORnet cohorts (breast cancer[32], amyotrophic lateral sclerosis[33], and the consequences of healthy and unhealthy weight[34]) and ideal for patient centered economic outcomes research[35] called for with PCORI's reauthorization in 2019. At the site level, GPC's Snowflake distributed cloud services[36] also host self-service query and analysis applications, methods for distributing death records to sites, and privacy preserving record linkage[37] powered by Datavant® connecting over 1.5 million patients in common with the Department of Defense and Veteran's Administration Infrastructure for Clinical Intelligence (DaVINCI)[38] health records. In Phase 4 vanguard GPC sites will further PCORnet's precision health capacity by linking to sequence data from genomic testing[39].

7) *Protecting privacy, data security and human subjects*: All GPC sites consist of major healthcare systems and universities with IRBs and institutional procedures aligned with PCORnet's data security and privacy policies such as the PCORnet Master Data Sharing Agreement. GPC partners standardize electronic health record data behind institutional firewalls. All studies are reviewed by an IRB to ensure compliance with the Common Rule and HIPAA, and PCORnet ensures that patient data used in research are managed according to applicable laws, IRB approvals, and individual patient consent. GPC employs Privacy-Preserving Record Linkage[37] (PPRL) to link data across PCORnet and external partners through encrypted hash tokens determined to be de-identified data under HIPAA Expert Determination. GPC's central hosted services have adopted the Data Management Plan Self Attestation Questionnaire[40] (DMP SAQ) provided by the federal CMS Data Protection and Safeguard Program[41] (DPSP). Supported by Amazon Web Services (AWS)[42], Snowflake and Oracle, the cloud environment adheres to the National Institute for Standards and Technology Special Publication 800.53[43,44]: "Security and Privacy Controls for Federal Information Systems and Organizations", as well as HIPAA[45] (shown in Figure 7, Criterion 3). By adhering to these comprehensive data security, privacy, and research policies, GPC ensures the protection of patient information while promoting effective, patient-centered outcomes research, fostering a secure and trustworthy environment that enhances the credibility and reliability of the research conducted within the PCORnet framework.

Population and PCORnet Study Leadership and Participation: As shown in Table 1, the Greater Plains Collaborative encompasses a large population across three time zones ensuring PCORnet Studies can be national in scope and

representative of the nation. Currently, GPC participates in 14 PCORnet designated studies with participation by all initial Phase 3 GPC sites and all sites recruited to the NIH PREVENTABLE trial GPC (over 1500 patients). The Neuroendocrine Tumor - Reported Outcome study is led by Michael O'Rorke at UIowa, Mark Supiano serves on the PREVENTABLE lead committee with STAR, and Jim McClay (MU) and Betsy Chrischilles (UIowa) are Co-Is in the BASICS study with PaTH. This Spring WashU was awarded an NIH R01[46], "Choosing Immune Suppression in Renal Transplantation by Efficacy and Morbidity 2" involving GPC, STAR and OneFlorida CRNs and GPC has filed for PCORnet designation.
The Greater Plains Collaborative looks forward in Phase 4 to providing genomically enriched, higher quality data infrastructure, increasing readiness for prospective recruitment across a large segment of our nation, and expanding our research programs to consider patient economic outcomes along with broader engagement across diverse stakeholders.

Table 1. Clinical Research Network (CRN) Population	
Number of Unique Patients 38,455,948	*Total number of unique patients (% of patients)*
Demographics	
Age	
• Mean Age 44.78	
• 0-19	*7,126,450 (18.53%)*
• 20-44	*12,745,009 (33.14%)*
• 45-64	*9,083,600 (23.62%)*
• 65-74	*4,398,493 (11.44%)*
• Older than 75	*4,928,700 (12.82%)*
Sex	
• Female	*20,234,432 (52.62%)*
• Male	*18,101,244 (47.07%)*
• Other	*120,029 (0.31%)*
Race	
• American Indian or Alaska Native	*186,540 (0.49%)*
• Asian	*1,056,733 (2.75%)*
• Black or African American	*3,428,908 (8.92%)*
• Native Hawaiian or Other Pacific Islander	*120,864 (0.31%)*
• White	*22,446,259 (58.37%)*
• Multiple Race	*236,048 (0.61%)*
• Refuse to answer	*551,732 (1.43%)*
• Unknown	*5,318,158 (13.83%)*
• other	*4,490,337 (11.68%)*
Hispanic	
• Yes	*4,080,604 (10.61%)*
• No	*24,235,916 (63.02%)*
• Other	*9,874,091 (25.68%)*

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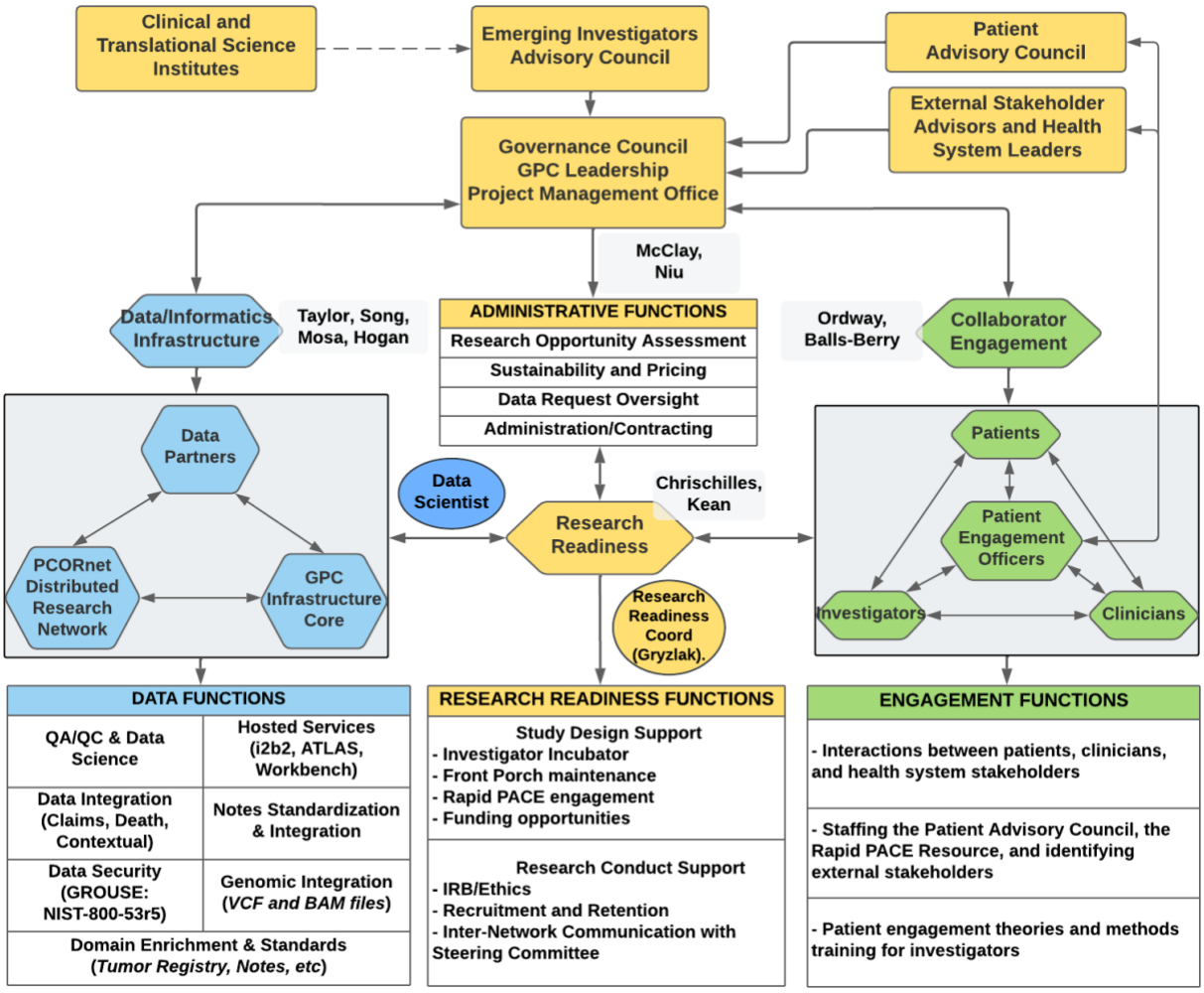
B. Approach for Phase 4 Participation in PCORnet governance, collaboration, and operations to facilitate national scope PCORnet® Studies of national scope. (Criterion 1 – Governance & Research Readiness).

1. CRN Governance: For Phase 4, GPC will maintain multidisciplinary leadership with Dr. McClay (Governance, Contact PI) Dr. Chrischilles (Research Readiness, Dual PI), Mr. Taylor (Data Infrastructure, MPI), Mr. Ordway (Patient Partner Co-I) and an inclusive model (Figure 1) integrating patients, clinicians, investigators, and external stakeholders.



The Governance Council, which includes the network PIs (McClay, Chrischilles, Taylor), patient partner Co-I (Ordway), and GPC Site PIs who represent their health systems, meets monthly to review and approve: (a) GPC policies and agreements; (b) new institutional members; (c) partnerships with other PCORnet networks and external organizations; (d) pre-award proposal support and budgeting; (e) and sustainability and pricing. The PIs and Governance Council oversee three core GPC activities: *1) Data and informatics infrastructure* (Taylor, Song, Mosa and Hogan) encompasses (a) managing interactions with current and new data partners (e.g., GPC institutions, insurers including Medicare, Datavant, data partners), (b) data request oversight, (c) the PCORnet Distributed Research Network, and (d) GPC staff maintaining distributed and centralized data infrastructure.

2) Research readiness (Chrischilles) is supported by the Research Readiness Coordinator (RRC) (Gryzlak) and facilitates (a) research opportunity assessment and response; (b) study design support and the investigator incubator; (c)

research conduct support including IRB/ethics and recruitment and retention methods; and (d) researcher engagement and interactions among clinicians, patients, and investigators to support PCORnet Studies and proposals.

3) Engagement (Ordway, Balls-Berry) encompasses (a) interactions between patients, clinicians, and stakeholders; (b) staffing the Patient Advisory Council, the Rapid PACE Resource, and identifying External Stakeholders and Health System Leaders; and (c) patient engagement theories and methods training for patients and investigators.

The Governance Council is advised by **two** stakeholder committees with site representation:

- The **Patient Advisory Council** (chaired by Mr. Ordway and Dr. Balls-Berry) participates in GPC activities (e.g. research opportunity assessment) and provides the Rapid PACE Resource for supporting investigators described further in Criterion 2. Mr. Ordway and Dr. Balls-Berry work with the external stakeholders and health system leaders to provide guidance on network research priorities and national activities for PCORnet and the coordinating center.
- With our Clinical Translational Science Institutes, the **Emerging Investigators Council** (EIC; mentored by Dr. Chrischilles) cultivates new investigators. The EIC advises leadership on resources to accelerate research in PCORnet studies of national scope, including recommendations for the Investigator Incubator. EIC members apply and are selected by the Governance Council.

The core administrative processes are led by the Administrative Director, Dr. Niu. The four main administrative function processes are described in the leadership plan and summarized here: *a) Research Opportunity Assessment* (ROA) disseminates and monitors response to Front Door collaboration requests and helps cultivate proposal development by investigators collaborating with GPC sites submitted via GPC's intake request form[1]. ROA is led by Dr. James McClay and is dually supported by the GPC Project Management Office (PMO) and RRC to ensure efficiency and review requests for alignment with the PCORI Strategies to Leverage PCORnet to Advance PCORI's National Priorities for Health. *b) Sustainability and Pricing* updates GPC infrastructure cost recovery models[2] and investigator Front Porch resource guide[3] with PCORnet infrastructure cost recovery guidelines. c) *Data Request Oversight Committee (DROC)* handles GPC-level requests[4] to execute queries and fulfill de-identified, limited, or identifiable data use requests[5] allowed by GPC's data sharing agreement[6]. d) *Administration and Contracting* for the GPC PCORnet contract and for many contracted studies but also supports sites when studies either contract directly or a GPC study will be led by another site.

Tactically, GPC starts each week with a GPC project call to review tasks, proposals, ongoing projects, and decisions to be supported by meetings or coordination throughout the week. GPC has streamlined operations by merging its informatics/development and project management calls into a single weekly Tuesday DEV/PM call with notes available publicly via the GPC Google Drive[7] linked from the GPC network Github Wiki[8]. Quarterly Institutional Review Board calls are coordinated by Utah and other forums are organized as required for projects such as the PREVENTABLE trial calls.

2. CRN Infrastructure to Enhance Research Efficiency and Collaboration: As GPC prepares for Phase 4, we highlight areas we see as specific strengths and how we will optimize and maintain them during the 4-year award period:

a) Streamlined, Standardized Federated Resources and Compliance with PCORnet Policies for Scalable Research: GPC sites have implemented and comply with PCORnet streamlined and standardized federated mechanisms for efficient and rapid conduct of PCORnet studies of national scope. All the GPC sites use centralized IRB and leverage this capability with funding opportunities through PCORI and other agencies such as the NIH, NSF, etc. All GPC sites have signed confidentiality and data sharing agreements. In addition, all sites have successfully implemented Datavant. In addition, GPC was instrumental in early support for SmartIRB[9] across CTSAs and PCORnet in partnership with the Trial Innovation Network. GPC established IRB reciprocity[1] early in 2015 which served as a key pilot. Similarly, the GPC reciprocal data sharing agreement (established in 2014-2015 during Phase 1) socialized and provided context for partners' subsequent alignment with the national PCORnet data sharing agreement that emerged later in Phase 2. In so doing, GPC sites comply with PCORnet governing policies, procedures, and core principles for PCORnet for the scalable, secure, and streamlined conduct of patient-centered, multi network research.

b) Participation in PCORnet Diversity, Equity, and Inclusion Practices: The GPC endorses PCORI DEI goals for PCORnet as expressed in the Maturity Model and commits to growing maturity in this domain. We have increased representation in

our network leadership and strengthened representation through our network characteristics. With respect to diversity at the GPC level, each site encompasses acute and ambulatory care settings across the lifespan and our breadth and expansion of sites (see partner summaries with addition of UCLA and UC-Davis) has increased representation of racial and ethnic minorities and safety net providers. As a network, we encompass a broad geographic region including urban and rural underserved populations and investigators and support teams experienced in engaging these populations. Our CDMs exceed 30 million patients which are linked to our integrated claims environment[10] that supports analysis across the entire beneficiary populations (over 25 million Medicare/Medicaid beneficiaries) and cancer registry characteristics.

c) Implementing PCORnet Data Security and Privacy Policies: As described in the Executive Summary and Criterion 3, GPC follows strong institutional protections at the site and best practices for federal compliance for GPC hosted services.

d) Active Engagement in PCORnet-Wide Activities: In support of increased use of the PCORnet infrastructure for the conduct of multi-network research, GPC has robust participation in PCORnet Steering Committee[11] (SC), SC Standing Committees and ad hoc Committees. Dr. McClay is an active participant in the PCORnet Steering Committee as the Phase 3 Dual PI and has 80% attendance overall. He will provide updates to the GPC site PIs after biweekly Steering Committee meetings. In Phase 4, a new Research Readiness component of the GPC organization (Figure 1) will be led by Dr. Chrischilles, Mr. Gryzlak and Dr. Chrischilles will serve as GPC representatives to the Research Committee. New in Phase 4, site data mart liaisons will participate in quarterly meetings with the Coordinating Center and Mr. Gryzlak will facilitate remediation of issues identified. Dr. William Hogan (MCW; prior OneFlorida Dual PI) will serve on the Data Committee. Dr. Joyce Balls-Berry (Washington University) leads an active patient engagement group with Patient Advocate and Patient Engagement officers from each site. Mr. Jeffrey Ordway (Missouri) is the GPC representative to the Engagement Committee, the PCORnet Engagement Coordinating Center, and PCORI reviewer. Dr. Xiaofan Niu is an active member of the CRN program management and query pricing meetings.

e) National Leadership, Participation, and Collaboration in Studies: In addition to successes noted in the executive summary, GPC has built upon our success with ADAPTABLE with strong recruitment to the PREVENTABLE trial. GPC holds meetings led by Dr. Mark Supiano (GPC's PREVENTABLE Steering Committee rep.) to discuss trial recruitment/retention. GPC leads the PCORnet-designated Neuroendocrine Tumors - Patient-Reported Outcomes study (O'Rorke, UIowa, PI) and newly PCORnet designated CISTEM2 (NIH R01) – including STAR and OneFlorida+ (Dharnidharka, WashU, PI)

GPC sites are participating in 15 out of the 26 currently active PCORnet designated studies.
ACTIV-6[12], BACK-OFF JSpA[13], BASICS[14], cvMOBIUS2[15]., ILD Care[16], NET-PRO[17], ODYSSEY RCC[18], PKIDS[19], PRECIDENTD[20], PRESERVE[21], PREVENTABLE[22], RECOVER[23] (Adult and Child), Using PCORnet to Compare Blood Pressure Control Strategies[24], and CISTEM2[25]
GPC sites led and were awarded multi-site proposals leveraging PCORnet infrastructure
*DRIVERs[26] (NIHR21) - junior investigator PI, multiple GPC sites, intended preliminary data for PCORI MMM priority area. *ALS4M[27] (NIH RO1) - rare disease, junior investigator - Song Xing, PhD, PI - University of Missouri *Chemotherapy Dosing in Patients with Obesity[28] (DOD R01) - Mary Schoeder, PhD, PI - University of Iowa
Other projects also successfully engage GPC network and multiple sites
*BESTMED: Observational Evaluation of Second-Line Therapy Medications in Diabetes[29] - Alexander Turchin, MD, PI *Personalized Machine Learning for Acute Kidney Injury Prediction and Prognosis[30] - Mei Liu, PhD, PI
Current Broad Pragmatic Trial Submissions: GPC provided researchers support to navigate FD intake and study designation
*DROOL-CONTROL - Richard Barohn, MD - University of Missouri *Knowing When: Advancing Evidence-Based Patient-Centered Decision-Making - Lisa Royse, PhD - University of Missouri *Evaluating implementation of obstetric patient safety bundles: A CER Study - Nichole Nidey, PhD - University of Iowa

f) Front Door Dissemination and Responsiveness: In order to facilitate PCORnet Front Door research study requests and identify local investigators to participate in the studies in a timely manner, GPC uses decentralized dissemination. All FD requests and opportunities are directly communicated to the GPC site PIs and PMs by the FD. Timely (within 10 business days) investigator interest responses are managed by the GPC site teams, and then reported to GPC central. GPC leadership also sends out reminders to the sites to ensure that sites are aware of these opportunities. FD tracking shows

consistent high GPC site interest. Since the start of Phase 3, GPC sites responded to 88.2% of 297 PCORnet FD queries on time with satisfactory results, network average 4.8 days, below the required five-day turnaround.

g) Maintain Collaborative Relationships. GPC is effective in maintaining relationships with other CRNs through the bi-weekly Steering Committee meetings as well as the monthly Project Management Office meetings of PCORnet. Drs. McClay and Niu are active in providing feedback and inputs on discussion topics. Site communication updates and milestone status tracking of all the multi-site projects with the lead study teams are shared and recorded on weekly Dev/PM meetings. Both GPC central and site study teams are very active in facilitating the communication between investigators and the corresponding Coordinating Centers of PCORnet.

Engaged patients, families, caregivers, and the broader health and healthcare community (Criterion 2 – Engagement)

The Greater Plains Collaborative is organized around a culture of engagement which incorporates patient partners in the use of the electronic health information they co-create.[1, 2] Building on evidence of the increasing role patients play in improving care and safety[3] as well as the accuracy of their medical records,[4] we have learned that patients remain intensely vested, and that researchers continue to need help to see opportunities and cultivate culturally appropriate relationship with patients to add value research being proposed and conducted. A lesson learned early on that continues to inform our engagement work is that each site's engagement leaders bring a unique lens to this work.[5] The GPC engagement track record documents important improvements that support patients in participating meaningfully in big data studies and pragmatic trials. Our network's unique size and geographic span as well as a diverse array of study topics challenge us to innovate and grow our engagement approaches and resources. In Phase 4 GPC's engagement efforts will continue to (a) nourish long-term relationship with the GPC network for stakeholder-engaged governance, (b) focused shorter-term engagement for specific projects to impact research in all phases, but especially during the earliest phases of feasibility and research question refinement, and (c) additional focus to support investigators.

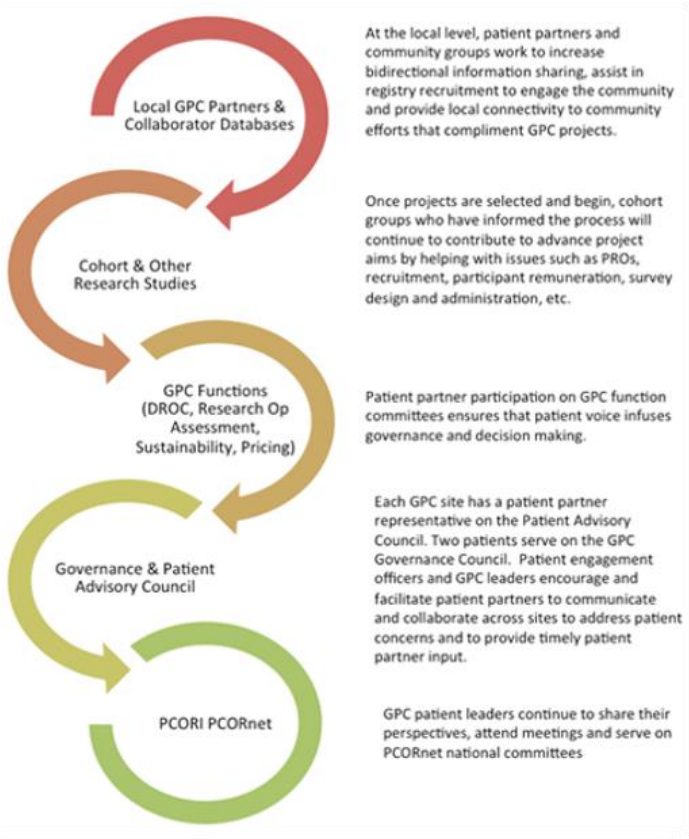


Figure 2. GPC Patient/Community Engagement

1) Stakeholder participation in decision making: Patient participants have varied reasons for doing this work. Some see it as a way to support their local site partner; others see the opportunity to influence PCORnet and national efforts to engage patients in big data while still others see it as a way for them to bring historically minoritized individuals and underrepresented voices into research. Accordingly, patients, health system leaders, and external stakeholders who have a deep interest and understanding of the PCORnet informatics infrastructure and goals have been tapped for governance input and all receive updates via listservs as well as monthly Global Calls. During Phase 4, these partners will remain as voting members of the GPC Governance Council and the Data Request Oversight Committee and represent the Patient Advisory Council on governance issues including service on the PCORnet Steering Committee. As shown in Figure 2, we have had an engagement model that highlights what we refer to as "engagement circles" of influence and leadership. The addition of our Patient Partner Co-Investigator will add a new level to the inclusion of our partners in the overall governance of the GPC.

2) Engage Patients and stakeholders in all phases of research: In addition to governance, oversight, communications, and patient matchmaking as study partners, GPC will continue its successful *Rapid Patient and Community Engagement (PACE)*. The engagement team developed a platform to encourage patient engagement for investigators using the GPC, especially if they are unable to marshal the resources needed for engagement at their local site. Rapid PACE[6] coordinates one-hour sessions that begin with the investigator sharing their GPC research project. Investigators are provided with guidance and a limited number of PowerPoint slides with a prescribed outline to use during this brief, 10-15-minute presentation. Afterward, the lead

engagement officer facilitates a discussion of the project with each patient participant weighing in to provide their insights, questions, and recommendations. Evaluations by both investigators and patient partners following Rapid PACE sessions document direct value to the project and is an experience patient partners point to as fundamental in strengthening their abilities to truly feel they are influencing the research process. We were able to increase Rapid PACE involvement in Phase 3 with promotion through the GPC "Front Porch" and review by the Research Opportunity Assessment team. This will continue through Phase 4 and provide availability at all phases of a project, from refining the research question, to recruitment and retention, implementation, and to dissemination of results. Since Phase 3, following the Rapid PACE we are testing the use of a short survey for patient partners to provide additional feedback and if needed endorse a research study.

Further, five GPC health systems or affiliates are members of PCORI's Health System Implementation Initiative (HSII)[7]: Intermountain Health, Iowa City VA Health Care System, Saint Luke's Health System, the Nebraska Medical Center, and the University of Missouri Health Care System. HSII is a multiyear effort to increase uptake of comparative effectiveness research in care delivery and these HSII participants are in an ideal position to provide feedback regarding PCORNet studies. In Phase 4 we will engage our HSII leaders and PCORI regarding how we can connect the two initiatives so that these experienced health system voices can provide feedback regarding study development, dissemination, and impact.

3) Support investigators to compete for funding and conduct of multi-network research: The GPC engagement team remains vigilant and committed to training the research community in engagement and patient centered outcomes research. One tangible way the engagement team makes a durable contribution is through a self-paced curriculum with modules for researchers and their teams that we are developing for delivery through the 'Front Porch' and which may become a required prerequisite to using the GPC's infrastructure. The goal of the curriculum is to use examples of patient and community engagement that leads to culturally appropriate research question development, study design, implementation, analytic, and/or dissemination strategies to increase health improvement as well as to ensure adherence to the newly established PCORnet Engagement Policy.

The foundation of this research centers on the work of our Patient Partner Co-I, Jeff Ordway. He has co-led the Engagement Core's development of a toolkit of engagement resources that are accessible through the PCORnet Knowledge Repository. Mr. Ordway understands the different resources that are available from all PCORnet sources will inform the development of the Investigator Incubator for our emerging researchers (see Criterion 5 below).

4) Onboard and train partners: The GPC onboards and trains partners by setting up an initial conversation between the new partner and our Engagement Lead and our Lead Patient/Patient co-investigator to gain an understanding of the new partner's lived experience and to assess their knowledge of research and PCORnet. Tailored training is then designed for each partner to bring them up to speed in the workings of the GPC and PCORnet and to develop them as full partners in the CRN. We also utilize a "buddy system", where we match each new member with a more established member of the GPC engagement team for support. Ongoing training takes place at monthly meetings, as well as at our LEC, to support the partners in growing their understanding of research methods. We are adding the Investigator Incubator to our training processes to ensure that we are supporting our emerging researchers with the information and training necessary for them to understand the impacts of engagement on research, and to efficiently and effectively utilize PCORnet for their research aims.

5) Identify and engage partners in PCORnet: Each GPC site designates a patient engagement officer and a lead patient research advocate to work together. This model provides direct impact on local site activities and it contributes to the engagement learning environment collectively; it will continue into this phase of the GPC. All sites recognize the importance of nominating diverse and representative voices from their local communities, and this attention has ensured that the GPC maintains a racially, ethnically, culturally and socioeconomically diverse patient advisory council. In addition to this dyad, we have stood up an additional External Stakeholder Advisory whose members represent other health interests including: 1) Dennis Ridenour President and CEO of BioNexus KC - a biomedical products and services

group; 2) Andwele Jolly, President and CEO of Integrated Health Network - nonprofit network of health care systems, public health departments and FQHCs in the St. Louis Region, and 3) Caroline Hoedemaker, Entrepreneur - Medical instruments and biotech research services who served on the PCORnet steering committee as a voting member.

6) Support diverse participation: GPC's health system service areas span urban and rural populations from Texas to Minnesota and Illinois to California. This breadth provides the geographic substrate for PCORnet to meet its objective of reflecting the diversity of the nation for definitive studies. This environmental diversity is complemented by strong community and patient engagement programs at our sites where the majority have dedicated community engagement components associated with their Clinical and Translational Science Institutes as well as specialized cores such as Dr. Balls-Berry's health disparity core[8] for the Knight Alzheimer Disease Research Center. The GPC engagement team and the site level expertise support not only increasing study recruitment diversity but also engaging varied stakeholders in participating across all aspects of the research enterprise in their communities as well as opportunities for national participation.

7) Foster Diversity, Equity, and Inclusion: Dr. Joy Balls-Berry, our lead patient engagement officer, served as a PI of a PCORI Eugene Washington Engagement Award in 2016 to 2018 and is currently the PI of an NIH grant to create opportunities to increase diversity in biomedical research using the foundation of community and patient engagement in research. Through her research efforts she has created curriculum related to community engaged research, assisted with the establishment of numerous diversity, equity, and inclusion programs for researchers, their partners, and future investigators including the Minority Women Research Network (PCORI funded), serving as the co-chair of the Diversity Committee for the Association of Clinical and Translational Science, and other roles within her former academic home at Mayo Clinic and her current role at Washington University. This work is done with multiple patient and community partners to ensure their voices are heard in the research process. Dr. Balls-Berry will continue to apply these approaches to GPC governance, education and training for Phase 4 to increase research readiness in collaboration with Mr. Grylzak (Research Readiness Coordinator) and Mr. Ordway (Patient Co-Investigator).

8) Align with PCORI activities to advance the science and practice of engagement: Mr. Ordway and Dr. Balls-Berry as our CRN engagement dyad are ideally positioned to increase GPC's alignment with PCORI and Coordinating Center (CC) activities, which includes creating a plan to operationalize and implement the new PCORnet Engagement Policy within the GPC. Mr. Ordway, our patient co-investigator, will continue his work with the Engagement CC after completing work together with Dr. Kim Kimminau (initial Phase 3 GPC lead patient engagement officer) to develop the PCORnet toolkit of engagement resources, as well as providing input in the continued development of policies for engaged practices through PCORnet, and also continuing service on the engagement committee. Together with Dr. Balls-Berry, they cover the spectrum of engagement science and application and can work within all levels of our governance structure to ensure all network and site activities are done in collaboration with PCORI directed activities.

Learning Engagement Conference (LEC): Finally, in Phase 4 we will maintain the rewarding annual LEC meeting which has served as a venue for culture building, engaged policy development, research sharing, and fostering trust. Each year, the engagement work of the GPC is highlighted from the podium, in breakout sessions and in introducing new ways of engagement participants to influence governance, policy adoption, learning across the Network, and develop novel ways to increase patient centered outcomes research. A PCORnet and GPC introductory bootcamp training is provided for all new partners and was recorded for onboarding conducted by the PCORnet Coordinating Center Engagement Core. In past LECs, engagement participants have conducted a poster walk, facilitated by one of the patient engagement officers, to encourage dialogue between researchers, team scientists, patient partners and informaticians to develop and successfully complete deliverables. Breakout topics have included a session on IRB compliance, meeting with informaticians to discuss de-identified data, and holding discussions around the Common Data Model. Feedback from patient partners speaks to this event as being a highlight feature of their participation.

High-quality, analysis-ready standardized data, use of the PCORnet® Common Data Model, and preserving privacy and data-security protections (Criterion 3 – Data) (5-page limit): *Sustained Quality*: To date in Phase 3, all initial GPC sites successfully completed 10 data curation refreshes (cycles 11 - 15, refreshes 1 and 2) and Empirical Data Quality (EDC) approval by the Coordinating Center. In 2023, we successfully added UCLA to GPC and PCORnet and they passed their first required check for refresh 15 this Spring. We note however that while San Antonio's CDM was approved by the Coordinating Center, their inpatient and emergency care data completeness was degraded given the departure of their University Hospital partner. We worked closely with their leadership throughout Phase 3 to see if this could be resolved but unfortunately, their robust and diverse practice lacks complete care environments until they complete their new hospital or restore data access to University Hospital. With remorse, we have removed San Antonio as a Phase 4 partner.

National Scope: Given the goal for greater national representativeness, we received approval from PCORI to add University of California Davis Health (UCD) as a partner for Phase 4. As part of the UC System, UCD and UCLA share Epic as an EHR vendor and participate in state data warehousing using the OMOP[1] common data model. UCD was previously part of PCORnet during Phases 1 and 2 and is committed to working with GPC before Phase 4 to ensure a compliant CDM for full participation. Table 1 from the Executive Summary and our individual network partner summaries now estimate GPC's total population to exceed 38 million patients, across all age groups, races, and ethnicities, in community and academic integrated delivery systems, delivering primary to quaternary care, across all settings, and in 14 states. As illustrated in Figure 3 below, GPC sites have excelled since Phase 1 in participating in multinetwork PCORnet® Studies that generate definitive national evidence as exemplified by all the sites in GPC at the time supporting the Bariatric[2] Study, the Childhood Antibiotic Study[3], ADAPTABLE[4], PREVENTABLE[5], and the highest number of sites per CRN supporting CDC COVID surveillance[6], NIH RECOVER[7], PROVIDE-HF[8], NET-PRO[9], and BASICS[10].

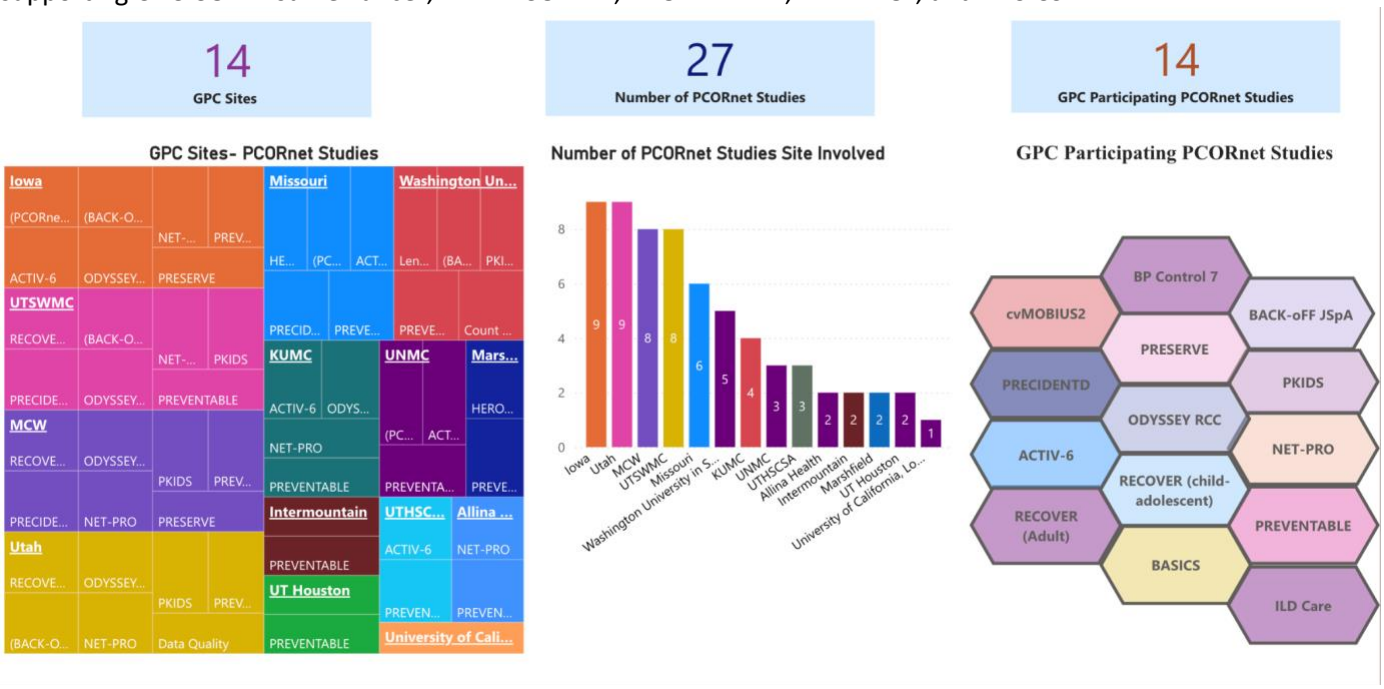


Figure 3. GPC PCORnet Designated Study Metrics Dashboard.

For Phase 4, GPC will build upon our improvements and innovations in Phase 3 by:

a) continuously improving data quality, interoperability, and data comprehensiveness by incorporating more domains from our EHRs, registries, and genomic testing,

b) using Datavant[11] for Privacy Preserving Record Linkage (PPRL) aligned with PCORnet and federal partners,

c) distributing vital status from the National Technical Information Service (NTIS)[12] to sites and CRN partners using PPRL,

d) GROUSE EHR/CMS Claims environment for research studies and data completeness analyses/remediation quarterly
e) extending the use of i2b2[13] and ODHSI's ATLAS[14] self service query/analysis tools, and
f) providing scalable, distributed computing to sites to further concurrent query throughput.

1) Data Mart Liaisons (DML) and Remediation: GPC data mart liaisons (see Criterion 4) are experienced in this role for their sites and will attend quarterly meetings with the PCORnet Coordinating Center to address and remedy any issues identified by data curation metrics and/or PCORnet Study teams. These gaps will also be communicated in existing weekly GPC calls and email communications to ensure all sites are aware also at the project management officer and PI level. The CRN Research Readiness Coordinator (RRC) will work with data mart liaisons to ensure that data marts promptly remediate any identified data quality issues that are out of compliance with the established PCORnet Steering Committee data quality service levels. Likewise, the RRC will support query prioritization and coordination to ensure prompt communication and responsiveness in alignment with those service levels.

GPCs governance (see Executive Summary, Criterion 1) has sustained high quality data for PCORnet since Phase 1 and will further enhance its processes and infrastructure in Phase 4 to meet requested characteristics specified below:

2) Quarterly Data refreshes and <60 days lag period: All GPC sites have completed required quarterly refreshes along with extract transform load (ETL) modifications to accommodate new attention to priority areas such as patient reported outcomes (e.g. depression screening and assessment) and value set reference changes. GPC sites participating in CDC COVID surveillance also refresh the CDM monthly or biweekly. All current sites have been providing refreshed data with lags <= 30 days. Sites will continue to generate quarterly updates with lags <= 60 days. Additionally, GPC central will continue to work with sites to resolve any identified issues within three months.

3) LOINC and RxNorm Mapping: GPC is committed to advancing data interoperability and will continue to improve LOINC and RXNorm mapping. As shown in Figure 4, all continuing sites are currently meeting the 80% threshold for RXNorm mappings; all of these sites have also met the LOINC criteria for the entirety of Phase 3. GPC has also advanced interoperability with UNMC collaborating with the National Library of Medicine and the CTSA community to retain mapping of retired NDCs to RXNorm and also leading efforts to map clinical observables to LOINC for clinical assessments[15,16] and developed SNOMED terminology standards for encoding molecular test results.[17,18] MU and MCW organized clinical notes using the LOINC document ontology deployed[19] across GPC to support natural language processing and de-identification[20].

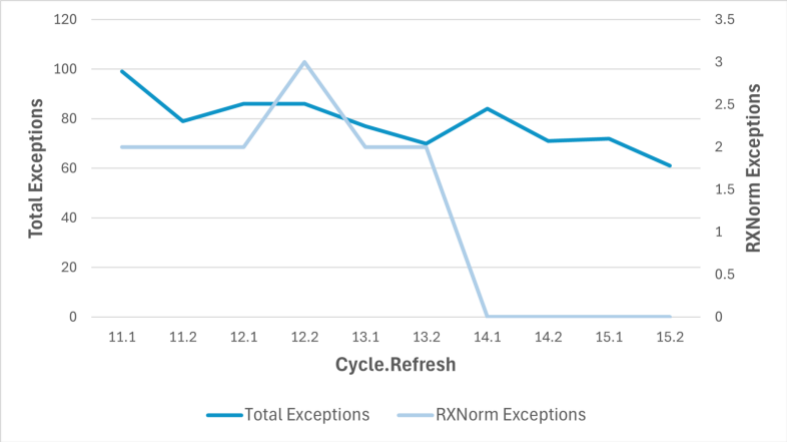


Figure 4. LOINC and RXNORM Mapping Rates Over Cycles

4) Data Completeness (> 75%), Persistence (decreases < 5%) , and Plausibility (> 80%): During Phase 3, GPC sites have met data completeness goals across encounters (San Antonio exception noted). Data persistence overwhelmingly increased with exceptions for when interpretation of CDM guidance changes. For example, Houston addressed deficient RxNorm mapping to discover that many home medications were brought into the PRESCRIBING Table and when removed this led to a >5% decrease. GPC sites throughout Phase 3 have maintained 80% of encounters with at least one face-to-face diagnosis and vital measurement though the rate has trended somewhat lower due to increased use of telehealth as a result of the COVID-19 pandemic.

5) Data Quality Investigation and Remediation: Working collaboratively with the PCORnet Coordinating Centers and DMLs, Dr. Spinka (GPC data scientist) will be joined by Mr. Gryzlak as RRC to continue reviewing EDC reports and Annotated Data Dictionaries (ADD) after each quarterly refresh. Any investigative data checks will be identified,

reported, and discussed on weekly GPC DEV/PM calls. The RRC will help facilitate investigation of the causes of any failed investigative data checks and will assist sites to develop a plan to resolve any investigative check errors not caused by source data constraints within two months (e.g. Surescript claims for retail dispensing lag clinical datastreams). In addition, a quarterly report will be prepared by GPC staff to highlight any investigative data check exceptions that are identified by GPC sites. This report will also determine which of the checks are remediable and which are irremediable and identify the reasons behind irremediable errors not caused by source data constraints within three months. This report will be utilized by the CRN Research Readiness Coordinator to facilitate the resolution of remediable exceptions.
6) Advancing Complete and Comprehensive Data Through Linkage: GPC will continue to enhance its integrated data environment, GROUSE[21], for linking claims data to GPC sites' CDMs and use Datavant for privacy preserving record linkage[11], distribute vital status from the Limited Access Death Master File[12] (LADMF) to our sites, and link to genomic testing results. GROUSE uses the federally supported, linkage approach with CMS to continue integrating Medicare/Medicaid claims data with GPC EHR/CDM/registry data as well as subsequent geocoding based linkage to social determinants of health proxies such as the American Community Survey[22,23]. This provides a unique resource for data-driven research by leveraging multiple health systems data integrated with Medicare and Medicaid claims (currently 25 million beneficiaries) to complete the picture of care received outside tertiary health systems. We applied 11 data completeness heuristic filters to patients who only have EHR/CDM data ("EHR only") versus those who had both EHR/CDM and CMS data ("Crosswalked"). The heuristic filters were based on availability of clinical facts, echoing the study by Weber et al[38] for evaluating data completeness: at least one observed record of a) diagnosis ("has_dx"); b) medication ("has_med"); c) outpatient medication ("has_med_out"); d) office visit ("has_office_visit"); e) outpatient visit ("has_op_visit"); f) procedure ("has_px"); g) routine visit ("has_routine_visit"). As shown in Figure 5, we see significant increase of patient retainment for the "Crosswalked" cohort, especially when filtered by medication and outpatient visits. We will build upon this work to consistently evaluate data partnerships and their capability to increase data completeness. In addition to supporting our ongoing disease cohorts (amyotrophic lateral sclerosis, breast cancer, and obesity), GROUSE has been approved to be reused by our NIH funded trial[24], "Remote Monitoring and Virtual Collaborative Care For Hypertension Control To Prevent Cognitive Decline (vCCC)" at KUMC and Utah and the newly funded NIH study[25], "Choosing ImmuneSuppression in Renal Transplantation by Efficacy and Morbidity (CISTEM2)" involving GPC, STAR and OneFlorida CRNs.

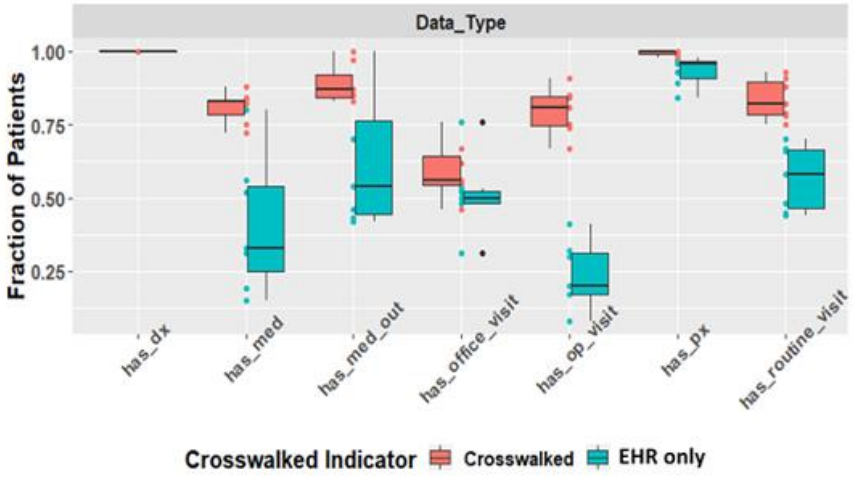


Figure5. Data Completeness Comparison Between CDM/EHR-only population and Crosswalked population

Led by Dr. Kean at UUtah, GPC and the REACHnet CRN have worked with the Department of Veterans Affairs (VA) and Department of Defense (DoD) on Brain Injury Data Sharing (BIDS), a project funded by the Joint Incentive Fund (JIF) to realize a patient-centric, longitudinal data source reflecting the complete care horizon for service members with traumatic brain injury. BIDS links the DoD/VA Infrastructure for Clinical Intelligence (DaVINCI) health records to PCORnet records using standard PCORnet Datavant tokens. In 2023, GPC completed the first phase of the linkage project on administrative preparedness, setting up a secure pipeline for Datavant hash token generation and exchange, and performed a general overlapping analysis resulting in a shared population exceeding 1.5 million patients with the software and results shared in our Github[26] commons. For the next phase, we will develop and distribute query packages

to collect detailed study-specific data for the Traumatic Brain Injury (TBI) population and investigate standard-of-care (SOC) variations and impact of community care.
While Datavant no longer offers distributing vital status from the social security administration as a service, GPC will return to obtaining certification to license the LADMF[12] directly from NTIS and seek use by GPC partners and PCORnet as other CRNs may also benefit from enhancing vital status completeness.
Finally, building upon PCORI stakeholder interest in molecular guided therapeutics and our Rapid Cycle Research Study[27], GPC (MCW) will standardize site level linkages to genomic test results[28,29] that are increasingly returned to health systems in standardized formats for variant call files as well as the detailed binary alignment map (BAM) files.
7) Site-specific query results: The GPC follows a distributed data model where queries go directly to the sites. In turn, the sites directly respond to queries. Additionally, GPC developed a site breakdown plugin[30] for i2b2 self-service queries.
8) Network-wide improvement efforts: GPC in consultation with PEDSnet has also developed[31] and deployed[32] PCORnet rule based quality checks to detect other logical and clinical inconsistencies in sites' CDMs and upstream systems. Because GPC operations are embedded within healthcare facilities, we have the unique ability to reach back to the original health records and the systems and processes through which data originate. Rules and feedback reports are generated for further investigation and remediation of data quality problems and the project's software is publicly available at our QUAIL[33] (Quality, Usability, Accessibility, Interoperability, Latency) Github site. GPC has started leveraging quality assessment tools developed by the OHDSI[34] consortium and N3C within QUAIL, and piloting data quality assessment methods developed by PEDSnet and alternative programming languages for the EDC with the Coordinating Center. GPC sites will also continue to pilot quarterly EDC code early and will track activity to ensure datamarts respond.
9) PCORnet CDM enhancement, expansion and evolution: GPC consistently provides feedback to the data committee regarding CDM enhancement and expansion. Since PCORnet's beginning, the GPC has prioritized inclusion of tumor registry data in each institution's datamart leading to grants and publications (referenced below in Criterion 5's vignette). The Cancer Collaborative Research Group (CRG) was funded by PCORI between 2017 and 2019 to promote multi-network cancer research and led to the development of a Tumor CDM table formatted according to standards published by the North American Association of Certified Cancer Registrars[35] (NAACCR). The Tumor table documentation on the GPC Github[36] includes specifications for data formats, quality check software, and relationships with other CDM tables allowing queries of the NAACCR data and CDM to be quickly deployed across the network. In Phase 3, GPC and NET-PRO study sites implemented the tumor table and is now being used for the development of a follow up to the PCORnet Designated BASICS[10] study (BASICS2) for the National Cancer Institute. GPC's lead role in the BEST-MED[37] designated study as well as the Maternal Morbidity and Mortality workgroup have also led to the specification for a Patient Reported Medications table lacking from the current CDM.
10) Support Query Execution: As a large network, GPC has strived for synergizing all partner sites to respond to participate in all front door queries and are committed to supporting the 30 Front Door queries per year within five days of receipt. From July 2022 to February 2024, GPC sites had received 23 queries and all sites responded, with 12 (out of 13) sites having data included in final reports on at least 90% of the queries (Figure 6.A). Among the qualified query responses (on time and data included in the final report), the median response time (in days) is 4.7 with the majority of GPC sites having their query execution time skewed to the shorter range (Figure 6.B). GPC has established a central REDCap project to facilitate transparent communication of potential data issues by collecting and analyzing EDC and ADD reports. Our data scientist (GPC SAS analyst) will generate and provide periodic analysis reports (similar to what are included in the progress report but with greater details) for sites to review and reflect. Besides leveraging PMO and Dev weekly joint calls where broad discussions on data issues are facilitated, GPC central will also organize one-to-one meetings with sites to help address data issues upon requests or identification of critical issues. GPC has also established a central github repository for better code and knowledge sharing.

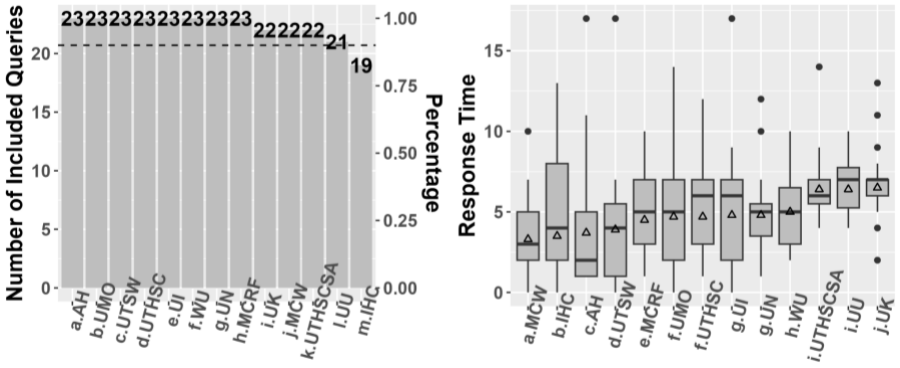


Figure 6. FD Query Completion Status and Trial Participation Statistics.

Additionally, the MU's CDM is deployed in the Snowflake[38] database using a SAS connector; reducing query execution time and enabling concurrent SAS queries. We will propose expanding to GPC sites in response to PCORI's May 2nd, "Enhance infrastructure to support efficient and effective development and execution of PCORnet® Studies" opportunity. GPC will monitor execution time to ensure that sites respond within 5 days Communications will occur across multiple venues, including dev/pm calls, governance calls, GPC listservs, and directly with sites as needed.

11) Implementation and maintenance of a publicly available PCORnet-wide self-service query tool: In Phase 3, GPC (MU) was funded as part of the PCORnet query fulfillment coordinating center and implemented[30] a i2b2-based self-service query (SSQ 2) tool and also piloted tested ETL software for the SSQ 1 simple query tool. SSQ 2 was first deployed for all GPC sites (1150+ queries; 38+ users) and then expanded to other PCORnet pilot sites. We also adapted OHDSI ATLAS[14] query tool to access the PCORnet CDM and are participating in the Phase 4 PCORnet Data Coordinating Center proposal to maintain the PCORnet CDM compliant i2b2 and ATLAS tools for self-service query infrastructure.

12) Privacy, security, research and human subjects compliance: As described in "*Protecting privacy, data security and human subjects*"of the Executive Summary, GPC is compliant with applicable laws, regulations, and legal requirements at each GPC site and in processes and systems managed by GPC centrally. MU's centralized GPC data architecture is shown in Figure 7 below. Data security is managed in accordance with federal, state, and institutional policies including NIST 800-53: Security and Privacy Controls for Federal Information Systems and Organizations[39] and HIPAA[40] compliance requirements to ensure strong security, governance, and data protection mechanisms. AWS "infrastructure-as-code"[41] capability provides security automation[42] to programmatically detect, investigate and remediate security threats by identifying incoming threats, triaging and prioritizing alerts as they emerge, then responding to them in a fashion that is significantly timelier than the manual procedures. The PCORnet, GPC Data Sharing Agreement and its External Institution Collaborator agreement, and GROUSE Data Use Agreements for claims linkage are signed and the GPC data request oversight committee (DROC) managed by honest brokers ensures compliance with human subjects and data sharing.

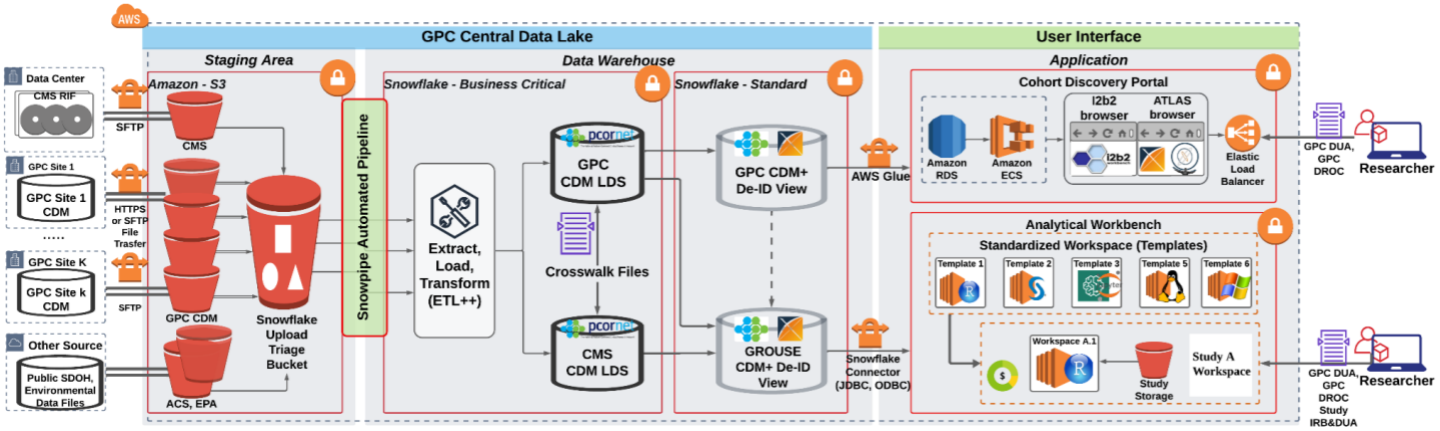


Figure 7. AWS and Snowflake cloud-based GPC Hosted Services Architecture

Dissemination and Resource Sharing (Criterion 5 - Dissemination) (2-page limit)

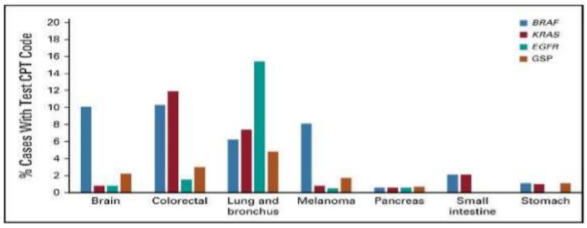
1) Outreach to promote awareness of CRN, PCORnet and use for CER: GPC governance and operations support resource dissemination and sharing both *within* our geographically dispersed network and *across* PCORnet and the public. In Phase 3, we enhanced these efforts in both directions with a GPC website[1] 'Front Porch', supported by centralized project management and research/query development support to fuel patient-engaged research. In Phase 4, we will enhance this with the new Emerging Investigators Council (Figure 1) and a pro-active Investigator Incubator.

Vignette: Dissemination and Resource Sharing to Develop a Patient-Centered Cancer Research Agenda

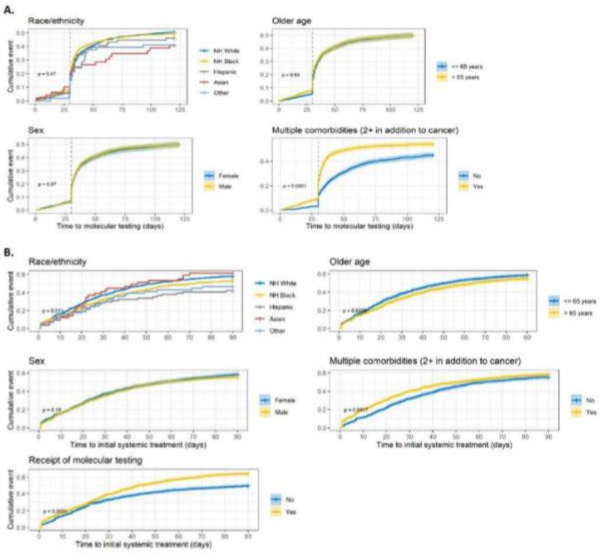
Stakeholder Engagement, Tools on iMeet and GitHub, Cohort Identification Queries

- Cancer Collaborative Research Group (CRG), Computable Phenotype for Systemic Therapy with RXCUIs, PCORnet CDM Tumor Table[4] used for PCORnet NET-PRO and BASICS studies; Cancer CRG Front Door Queries, Neuroendocrine Tumor (NET-PRO) computable phenotype node-to-node query; NET-PRO PCORnet Best Practices webinar.

Sample Study Results – PCORnet Molecular Testing Study:



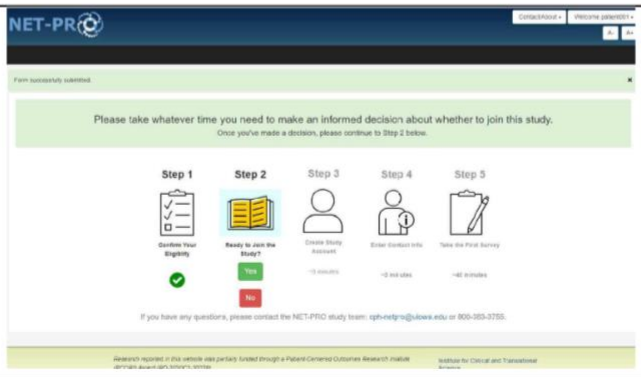
PCORI Rapid Cycle Project on PCORnet Molecular Testing (References 5-8) Percent of patients who had tests with Current Procedural Terminology (CPT) codes for BRAF, KRAS, EGFR, and genome sequence panels (GSPs), at 11 study institutions, by cancer types most commonly associated with these tests



(At right) Kaplan-Meier curves (A) cumulative incidence of molecular testing within 120 days of index date (ie, 30 days before and 90 days after diagnosis of metastatic lung cancer). Dashed grey line indicates index date of metastatic lung cancer diagnosis. (B) cumulative incidence of initial systemic treatment within 90 days of index date. (Reference: Osazuwa-Peters, Oyomoare L., et al. "Factors Associated With Receipt of Molecular Testing and its Impact on Time to Initial Systemic Therapy in Metastatic Non-Small Cell Lung Cancer." Clinical lung cancer 24.4 (2023): 305-312)

NET-PRO Study Tool to Engage Patients and Return Results to Participants:

The NET-PRO study customized the Iowa Personal Health Record as an interactive patient portal that gives patients control of their data and returns their survey answers and other information to them.



2) Share resources: The GPC website, listservs, wiki[2] and ticket management, and liberal use of GitHub[3] are publicly accessible and GPC PMO submits materials to the PCORnet online resource sharing library (aka "commons"). The GPC patient-centered cancer research agenda exemplified by NET-PRO in the **Vignette** above illustrates how GPC and PCORnet-level sharing foster PCORnet studies and resources. Materials are bidirectionally shared with PCORnet via the depositing GPC materials on the PCORnet Commons and sharing PCORnet Introduction Slide Deck[9] and the master

PCORnet iMeet workspace[10] with stakeholders and investigators. In Phase 3, GPC added its Front Porch; enumerating resources with a focus on *how* to actively engage with the GPC including site-level information, how researchers can submit requests to partner with GPC sites, and pricing information. The patient section includes GPC and PCORnet patient engagement resources, and how patients can participate in GPC activities. In Phase 4, we will expand the GPC Front Porch to host the *Investigator Incubator* (below).

GPC also has a long history of active dissemination through the LEC where sites share work in breakout sessions and the poster presentations. We plan to expand these opportunities with network patient advisors and patient engagement officers assisting in developing dissemination plans for research conducted across PCORnet. We will use the PCORI Dissemination and Implementation Framework[11] as the foundation of this work which fosters shared leadership in determining the strategies for dissemination. We will work with our stakeholders to identify priority areas based on the stage of research being conducted across the network. We will then determine the goals which include the messages and audience that we plan to reach based on the priority areas and plan dissemination using the *PCORI Dissemination and Implementation Toolkit*[12]. A key feature of this process also means that we must consider the end-users of this process we are designing so messaging must relate directly to these groups. As we move forward with this process, we evaluate areas of success and opportunities for growth in this dissemination.

3) Support of Dissemination and Resource Sharing Including the PCORnet Online "Commons": The GPC Project Management Office (PMO) will continue to maintain GPC list-servs; webinar software; site, committee, and workgroup contact information; and the GPC website. The PMO and RRC will maintain the 'Front Porch' linking to tools and other resources developed by PCORnet and member sites (e.g., code, engagement materials). The PMO holds weekly joint calls with site teams, maintains a database of all publications co-authored and tools developed for or from PCORnet infrastructure, and will submit notable materials to the PCORnet shared resource library[13].

4) Exchange best practices to increase research readiness: In Phase 4, GPC will incorporate a speaker's bureau with live webinar series recorded for asynchronous use as well as office hours staffed by the RRC. Invitations to webinars will be widely distributed. The *Investigator Incubator* will additionally include the dedicated GPC analyst (launched in Phase 3) to help better prepare investigators for making Front Door queries and support GPC-level feasibility and advanced analytic queries to minimize "self-inflicted errors" and loss of rigor and reproducibility[14]. Focus groups, member surveys, and consultations with the Emerging Investigators Council will engage stakeholders in *Incubator* development.

5) Return results: In Phase 3, an innovative tool for engaging patients and returning their research results was developed in the NET-PRO study using a Personal Health Record platform (Vignette above). In Phase 4 we will charge the Research Opportunity Assessment (ROA) committee with ensuring that proposals from GPC investigators include a plan for sharing results with patients and other stakeholders. In addition, the Investigator Incubator will accumulate and catalog presentations from PCORnet study investigators that involve GPC data. This will be incorporated in the annual report, publicly on the GPC website, and through invited presentations at the PAC/PEO and GPC Global monthly calls as well as the poster session at the annual LEC meeting.

6) Dissemination at National Meetings: Since PCORnet's inception, GPC has a long-standing tradition of promoting PCORnet notably at AMIA Symposia[15] for the informatics community and specialty meetings[16]. GPC also invites external investigators and stakeholders to its annual LEC meeting; notably hosting a workshop[17] with the Veterans Administration and Oracle Health (VA's EHR vendor) regarding data sharing for joint studies. In Phase 3, we strengthened dissemination to the clinical and translational science community by actively engaging the Association for Clinical and Translational Science (ACTS): the academic home for NIH clinical translational science, team scientists and trainees. At Translational Science 23, we organized a PCORnet panel[18] presenting capabilities, PREVENTABLE as exemplar study, supporting CDC COVID surveillance and the role of engagement. At TS24, we organized GPC/PCORnet workshop allowing more time for dialog and gathering feedback. In addition to broad presence at national meetings, we will continue focused PCORnet dissemination among the AMIA and ACTS communities.

Staffing and Organizational Capacity (Criterion 4)

The Greater Plains Collaborative will sustain the leadership, governance and communications approaches in Phase 4 that proved highly effective in the previous phases. These approaches are described in Criterion 1 of the GPC's Technical Proposal, leadership plan, and are represented within Figure 1. In conjunction with the direction provided by the Principal Investigators, the GPC will continue to utilize a network Governance Council composed of the Site PIs and the Patient Co-I with other stakeholders, as the deciding body for major decisions as outlined in Criterion 1 of the Technical Proposal. GPC is fortunate in that the majority of our site PIs have been engaged in PCORnet since its inception. With the healthcare organizational and leadership as well as site PI support committed by each of the GPC sites through established subcontracting relationships, we will enhance and evolve our approaches based on stakeholder feedback and operational experience.

GPC Governance

James McClay, MD, MS, FACEP, FAMIA, ACHIP, will serve as the contact Principal Investigator (PI) for the GPC during Phase 4. He is currently the GPC Dual-PI for Phase-3. Dr. McClay was the GPC Dual-PI for a portion of Phase 2 (before PCRF) and the prior site PI at the University of Nebraska Medical Center since the inception of the GPC. As required, Dr. McClay is a full-time employee of the prime applicant, the University of Missouri where he serves as a professor in the department of Biomedical Informatics, Biostatistics and Medical Epidemiology and as Chief Research Informatics Officer for the School of Medicine. For MU, Dr. McClay, the Principal Investigator of GPC, will be focused on overseeing the GPC's overall contracts. He will join effort with Dr. Chrischilles and Mr. Taylor in leading collaborations with the PCORnet Coordinating Center and other CRNs, and leading the planning and implementation of the GPC's collaboration with other data partners and research collaborators; All three MPIs will collaborate in leading the project direction. His effort for Phase 4 is budgeted at 32%, including his site PI duties.

Bradley Taylor, MBA, is the Chief Research Informatics Officer at the Medical College of Wisconsin, where he is the Director for the Center for Biomedical Informatics (CBMI) for Clinical and Translational Science Institute of Southeast Wisconsin (CTSI) and site PI for the MCW hub of the GPC since Phase 1. He will serve as an MPI and lead efforts to continuously refine and enhance the clinical data/informatics for the GPC and implement CDM V7.0. With Drs McClay and Chrischilles, Mr. Taylor will co-lead the collaborations with the PCORnet Coordinating Center and other CRNs, and the planning and implementation of the GPC's collaboration with other data partners and research collaborators. In addition, he will lead the GPC milestones related to linking genomic testing to the PCORnet CDM. His effort for Phase 4 is budgeted at 30%, including his site PI duties.

Elizabeth Chrischilles, PhD – GPC Dual PI and University of Iowa site PI - Dr. Chrischilles is Professor and Department Head of the Department of Epidemiology, College of Public Health at The University of Iowa, and Associate Director for Informatics in their CTSA. She has served as site PI for the Iowa site since Phase 1, led the cancer research portfolio for the network, and participated with Dr. McClay and Mr. Taylor on the GPC ROA committee since Phase 1. A trailblazer in pharmacoepidemiology whose innovative research and policy contributions have transformed national healthcare systems, Dr. Chrischilles is a leading expert on medication safety and effectiveness. Her multi-disciplinary, collaborative work resulted in creation of new FDA medical product surveillance tools and a model for pharmacist-delivered care for Medicaid patients. For Phase 4, Dr. Chrischilles will lead the GPC's Research Readiness activities, collaborating with the Research Readiness Coordinator, mentoring the Emerging Investigators Council, and overseeing the study design and research conduct support functions. She will work closely with the Collaborator Engagement leads to engage and enhance awareness by patients, external stakeholders, and health system leaders. Her effort for Phase 4 is budgeted at 25%.

Jeff Ordway - **Patient Partner Co-I.** Mr. Ordway will co-lead the Collaborator Engagement activities with Dr. Joyce Balls-Berry, including support for the Patient Advisory Council and the Rapid PACE function. He will provide his expertise

throughout the project by participating in monthly Governance Council meetings. He will collaborate with the Research Readiness Coordinator in supporting project/proposal development via structures such as the Investigator Incubator. Mr. Ordway (MU) has been a member of the Patient Advisory Council for GPC since Phase 2 and became the lead patient research advocate in Phase 3. He has played a major role in the Engagement Core for the Coordinating Center for PCORnet to create a well-organized PCORnet engagement strategies toolkit and serving as a senior project manager. Mr. Ordway will continue his work with the Core,and will continue to provide a patient voice in the areas of policy and dissemination of engagement strategies. He will represent the GPC on the PCORnet Engagement Committee. Mr. Ordway is committing 20% of his effort to GPC in Phase 4 to fulfill this role.

Joy Balls-Berry, PhD – Lead Patient Engagement Officer will continue her GPC and national level engagement as the GPC Patient Engagement Lead. Dr. Balls-Berry leads the Health Disparities and Equity Core at the Knight Alzheimer's Research Center, and Community Engagement for Precision Health at the Institute for Clinical and Translational Science at Washington University. Her research focuses on bidirectional engagement and the community's willingness to participate and determining the best approaches to giving under-resourced populations a voice in the research process and clinical care. She will work closely with Jeff Ordway, the Patient Partner PI, to lead the GPC engagement effort.

Xiaofan Niu, PhD - Sr. Project Director will continue as Administrative/Project Director building on 20 plus years' experience in independent research study design and execution, national research project coordination and management. She is also the Chair of the GPC Dev/PM meeting and has worked effectively in coordinating with all GPC sites on milestone completion and delivery. Dr. Niu has had significant multi-site management and complex project/program management experience. She is budgeted at 50% for each year during Phase 4.

Brian Gryzlak, MA - Research Readiness Coordinator (RCC) - Mr. Gryzlak will serve as GPC RCC in Phase 4, leveraging his expertise in managing multi-site national trials such as NET-PRO to cultivate research projects empowered by PCORnet infrastructure. He is currently in the project manager and the data liaison roles at Iowa for numerous PCORI funded studies and has a deep understanding of both administrative and technical requirements of these projects. Mr. Gryzlak is budgeted at 60% each year for his dual network RCC and site project manager roles.

University of Missouri and GPC environment: GPC network leadership will reside at the University of Missouri and will be housed at the NextGen Biomedical Informatics Center (Next-Gen BMI) in the MU School of Medicine which provides storage, high performance computing, GPU computing, physical servers, and virtual servers. NextGen BMI partners with SnowFlake and Amazon Web Services for managed Software-as-a-Service (SaaS) and Platform-as-a-Service (PaaS) for: (a) a research data lake, (b) curated and harmonized data models (PCORnet CDM, i2b2, OMOP), and (c) programming and computing environments for ETL and analyses. University of Missouri Health Care (MUHC) is a multi-hospital system owned by the University of Missouri System comprised of five hospitals and 50 primary and specialty clinics statewide. With 14 sites, the GPC has broad access to leaders in the fields of comparative effectiveness research and pragmatic trials, epidemiology and research design methodologies, informatics patient engagement, clinical research administration and project management. Most sites leverage CTSA infrastructure. GPC holds virtual and in-person meetings with site personnel to foster organizational commitment across all institutions. Throughout the previous phases, the GPC demonstrated the ability to engage the required expertise across all partner sites to support its efforts.

Site Principal Investigators (with brief description of their site environments) and other key personnel include:

Dr McClay, Contact PI, Dr Chrischilles, Dual PI and Mr. Taylor, MPI each serve as the Site Principal Investigators for their sites (University of Missouri, University of Iowa, and Medical College of Wisconsin, respectively. The other Site Principal Investigators and key personnel are:

Abbey Sidebottom, PhD - Allina Health - Dr. Sidebottom is the Principal Research Scientist and Epidemiologist at Allina Health. Allina Health delivers health care services to patients in Minnesota and western Wisconsin and includes 12 hospitals, 90 clinics, and 52 rehabilitation sites. Dr. Sidebottom's career highlight includes extensive use of electronic health record data for population health and clinical research and conducting and coordinating applied research across

several clinical service lines. She is experienced in identifying research partners, implementing studies and overseeing data collection, data sharing, and contracting.

Kirk Knowlton, MD - Intermountain Healthcare - Dr. Kirk Knowlton is Director of Cardiovascular Research at Intermountain Healthcare and a member of the Intermountain Research Leadership Committee. Dr. Knowlton has served as the site PI for over 7 years. He has published his research Nature Medicine, Science, Circulation, and the Journal of Clinical Investigation. He has served on numerous research committees with the American Heart Association and the Sarnoff Foundation. Dr. Knowlton also maintains an active clinical practice as a general cardiologist with a focus on heart failure and pulmonary hypertension. IHC Health Services, Inc., (Intermountain Healthcare) is a not-for-profit healthcare system based in Salt Lake City, Utah, with 33 hospitals (and a "virtual" hospital), about 385 clinics, and a health plan.

Jeffrey VanWormer, PhD – Marshfield Clinic Research Institute - Dr. VanWormer is a behavioral epidemiologist with research interests in the primary prevention of cardiometabolic disease, with a particular focus on community-level risk factor surveillance and lifestyle interventions. Dr. VanWormer is an investigator member in the national Health Care Systems Research Network and the University of Wisconsin Institute for Clinical and Translational Research. Marshfield Clinic Research Institute is the research 'arm' of the larger Marshfield Clinic Health System (MCHS), a large multispecialty integrated care system serving the predominantly rural north-central Wisconsin. MCHS approximately 90 clinical specialties in 65 clinic locations and 11 hospitals across northern, central, and western Wisconsin.

William Hogan, PhD - Medical College of Wisconsin - Dr. Hogan is a professor and the Director of the Data Science Institution at the Medical College of Wisconsin. He has over 20 years' experience in biomedical informatics, including building large-scale informatics infrastructure, enhancing public health surveillance, developing data standards, and applying artificial intelligence and analytics to public health and healthcare. He will utilize his extensive PCORnet experience and expertise--from his prior role as the dual PI with clinical informatics expertise on the OneFlorida+ Clinical Research Network—to assist the GPC including serving on the PCORnet Data Committee

Sravani Chandaka, MS - University of Kansas Medical Center - Ms. Chandaka has wide experience in delivering complex informatics/analytics solutions in healthcare delivery and clinical research settings. At KUMC, she has been heavily involved in collaborative medical research through Greater Plains Collaborative (GPC) since its inception. She has served the role of a data manager for a number of PCORnet clinical trials. She is also the lead architect for the PCORnet Common Data Model-based warehouse at KUMC. University of Kansas Medical Center has over 100 clinical sites including 1 hospital,11 primary care practices, 86 specialty care practices, and 1 federally qualified health center.

Abu Mosa, PhD - University of Missouri - Dr. Mosa, the Senior Director of Information Technology and an Associate Professor of Biomedical Informatics. His expertise bridges computational and health sciences, integrating data-driven artificial intelligence and will be responsible for GPC hosted service IT infrastructure.

Carol Geary, PhD – University of Nebraska Medical Center - Dr. Geary is an Assistant Research Professor and the Deputy Director for Research Networks for the University of Nebraska Medical Center (UNMC) Research, Education, Analytics, and Design for Health Informatics Core. Her research focuses on use of electronic health record data for research, quality evaluation and patient and stakeholder engagement in research. Dr. Geary is the site PI for the Nebraska Medical Health System. In Phase 4, UNMC will add Children's Hospital of Nebraska data into its CDM to bring more complete records for a substantial number of patients who are seen at both hospitals. Afterwards, UNMC provides data from 5 hospitals, 35 primary care practices, 131 community clinics serving eastern Nebraska, western Iowa, northern Kansas and Missouri.

Elmer Bernstam, MD, MSE - University of Texas Health Science Center – Houston - Dr. Bernstam is the Associate Dean for Research at UTH. He has focused on the quality and accuracy of health information online and has worked on identifying consumer attitudes toward molecular testing (i.e., in support of personalized cancer therapy) and related education and privacy issues. He has been the Director of Biomedical Informatics for the Center for Clinical and Translational Sciences (the CTSA program at UT-Houston) since 2008. Dr. Bernstam leads clinical informatics at the UT

School of Biomedical Informatics at Houston. The UTH encompasses a large multi-specialty practice (UT Physicians) with 100 community clinics and 5 affiliated hospitals including Memorial Hermann Hospital System and Harris Health.

Douglas Bell, MD, PhD - University of California, Los Angeles - Dr. Bell leads the CTSI Biomedical Informatics Program and serves as UCLA's honest broker for research use of electronic health record data. He is also the Director of the Los Angeles Data Repository (LADR), a federated data repository system that spans four local medical centers. His ongoing research includes work on clinical decision support, data quality, data sharing, and patient outreach particularly for research recruitment. Dr. Bell is the program director of UCLA's fellowship program in clinical informatics. His past research has contributed to the fields of electronic prescribing, clinical decision support, and online physician education. The UCLA affiliated hospitals serve the 2nd largest metropolitan area in the US and enhance PCORnet diversity.

Nicholas Anderson, PhD - University of California, Davis - Dr. Anderson is the Chief of Division of Health Informatics and the co-Chair of CITRIS Health consortia. He has over 25 years of experience in biomedical informatics in both industry and academics and has been involved in translational data science that spans bench to bedside domains, including computational and information management tools and methods. GPC proposes UC Davis as a site in Phase 4.

Lindsay Cowell, PhD – University of Texas Southwestern Medical Center - Dr. Cowell is an Associate Professor in the Department of Population and Data Sciences and a member of the UTSW Cancer Center's Population Science Program. Her research focuses on informatics methods for studying the immune system and its role in infectious diseases, autoimmune diseases, and cancer, resulting computable representations of qualitative biological and clinical information. She works closely with the UTSW Academic and Administrative Information Resources group which maintains our UTSW Clinical Data Warehouse and GPC CDM. UTSW contributes clinical data from our healthcare system which includes two university hospitals and 51 clinics as well as billing data from Parkland and Children's Health.

Jacob Kean, PhD – University of Utah – Dr. Kean is an associate professor in the Population Health Science Department and a research speech-pathologist at the Veterans Affairs. His team will continue to provide linkage and research engagement with the Department of Veterans Affairs and its DaVINCI data warehouse. U of U Health is the Intermountain West's only academic health care system, combining excellence in patient care with the latest in medical research and teaching. U of U Health includes five hospitals; 11 community clinics; and specialty centers including Eye, Cardiovascular, Clinical Neurosciences, and Diabetes centers.

Albert Lai, PhD, FACMI – Washington University - Dr. Lai is the Chief Research Information Officer for the Washington University School of Medicine (WUSM) and Deputy Director of the Institute for Informatics. He has extensive experience and expertise with electronic phenotyping, cohort discovery, data sharing, clinical research, clinical trials recruitment, and mobile health. Dr. Lai's research focus is on the use of structured and unstructured data from the electronic health record to pre-screen patients for clinical trials. Washington University is a network of 15 hospitals and clinics across Washington University in St. Louis and BJC HealthCare, providing services throughout Missouri and Illinois.

Xing Song, PhD (MU) will be the GROUSE Administrator for GPC. Dr. Song's expertise is in machine learning and statistical learning algorithms, biomedical informatics, data mining and knowledge discovery. Her research leverages multiple GPC CDM data marts and develops machine learning models as well as techniques for explaining model transportability. She is the lead faculty for the GPC's GROUSE that integrates Medicare/Medicaid claims across its states and the health systems Common Data Models (CDM) containing EHR, billing and registry data.

Christine Spinka, PhD (MU) will be the lead SAS analyst for GPC. Dr. Spinka a biostatistician and has served as the GPC data scientist/SAS analyst since Phase 3. She has been leading the effort to remediate GPC site data quality and facilitates research related to EHR and claims analysis.

The participating GPC sites are committed to adequate staffing to meet the Phase 4 objectives and key milestones. Each site is funded to support a core staff infrastructure of a Data Mart Liaison, an Honest Broker, a Project Manager and a Patient Engagement Officer. Additional site funding has also been provided for leadership roles assumed for overall GPC activities. Specifically, the GPC is engaging the following additional personnel in GPC network roles in Phase 4: Brad Taylor – Research Opportunity Assessment (ROA), Elizabeth Chrischilles – Dual PI, Research Committee and ROA, James

PRINCIPAL INVESTIGATOR (MCCLAY, JAMES, C.):

McClay – Contact PI and ROA, Annie Risenmay - IRB group lead, William Hogan – Data Committee, and Jeff Ordway - Engagement Committee.

PROTECTION OF HUMAN SUBJECTS

Describe the protection of human subjects involved in your network.

During Phase 3, the GPC IRB Consortium met on a monthly basis and was chaired by Annie Risenmay at the University of Utah. Standard operating procedures have been created to guide and streamline our IRB collaboration. GPC institutions have a single IRB process through the use of the SMART IRB agreement (e.g. https://smartirb.org/). The GPC IRB Consortium provides a mechanism for our institutions to efficiently communicate and reach consensus on a variety of regulatory topics. We have noted that each of our individual IRBs has developed areas of expertise that allows learning among the GPC institutions. Further, the institutions have committed to an ongoing process of sharing and developing best practices for meeting regulatory standards and implementing collaborative research. The consortium regularly updates guidance and processes for investigators on a dedicated section of the GPC Website (e.g. https://gpcnetwork.org/policies-irb/). The GPC also holds specific breakout sessions at our annual Learning Engagement Conference (LEC) for the IRB Consortium and also specific joint sessions with the GPC Patient Advisory Council and Informatics teams to increase dialog and engagement with patients and stakeholders (e.g https://gpcnetwork.org/wp-content/uploads/Events/LEC2022/2022-Learning-Engagement-Conference-DRAFT-Agenda-October-4th-2022-v1.9.pdf https://gpcnetwork.org/wp-content/uploads/Events/LEC2023/LEC-VA-Oracle-Workshop-General-Information-Agendas.pdf.).

The GPC IRB Consortium has also been invited to present on our single IRB processes at local and national meetings. This demonstrates the leadership that GPC IRB Consortium members in this area. Select past and upcoming presentations are:

- PRIM&R Advancing Ethical Research Conference 2019. (November 20, 2019) “Strategies for Conducting an Effective Local Context Review as a Relying Organization”, Kimberly Summers (UTHCSA) and Sarah Mumford (Utah).
- Riches, N.O., Johnson, E., Frost, C.J., Johnson, A., Mumford, S., Baumann, J., Johnson, B., & Rothwell, E. (October 2019). “Creating a biobanking graphic database: A pilot and feasibility study,” poster presentation at the Greater Plains Collaborative Clinical Research Network meeting, Kansas City, Missouri.
- Association for the Accreditation of Human Research Protection Programs, 2021 Annual Conference. (May 19, 2021) “Components of Community Consultation Plans for Exception from Informed Consent (EFIC) Studies.” Sarah Mumford (Utah) and Rhonda Oilepo (UTSW).
- OHRP Research Community Forum Hosted by University of Texas Southwestern Medical Center. June 15-16, 2021. Plenary Session, “Regulatory Considerations for Planned Emergency Research” Sarah Mumford (Utah) and others.
- Burr JS, Johnson A, Risenmay A, Bisping S, Serdoz ES, Coleman W, Sward KA, Rothwell E, Dean JM. Demonstration Project: Transitioning a Research Network to New Single IRB Platforms. Ethics Hum Res. 2022 Nov;44(6):32-38. doi: 10.1002/eahr.500149. PMID: 36316971; PMCID: PMC10328109.
- Hernandez, J., Morain, S., & Risenmay, A. (2022, November). *Communication in minimal risk research using waiver of consent*. Presentation at the Public Responsibility in Medicine and Research Conference, online.
- Trullinger, A., Serdoz, E., Caldwell, C., Moore, B., & Risenmay, A. (2023, April). *Single IRB coordination models: Innovative approaches from four CTSAs*. Presentation at the Association for Clinical and Translational Science Conference, Washington, D.C.

- Trullinger, A., Serdoz, E., & Risenmay, A. (2023, December). *Single IRB coordination models: Innovative approaches from four CTSAs*. Paper presented at the Public Responsibility in Medicine and Research Conference, Washington, D.C.

For most research projects, plans to protect human subjects require researchers to categorize the research project as falling into one of six possible domains, as outlined in the six possible scenarios given in PHS 398. We anticipate research projects in the GPC going forward will fall into all six domains. Thus, we need to develop a plan to protect human subjects that is flexible enough to deal with any or all of the scenarios.

Some projects will not involve human subjects at all (Scenario A). That will occur when the data that we use are totally de-identified. According to OHRP, data are considered de-identified under the following criteria:

> *OHRP considers private information or specimens not to be individually identifiable when they cannot be linked to specific individuals by the investigator(s) either directly or indirectly through coding systems. For example, OHRP does not consider research involving **only** coded private information or specimens to involve human subjects as defined under 45 CFR 46.102(f) if the following conditions are both met:*
>
> *1. the private information or specimens were not collected specifically for the currently proposed research project through an interaction or intervention with living individuals; and*
>
> *2. the investigator(s) cannot readily ascertain the identity of the individual(s) to whom the coded private information or specimens pertain because, for example:*
>
> *a. the investigators and the holder of the key enter into an agreement prohibiting the release of the key to the investigators under any circumstances, until the individuals are deceased (note that the HHS regulations do not require the IRB to review and approve this agreement);*
>
> *b. there are IRB-approved written policies and operating procedures for a repository or data management center that prohibit the release of the key to the investigators under any circumstances, until the individuals are deceased; or*
>
> *c. there are other legal requirements prohibiting the release of the key to the investigators, until the individuals are deceased.*

Other projects will fall under scenario C, exempt human subjects research. We anticipate that the most likely projects of this type will be those that meet the federal criteria outlines in 46.101(b)(4): *Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.*

However, we expect much of the research in the GPC will be non-exempt. For those that are prospective clinical trials, the GPC will develop individualized plans for the protection of human subjects, taking into consideration the following factors:

<u>*Distinguishing when outcomes research or sharing of data/biological samples requires IRB oversight*</u>.

1) Outcomes research is closely aligned with quality improvement (QI) and quality assurance (QA) activities. The GPC leadership recognizes that developing a consensus approach to distinguishing QI/QA activities, which do not require IRB oversight for human subjects research, is critical for efficient GPC operation.

2) Receiving/exchanging data or biological samples will be common in GPC studies. Regulatory oversight will vary, depending on whether data or samples are directly identifiable or coded and if data/sample recipients are collaborating with individuals who have access to the code. The GPC Greater Plains IRB Consortium (GPIC) will develop guidelines to address these issues. Whenever feasible, sharing of data or samples will be coded or de-identified to minimize risk to study participants, lessen regulatory burden for the institutions and reduce the time from conception to implementation.

Regulation of subject identification and recruitment strategies. To facilitate study subject identification across the consortium, GPC members will be familiar with the rules governing medical records access at collaborating institutions. Developing uniform standards regarding who can access medical records for research purposes, who can make first contact with potential subjects, and what constitutes the allowed content for recruitment materials is essential for efficient operation of the reciprocal deferral model. In addition, if data warehouses are used for recruiting research subjects, consensus regarding the need for IRB oversight of these activities is likewise critical. Thus, the GPC has devoted significant effort to characterize variation in these areas and develop best practices as part of our GPC IRB Consortium.

Waivers and alterations of consent and authorization. With certain limits, federal regulations provide flexibility for IRBs to grant a waiver of documentation of informed consent and authorization, a complete waiver of informed consent and authorization, or alteration to the consent or authorization process. For efficient GPC operations, we have again developed guidelines regarding when this flexibility is appropriate and how it can be exercised, particularly in regard to use and extraction of data from medical records.

Identifying and assessing research risks. Given the close parallels between comparative effectiveness research and patient clinical care, developing standards for risk analysis of such research is essential for effective operation of the reciprocal deferral IRB model. The factors that an IRB considers in these analyses may significantly impact the regulatory determinations for a study, such as whether a waiver of informed consent can be granted, what should be included in a consent document, or if a formal data monitoring board is required. Thus, we have addressed these issues and will continue to develop practical and uniform guidance to use for risk analysis.

For each proposed study, the GPC IRB Consortium will evaluate the overall risks and benefits in each of these domains separately and then integrate them into an assessment of the risks and benefits of the study as a whole. This approach will require judgments when comparing one sort of risk to another. Communication of this complex risk/benefit information requires a balancing act. Detailed explanation of each separate risk may be overwhelming and confusing. Summaries of the risks may oversimplify or underemphasize particular risks. Evaluation of the acceptability of studies and of the adequacy of consent forms must reflect consideration and communication about these potential risks and benefits both separately and as a whole.

Inclusion of Women and Minorities

Our network will include 34+ million individuals. Any particular study will include a subset of these individuals. Our GPC IRB Consortium will continue to evaluate each project to ensure that women and minorities are included.

Vulnerable populations

Studies that include vulnerable populations will be evaluated in accordance with HHS policies.

Data Safety and Monitoring Board (DSMB)

There will be no overarching DSMB for this project. Individual research studies may require DSMBs. This will be determined by the GPC IRB Consortium on a study-by-study basis.

CONSORTIUM CONTRACTUAL ARRANGEMENTS

The Greater Plains Collaborative (GPC) consists of 14 academic medical centers and healthcare organizations across 14 states. This alliance is formed based on the initial PCORI vision of an integrated national data infrastructure to support practice-based outcomes and comparative effectiveness research. For Phase 4, the GPC will replace the University of Texas Health Science Center at San Antonio with University of California, Davis. GPC will expand its population coverage to >38M (Table 1) in Phase 4.

The primary applicant organization (MU) has had subcontract agreements in place with our partner sites and is ready to execute the agreements at the time of award. GPC sites all have well-established research programs as well as significant operational experience with both commercial EHR systems and informatics/data warehouse infrastructures. Additionally, the partners bring strong working relationships at both the localized level (between investigators and informatics/information technology organizations) as well as at the broader cross-institutional level. Each GPC site brings unique strengths and complementary areas of expertise. The majority of sites are also CTSA sites or are participants in a CTSA consortium. The specific strengths and diversity of the Greater Plains Collaborative institutions are described in the "Clinical Research Network Data Contributing Partners" documents at the end of the proposal.

As was the case in prior and current phases, there will be standard expectations for each partner site in terms of the delivery of key milestones. The scope of work and milestones to be performed by each participant in the GPC CRN will include the supporting activities necessary to allow the consortium to successfully complete all requirements over the four-year period of Phase 4. The associated work requirements for each partner focus on further optimizing each site's data infrastructure to support efficient and complex clinical research trials and to begin addressing increasing volumes of research queries and observational studies. Additionally, the network sites continue to work together on establishing the GPC as a sustainable resource for standardized, accessible data for patient-centered clinical trials. This is described at the end of this section.

Site Scope of Work and alignment with PCORI Phase 4 Milestones

We have provided the GPC sites with a list of anticipated milestones to govern the expectations in the execution of this contract. These milestones incorporated the updated requirements from PCORI for Phase 4, covering governance, data quality, engagement, research and operation areas of the network functions. GPC also has additional network specific requirements to enhance the quality and comprehensiveness of the CDM to support precision medicine research. These GPC site expectations along with the PCORI milestones form the basis of the Statement of Work for each of the GPC sites as is shown below.

Scope of Work for Participation as a Site in the Greater Plains Collaborative (GPC)

This Scope of Work (SOW) is based on two documents: (1) PCORnet Phase 4 GPC site Obligations and Expectations dated March 26, 2024, and (2) the PCORnet Phase 4 Milestones spreadsheet provided by the University of Missouri – Columbia.

1. Maintain a local site team composed of the following roles:

- A site Principal Investigator, who is an MD/PhD/ or Director-level supervisor within the organization who will attend and speak on behalf of their organization (and affiliated health system(s) if applicable) during monthly Governing Council calls.
- An experienced Project Manager
- A dedicated Datamart Liaison

- A patient engagement officer primarily with experience in prospective clinical trial participation
- A patient or caregiver/family member with a lived experience to join the GPC advisory council.
- Patient engagement work is important at the site level. GPC central will budget for patient engagement officer participation and compensation to help with transparency and consistency of reimbursement across GPC sites.
- PAC/PEO members need to participate at least 80% of the GPC engagement functions (Monthly PAC/PEO meeting & RAPID PACE)

2. All sites must accomplish the core PCORnet statement of work as articulated in the PCORI funding announcement.

Policy, procedure and participation

- Adhere to the GPC network engagement policy and site requirements to be articulated in the Engagement Plan. This will largely be a continuation of the current GPC Engagement Plan.
- Comply with PCORnet governing policies, procedures, and core principles for PCORnet for the scalable, secure, and streamlined conduct of patient-centered multi-network research. This will largely be a continuation of the current GPC network governance and data security policies.
- Implement and comply with all PCORnet data security, privacy, and other trust-building policies.
- Where possible, work GPC-wide and locally to create synergies between infrastructure maintenance and ongoing research projects.
- Lead and participate in a variety of multi-network studies (defined as those studies that receive PCORnet designation). Where possible and appropriate, leverage PCORnet innovative methods and infrastructure.
- Implement and comply with PCORnet policies to use streamlined and standardized mechanisms, including centralized IRB models and standardized data use agreements, for the efficient and rapid conduct of multi-network research.
- Actively engage and collaborate in PCORnet-wide meetings, ad hoc work groups, and teams that support operations, management, improvement of network infrastructure in support of increased utilization of the PCORnet infrastructure for the conduct of multi-network research.

Participation in Multi-network Projects and Studies

- Respond to research opportunities shared by the PCORnet Front Door by considering participation; where appropriate, disseminate research opportunities within the local site to identify and support local clinical investigators to participate in multi-network projects and studies.
- Lead or participate in the development and design of PCORnet Designated Studies
- Execute and return site-specific results for 20 PCORnet-approved and 10 PCORI-approved queries per year.
- Respond to PCORnet-approved queries within 5 business days of receipt.
- Respond to PCORnet Front Door requests for participation in multi-network studies within 10 business days of receipt.
- Facilitate collaborative relationships with other CRNs and the Coordinating Center of PCORnet, and external research partners and funders to support increased utilization of network infrastructure and the conduct of multi-network research.
- Adhere to the GPC network engagement policy and site requirements to be articulated in the Engagement Plan.
- Review and provide information to the GPC prime site for progress reports to PCORI. Progress reports include tracking metrics from the prime site for research opportunities, data submissions and publications.

Data Management and Submission

- Perform quarterly refreshes of the PCORnet CDM. From time-to-time, this will include modification of local extraction, transformation and loading (ETL) procedures to reflect changes to the CDM Implementation Guidance or Value Set Reference File, additions/modifications to the PCORnet Data Quality Checks. Submitted data must be certified by the Coordinating Center as research ready by quarterly refresh deadline.
- Ensure quarterly updates of the CDM have a data lag ≤ 60 days.
- Address quality issues identified by study teams. Quality problems are usually identified when those receiving data for studies use the data and encounter unexpected data, data coding or formatting in results or result-sets provided in response to study-specific queries.
- Mapping at least 80 percent of medications (by frequency) to the appropriate Tier 1 Preferred RxNorm CUI codes (fully specifying the ingredient, strength, and dose form) as specified in the CDM Implementation Guidance. The remaining medications should also be mapped to the most appropriate RXCUI as specified in the Implementation Guidance.
- Mapping the top 80 percent (by frequency) of labs to LOINC within two months, fully specifying the result and result unit. Participating in network efforts to validate LOINC mappings, which will involve investigation of the result unit, specimen source, and local values for the lab test name, result unit, and specimen source. Populating values for lab normal ranges when present in record-level results. Providing information on normal ranges for tests where record-level entries are not available.
- Maintaining data quality by investigating and aiding in remediation of data anomalies and fixing extraction, transformation, and loading procedures to remedy any failed required data checks within three months. This includes resolving recurring errors in the persistence data checks.
- Maintaining data quality by investigating the cause of any failed investigative data checks and developing a plan to remediate any investigative check errors not caused by source data constraints within three months.
- Advancing the quality and availability of complete and comprehensive data sets, including through linkages of disparate sources of complementary data (e.g., administrative claims data, vitals, health information exchange data).
- At least 75 percent completeness of encounters, diagnoses, or procedures in ambulatory, telehealth, emergency department, or inpatient settings within two months of each quarterly refresh.
- Ensuring data plausibility by maintaining that at least 80 percent of patients with a face-to-face encounter during the previous five years have at least one face-to-face diagnosis and one vital measurement.
- Ensuring data persistence by maintaining no more than a 5 percent decrease in the number of patients and records in a CDM table within two months of each quarterly refresh.

Required Infrastructure

- Maintain infrastructure to support concurrent Front Door query execution within 5 business days of receipt.

3. GPC specific elements to meet PCORI's expectations in the funding announcement include:

Policy, procedure and participation

- Continue the GPC data sharing agreement, external institutional collaborator agreement, and support the GPC model for infrastructure cost recovery for non-PCORnet funded research studies.
- Attend the GPC annual Learning Engagement Conference (https://gpcnetwork.org/?q=events) with PI, GPC-DEV lead, and PM (our budget picks up the patient travel).
- Core people from the site should make 80% attendance to regular GPC meetings (GPCDEV/PM, DROC, GPCPI, Engagement PAC and PEO, and IRB).

Participation in Multi-network Projects and Studies

- It is important for sites to derive value from GPC and be a public-spirited organization that also serves external investigators seeking to derive value from a vibrant, national clinical research network. All GPC sites are expected to develop a blended portfolio of writing grants that use PCORnet/GPC across other sites besides their own and to participate as a site in trials and other multicenter studies that originate outside the site institution.
- GPC sites are expected to execute and return results within standard response times for unfunded DROC requests from GPC investigators to support feasibility determination for studies being developed that seek to use GPC and PCORnet. Based on operational metrics from prior years, approximately 10 such requests are expected per year.
- GPC sites are expected to execute and return results within standard response times for unfunded DROC requests from other GPC sites in support of K scholars and GPC-site initiated 'lightly funded' pilots. Based on operational metrics from prior years, approximately 10 such requests are expected per year.

Data Management and Submission

- GPC sites are expected to obtain and maintain complete clinical data for inpatient and outpatient environments.
- GPC sites are expected to maintain transparency regarding policies, procedures, and algorithms for exclusion of data at the organization, patient, and encounter levels as well as algorithms used for de-identification.
- GPC sites will be expected to pursue local approvals necessary to obtain their local North American Association of Central Cancer Registries (NAACCR) Hospital Tumor Data File (also called the NAACCR hospital tumor registry). At such time as requirements for the CDM extension tables to house the tumor registry data, sites will be expected to
    - Refresh the tumor registry data in the CDM extension tables quarterly and
    - Standardize the NAACCR Hospital Tumor Data File into a Tumor Table linked to the rest of the PCORnet CDM on PATID, and
    - Participate in developing and testing cancer quality checks, and
    - Run cancer data quality checks and resolve identified exceptions quarterly.
- GPC sites are expected to refresh their LOINC document ontology yearly.
- GPC sites are expected to refresh the new PCORnet CDM Patient Reported Medications table quarterly.
- Work with GPC Prime to improve GPC CDM data quality by leveraging the claims data.
- The GPC Prime site will obtain a license of the social security death master file for ascertainment of additional death facts. The linked death facts will be provided back to GPC sites to enhance local clinical research at GPC sites (e.g. for CDM enhancement and recruitment exclusion criteria) .
- Vanguard GPC sites will design and pilot linking genomics data with CDM, and eventually provide consistent capability to support precision medicine pragmatic studies for PCORnet investigators.

Required Infrastructure

- GPC addresses the PCORnet claims data integration requirement by annually linking site level CDM data (limited data sets) to Medicare/Medicaid claims data. The environment where these data are managed is called "GROUSE" (https://gpcnetwork.org/?q=GROUSE). GROUSE has completed the transition to Amazon Web Services during Phase 3. GPC sites will continue the support to amend the local IRB submission covering site activities for GPC, local Information Security appraisal of site GPC activities, or local Data Governance approval

for submission or Snowflake distributed sharing of the Limited Data Set (LDS) to the secure AWS environment, and to participate in validation of data . GPC sites will update GROUSE quarterly.

- GPC will continue to use Datavant for PCORnet Privacy Preserving Record Linkage (PPRL) and continue discussions with Datavant to list GPC as a potential data partner and make partial GPC data visible via the Datavant overlap analysis tool. As such,
- Sites are expected to maintain a current installation of Datavant for PPRL, to run new hashes annually, and to populate the corresponding CDM tables for the purpose of updating the claims linkage.
- Sites are expected to seek local approvals necessary for inclusion in the GPC set for the Datavant overlap analysis tool. Note that sites can request that their identity as a site be blinded to those who use the tool. The GPC Coordinating Center will work with Datavant on this capability and during future Governing Council calls.

Greater Plains Collaborative Cost Recovery Strategy

Since its creation, the GPC has recognized the many challenges to creating a sustainable CRN. In response, the GPC has proactively implemented a number of complementary strategies to ensure its long-term vitality. These strategies encompass both strategic and tactical elements and capitalize on a number of resources and programs within our institutions and on the unique missions and roles of our collaborating health systems.

At a strategic level, GPC leaders recognized that the sustainability of the GPC is predicated on our largely academic medical centers' and health systems' core values of advancing clinical and translational science as a catalyst for serving as leading learning health care systems for their regions. These core values are reflected in the investments that each of our institutions makes in the translational science enterprise. At a more granular level, each of our institutions recognizes that its success in an era of accountable care depends on the ability to harness the power of big healthcare data and develop the informatics and analytical infrastructures to support the delivery of high value healthcare. Our institutions further recognize the growing synergies between the data needs of investigators and health system leaders and the expertise that is needed to conduct patient centered outcomes research and to develop innovative delivery models. Thus, a fundamental strategy of the GPC has been to advance understanding among health system leaders of the value of PCORnet participation and of linking GPC capabilities and activities to health system's needs.

At a tactical level, the GPC will pursue a number of strategies to ensure sustainability. These include: (1) establishing a critical mass of committed participating sites; (2) collaboration with institutional translational science programs; (3) retaining a service recharge model to support core infrastructure functions; and (4) use of low-cost and open-source technologies to decrease the shared cost of introducing innovative new tools and capabilities.

Critical mass of committed participating sites: The success of PCORnet depends on the ability to develop new research protocols for pragmatic studies and to rapidly respond to opportunities to participate in studies proposed by other groups. Thus, the ability of the GPC to have a critical mass of institutions that share a common vision, provide care to diverse populations, and house research programs with a wide range of methodological expertise is essential. Our network model continues to consist of institutions that have 1) the regional reach of their healthcare systems, 2) their strong EHR adoption and health services research and informatics expertise, and 3) a blend of institutions using Oracle Health's EHR (IHC, MCRI, MU), which complements the predominant use of the Epic EHR in the original GPC institutions. We believe that the fourteen sites that will participate in Phase 4 position the GPC to participate in a wide range of PCORnet studies and in new initiatives from the NIH, CDC, FDA, VA/DoD, and to be of value to new partners, including the insurance, pharmaceutical and device industries.

Collaborations with translational science programs: As noted previously, the GPC has benefited from collaborations with NIH CTSA and CTR programs and similar translational science programs at non-CTSA institutions, which enabled sites to significantly share resources provided by NIH and PCORI. The collaborations were particularly beneficial in developing

data warehouses, REDCap and other informatics tools, shared IRB and contract models, and SOPs in Phase 1. During Phase 2 and People Centered Research Foundation contracts, these collaborations will be expanded to promote efficient patient recruitment, engage a broader spectrum of stakeholders, and facilitate multi-site research studies across GPC and led by GPC investigators. A continued area of collaboration will be support for CTSI pilot programs to engage investigators in using PCORnet as a national resource while also supporting new scholars.

Cost Recovery Pricing and Service Center: An important element in our plan for long-term sustainability is the continuation of consistent pricing and a service recharge model in which much of the costs of maintaining central GPC and site-level infrastructures are supported by individual projects that utilize the GPC. GPC has developed and continues to refine our cost recovery pricing in alignment with the standard pricing model developed by the Coordinating Center. GPC supports sending data to external investigators leveraging our external institutional collaborator agreement. GPC is focused on the sustainability of the PCORnet infrastructure. GPC PIs collaborated to develop and agree upon a comprehensive pricing model for studies that leverage PCORnet infrastructure. The GPC pricing model addresses the PCORnet Infrastructure Recovery Costs, Analysis as a Product, Data as a Product, the use of Medicare and Medicaid claims in the GROUSE environment and GPC requirements for letters of support. The pricing model supports PCORnet cost recovery objectives at the GPC network operating level.

GPC has developed and implemented a GROUSE subsidy model to support students and research studies that focus on the three approved cohorts as well as improving data quality. The lower pricing is to encourage students and their supervising faculty to gain experience using PCORnet resources and the common data model.

These cost recovery models will be supported by enhanced institutional support from the University of Missouri System's NextGen Precision Health Initiative and Data Science and Analytics Innovation Center co-directed by Dr. James McClay. GPC leverages both our cost recovery model and a network lead service center to facilitate GPC service payments to sites. Sites invoice the cost center for services provided in support of individual projects. The funds generated from such invoices will be used to support a number of site-level infrastructure expenses (e.g. data standardization, data querying, enhancing shared IRB agreements, oversight of requests for data, PCORnet Infrastructure recovery costs). In addition, the service recharge model will support a number of essential central functions that are described below.

1) *Supporting GPC honest broker functions that involve central analysis of data from individual GPC sites and/or the creation of de-identified or limited datasets to support external investigations*.
2) *Study feasibility queries including projects that employ automated federated access approaches (e.g., SHRINE)*.
3) *Developing REDCap projects to support the collection of patient reported outcomes for PCORnet studies*.
4) *Developing EHR tools (e.g., alerts) for interventional studies that can be installed at multiple sites*.
5) *Integration of payer and insurer data to capture out of system healthcare delivery and to create comprehensive longitudinal data warehouses for our captured populations*.
6) Data integration (eg. National Cardiology Disease Registry CathPCI[1]) aligned with quality improvement initiatives
7) Support additional patient engagement activities as research needs rise.

The service recharge model for site payments supports essential core functions and is dependent on the ability to create a steady stream of external funding through the development of new research proposals by GPC investigators and by attracting studies proposed by external investigators and organizations. In addition to national PCORnet studies, several proposals using the GPC have been based on our data sharing agreement for non-commercial use.

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CLINICAL RESEARCH NETWORK SITES

Table 1. University of Missouri Health Care Site Population	
Number of Unique Patients 2,208,148	*Total number of unique patients (% of patients)*
Demographics	
Age	
• Mean Age	*50.14*
• 0-19	*243,675 (11.04%)*
• 20-44	*708,106 (32.07%)*
• 45-64	*547, 252 (24.78%)*
• 65-74	*289,927 (13.13%)*
• Older than 75	*361,596 (16.38%)*
Sex	
• Female	*1,116,868 (50.58%)*
• Male	*1,074,915 (48.68%)*
• Other	*16,365 (0.74%)*
Race	
• American Indian or Alaska Native	*1,928 (0.09%)*
• Asian	*27,881 (1.26%)*
• Black or African American	*104,745 (4.74%)*
• Native Hawaiian or Other Pacific Islander	*1,081 (0.05%)*
• White	*1,310,003 (59.33%)*
• Multiple Race	
• Refuse to answer	*14,805 (0.67%)*
• Unknown	*719,019 (32.56%)*
• other	*28,686 (1.30%)*
Hispanic	
• Yes	*31,100 (1.41%)*
• No	*1,066,591 (48.30%)*
• Other	*1,110,457 (50.29%)*

Summary of CRN Site Care Settings:

Site Name	Medical Institutions (#)	Hospitals (#)	Physicians (#)	Primary Care Practices (#)	Emergency Departments (#)	Community Clinic (#)	Geographic Coverage: State Name(S)
MUHC	1	10	1266	10	2	1	Missouri

The University of Missouri Health Care (MUHC) is a multi-hospital and academic health system owned by the University of Missouri System comprising five hospitals: University Hospital, Missouri Orthopaedic Institute, Missouri Psychiatric Center, Missouri Rehabilitation Center, and Women's and Children's Hospital. It also has over 50 specialty clinics. University Hospital, the flagship hospital of the University of Missouri Health Sciences Center, is a 307-bed tertiary care

center that provides a full range of medical services. With ten University-owned primary care practices in Boone County, and additional practices in surrounding counties, MUHC also provides a substantial percentage of the primary care in central Missouri. Moreover, the three primary care departments (Family and Community Medicine, Internal Medicine, and Child Health) have all committed to transforming their practices into patient-centered medical homes. University of Missouri Health (MU Health) is one of the most comprehensive health care networks in Missouri. It includes: University Hospital; 50 primary and specialty clinics statewide; University Physicians, a group practice with over 600 members; Women's and Children's Hospital; Ellis Fischel Cancer Center; Missouri Psychiatric Center; Missouri Orthopaedic Institute; Mizzou Quick Care clinics in the three Columbia Hy-Vee grocery stores; and the Missouri Telehealth Network, which serves more than 60 Missouri counties and allows patients to stay in their own communities while being seen by a physician at a major medical center. The Health Network of Missouri also includes 5 smaller, predominantly rural hospitals or health systems: Lake Regional Health System in Osage Beach, Bothwell Regional Health Center in Sedalia, Hannibal Regional Healthcare System, Capital Region Medical Center in Jefferson City, and Saint Francis Healthcare System in Cape Girardeau. MPact Health is a network spanning four states, including MU Health Care, Mosaic Life Care, and the Mercy System.

Summary of CRN Site participation in PCORnet® Studies:
The University of Missouri (MU) joined GPC in PCORnet Phase 2 and has been a CRN coordinating center in PCORnet since 2023. MU executed all of the agreements for participation in GPC and PCORnet. MU personnel have been highly engaged in research activities using PCORnet infrastructure, workgroup, patient engagement, and infrastructure innovations. Dr James McClay will serve as site PI as well as contact PI for GPC with Dr. Abu Mosa (prior site PI) continuing to advance cloud infrastructure and develop self-service query capability for GPC and the PCORnet coordinating center. MU's patient engagement officer (Lisa Royse) and patient representative (Bill Stephens) in GPC were actively engaged and contributed to the patient-centered research design activities at the site and network level. MU successfully completed the first PCORnet designated study titled "Aspirin Dosing: A Patient-Centric Trial Assessing Benefits and Long-term Effectiveness (ADAPTABLE), ClinicalTrials.gov Identifier: NCT02697916" and recruited 178 patients. MU is actively participating in the following studies that are either characterized as PCORnet demonstration studies or PCORnet designated studies: (a) Pragmatic Evaluation of Events And Benefits of Lipid-lowering in Older Adults (PREVENTABLE), an NIH funded study; (b) PRECIDENTD - PREvention of CardIovascular and DiabEtic kidNey disease in Type 2 Diabetes, a PCORI study (c) The RECOVER Post-Acute Sequelae of SARS-CoV-2 (PASC) Electronic Health Record Cohort Study[1].(d) Bariatric Surgery Impact on Cancer Screening (BASICS), (e) Using PCORnet to Compare Blood Pressure Control Strategies[2], and (f) ACTIV-6: COVID-19 Study of Repurposed Medications. The investigators at MU also submitted or participated in numerous grant applications using PCORnet/GPC infrastructure to PCORI, NIH and other funding agencies. MU has been highly responsive to the PCORnet Front Door data queries responding to all requests through the PopMedNet query tool with 96% of queries submitted on time and having data in the final report. Further, MU submitted 90% of data curations on time, with less than 90-day latency and 1 and 4 exceptions for the most recent two refreshes. A recent update to the ETL procedures removed home medications from the prescribing table, temporarily causing a 5% decrease in records but improving data quality. Additionally, MU meets all RXNorm and LOINC mapping rate criteria. MU also participating in the CDC COVID-19 Health Data Initiative Project and responded to all queries submitted through PopMedNet. MU has been refreshing the full CDM data lake monthly to fulfill the requirement of participating in this nationally important CDC COVID project. MU actively engages clinical researchers for the PCORnet Front Door network collaboration requests that are being disseminated in collaboration with the School of Medicine's Office of Research. Overall, MU has been active in all PCORnet activities and will continue to do so for Phase 4 of the funding cycle.

CLINICAL RESEARCH NETWORK SITES

Allina Health System

Table 1. Allina Health System Site Population	
Number of Unique Patients	*2,821,189*
Demographics	*Total number of unique patients (% of patients)*
Age	
• Mean Age	*45.4*
• 0-19	*470,464 (16.68% of patients)*
• 20-44	*972,023 (34.46% of patients)*
• 45-64	*702,040 (24.89% of patients)*
• 65-74	*332,833 (11.80% of patients)*
• Older than 75	*343,653 (12.18% of patients)*
Sex	
• Female	*1,478,538 (52.41% of patients)*
• Male	*1,342,507 (47.59% of patients)*
• Other	*144 (0.01% of patients)*
Race	
• American Indian or Alaska Native	*22,247 (0.79% of patients)*
• Asian	*119,403 (4.23% of patients)*
• Black or African American	*255,814 (9.07% of patients)*
• Native Hawaiian or Other Pacific Islander	*8,607 (0.31% of patients)*
• White	*2,241,476 (79.45% of patients)*
• Multiple Race	*N/A*
• Refuse to answer	*168,430 (5.97% of patients)*
• Unknown	*5,212 (0.18% of patients)*
• other	*N/A*
Hispanic	
• Yes	*141,514 (5.02% of patients)*
• No	*2,543,047 (90.14% of patients)*
• Other	*136,628 (4.84% of patients)*

Summary of CRN Site Care Settings:
The Allina Health System ("Allina Health") is a Minnesota nonprofit corporation that delivers health care services to patients in Minnesota and western Wisconsin. Our integrated health system offers a full range of inpatient and outpatient primary and specialty care services, and includes 11 hospitals, 90 clinics, 52 rehabilitation sites, 15

pharmacies, 2 ambulatory care centers, hospice care, and emergency medical transportation. Table 1 represents the demographics of 2,821,189 patients in the large, diverse population served by Allina Health.
More than 28,000 employees and 6,000 associated and employed physicians share the Allina Health mission, vision, values and promise: "*We serve our communities by providing exceptional care, as we prevent illness, restore health and provide comfort to all who entrust us with their care.*"

Site Name	Medical Institutions (#)	Hospitals (#)	Physicians (#)	Primary Care Practices (#)	Emergency Departments (#)	Community Clinics (#)	Geographic Coverage: State Name(S)
Allina Health	*5*	*11*	*6,000*	*N/A*	*13*	*90*	*Minnesota Wisconsin*

Allina Health Research provides the necessary infrastructure for advancing research across the organization and fosters a supportive environment for the research community. In 2022, Allina Health conducted 184 active clinical studies with more than 5,083 patients enrolled or screened. Researchers contributed to advancing health care through 151 national presentations and posters, and through 100 peer-reviewed publications. Research Operations is responsible for research contracts, finance, billing compliance, and grant management. Allina's Human Subject Research Protection Program manages the daily operations of the Allina Health Institutional Review Board (IRB); coordinates review by external IRBs; and provides quality monitoring, training, and education. Allina has implemented SMART IRB. Allina's Research Compliance Program is a collaboration among many stakeholders including researchers, Compliance, Research Operations, Legal, Human Research Protection Program and others to ensure proper systems exist to support Allina Health Research from a compliance perspective. Clinical research studies include clinical trials, cancer genomics studies, pathology-based studies, and care delivery improvement studies. Allina Health is nationally recognized for its Infectious Disease research and was the only clinical trial site in Minnesota to participate in the Johnson & Johnson (Janssen Pharmaceutical) COVID-19 vaccine study.

Summary of CRN Site participation in PCORnet® Studies:
Allina's PCORnet participation began in 2015 with LHSNet, and in 2018, we joined The Greater Plains Collaborative (GPC). Allina's CRIA team openly shares tools, codes and methods and our data architect collaborates with other GPC sites on ways to tackle data issues. Allina consistently refreshes its CDM quarterly, meeting specs and deadlines. For both Cycle 15 refreshes, Allina consistently had approval by the deadline, only 1 data check exception, mapped at least 80% of the medications to the appropriate Tier 1 RX Norm CUI codes, and mapped at least 80% of labs to LOINC. Our patient population generally increases. Our response rate to Front Door queries is 96% meeting deadline. Allina participated in these studies that have been completed: ADAPTABLE [1,2], DS-DETERMINED (aka, DS-CONNECT), REVEAL (Alliance) ASCVD, and AFib/HF PCORnet. Allina has been highly responsive to data requests, and we are participating in numerous PCORnet-enabled research, including: BESTMED Study, CDC COVID Refresh (CDM Registry) aka CDC Global Task force, NET-PRO Study[3] (we have been a high recruiting site), CardioHealth Alliance, PREVENTABLE.

We plan to participate in the new *REducing future fractureS and improving ouTcOmes of fRagility fracturE" (RESTORE) study.* Recently (March 2024) Allina Health was invited to apply for four separate PCORI opportunities, and we look forward to both initiating and participating in more PCORnet-enabled research studies. Allina's PEO and Patient representative participate in updates and the GPC annual meeting. Allina's site PI, site PM, and data architect/lead analyst consistently participate in meetings and collaborate with colleagues across the network.

CLINICAL RESEARCH NETWORK SITES

Summary of CRN Site Care Settings: IHC Health Services, Inc. (Intermountain Health) is a not-for-profit vertically- and horizontally-integrated healthcare system based in Salt Lake City, UT, and covering 7 states with 33 hospitals (including a "virtual" hospital), 385 medical clinics, telehealth services (begun in 2014), a Medical Group with 3,800 employed physicians and 9,300 affiliated physicians, a broad range of medical services, and a health plans division called SelectHealth. Intermountain is the largest private employer in the Intermountain West with more than 65,000 employees. Until 2022, it had 24 hospitals and 215 clinics but acquired SCL in 2022.

Intermountain includes multiple cancer hospitals as part of an NCI Designated Cancer Center (Huntsman Cancer Institute) and the Intermountain Medical Center Heart Institute that is a top 50 cardiovascular hospital in the US. Intermountain's first electronic health record (EHR) began in the 1960's, the first EHR in the world. A robust system-wide Intermountain EHR (serving hospitals and outpatient clinics) has been in place for more than three decades.

Intermountain's mission is helping people live the healthiest lives possible. Clinical research is integral to achieving this mission. The research program spans population health/primary care through tertiary and quaternary care. Intermountain research investigators are well experienced in clinical trials including pragmatic trials and, with the rich electronic data warehousing, are well-published in observational EHR-based studies.

Table 1. Intermountain Health Site Population	
Number of Unique Patients	*4,521,578*
Demographics	
Age	
• Mean Age	*38.7 years*
• 0-19	*25.8%*
• 20-44	*36.7%*
• 45-64	*19.8%*
• 65-74	*8.3%*
• Older than 75	*9.4%*
Sex	
• Female	*50.6%*
• Male	*49.3%*
• Other	*0.1%*
Race	
• American Indian or Alaska Native	*0.8%*
• Asian	*1.9%*
• Black or African American	*1.5%*
• Native Hawaiian or Other Pacific Islander	*1.3%*
• White	*81.9%*
• Multiple Race	*unknown*
• Refuse to answer	*unknown*
• Unknown	*12.0%*
• other	*0.5%*
Hispanic	
• Yes	*13.0%*
• No	*73.9%*
• Other	*13.1%*

Summary of CRN Site participation in PCORnet® Studies: Intermountain joined the Learning Health System CDRN (LHSnet) in Phase II (2015) and developed the common data model (CDM) from its 24-hospital and 215-clinic health system (expansion occurred in 2022). Intermountain was active in CDM refreshes, clinical trials, and observational research. This included participation in ADAPTABLE (PI: Matthew T. Roe, MD MHS, Duke University; site PI: Kirk Knowlton, MD), an observational Heart Health Survey study of heart failure patients whose first two papers were published in 2024 (PI: Dr. Alanna Chamberlain, PhD, Mayo Clinic; site PI: Kismet Rasmusson, DNP), and an observational survey study of osteogenesis imperfecta (PI: Dr. Rebecca Jackson, MD, the Ohio State University; site PI: Lorenzo Botto, MD). Intermountain contributed to, "The PCORnet CDM as a surveillance tool for uncontrolled hypertension," an observational study from the health services research CRG for Intermountain, the University of Utah, and the Utah Department of Health (site PI: Shan He, PhD).

PRINCIPAL INVESTIGATOR (MCCLAY, JAMES, C.):

Joining the Greater Plains Collaborative (GPC) CDRN in 2019, Intermountain is active in research studies, clinical trials, and grant applications. This includes the PREVENTABLE trial in which Intermountain is a high-enroller of subjects (PI: Karen P. Alexander, MD, Duke University; site PI: Jeffrey L. Anderson, MD). Joining in May 2020, Intermountain remains one of the 40 active participating sites in the COVID-19 CDM surveillance project of the Centers for Disease Control and Prevention. Intermountain also continues to participate in the NIH RECOVER-EHR project that began in 2021 as part of the RECOVER post-acute sequelae of COVID-19 (PASC) initiative, contributing patient information to both the pediatric and adult RECOVER-EHR studies (mPIs: Drs. Horwitz, Katz, Troxel; site PI: Benjamin D. Horne, PhD). Intermountain participated in multiple NIH ACTIV COVID-19 clinical trials in response to a PCORnet-wide request for submissions.

Other observational PCORnet studies that Intermountain participated in include, "Using PCORnet to Compare BP Control Strategies" (PI: Mark Pletcher, MD, UCSF; site PI: Kirk Knowlton, MD), "the Characterization of Patients with Heart Failure and Patients with Atrial Fibrillation and Atrial Flutter in PCORnet data" (PI: Manesh Patel, MD, Duke U.; site PI: Heidi T. May, PhD), the "Veteran Suicide Prediction/Prevention Using Electronic Health Records" (VESPER) study (PI: Jeffrey Swanson, PhD, Duke U.; site PI: Heidi T. May, PhD), and the "Observational Evaluation of Second Line Therapy Medications in Diabetes" (BESTMED) study (PI: Alexander Turchin, MD, Harvard U.; site PI: Benjamin D. Horne, PhD).

Intermountain has participated in a multitude of grant applications through PCORnet, including Front Door requests for collaborators and direct contact invitations from PIs at other PCORnet sites. While many of these have not been funded, others await funding decisions currently and Intermountain continues to be active in responding to requests for collaborators. For example, Intermountain is very interested in and joined the application for grant funding for the NOTIFY trial that will use coronary calcium to guide treatment in atherosclerotic cardiovascular disease (2024 PCORI submission, mPIs: David Maron, MD, Stanford University, and Pamela S. Douglas, MD, Duke University). An application for funding for a study, "Prevention of Nephrotoxic Acute Kidney Injury," (2024 NIH submission, PI: Benjamin Griffin, MD, University of Iowa) will validate a risk prediction algorithm and then implement it in clinical care.

Intermountain in the cycle 15 refreshes received data curation approvals by the deadline and had 6 and 3 investigative checks in refresh 15.1 and 15.2, respectively. For refresh cycles 15.1 and 15.2, Intermountain had 96.6% and 94.8% of medications in Tier 1 Preferred RxNorm CUI codes, mapped 100% of laboratory results to LOINC, had <5% change in patient and record numbers in the CDM, and had ≤90-day data latency. Intermountain has successfully responded to >80% of Phase 3 Front Door queries by the deadline with results included in final query report.

Intermountain electronic resources include data on >4.5 million patients in the current CDM and additional data for research in: 1) iCentra (Cerner EHR since 2016 in UT, ID, WY) and EPIC (NV, CO, KS, and MT facilities)—note: all facilities will be EPIC by 2025, 2) the HELP2 system (pre-iCentra hospital EHR), 3) Clinical Workstation (pre-iCentra clinic EHR), 4) the Intermountain Biorepository (biobank of >4.5 million biological samples from cancer patients), 5) a tumor registry (with data from decades of tracking), 6) the INSPIRE biobank (ongoing 31-year old DNA and plasma biobank of >35,000 cardiac cath lab patient samples with whole genome sequencing and patient-reported socioeconomic, dietary, exercise, and other lifestyle data), 7) medication claims data from SelectHealth (representing about one quarter of patients in the CDM), 8) Social Security death master file mortality data, 9) Utah Department of Health electronic death certificates, and 10) Medicare/Medicaid Claims in the GPC GROUSE environment. Intermountain is committed to future CDM expansions.

Site Name	Medical Institutions (#)	Hospitals (#)	Physicians (#)	Primary Care Practices (#)	Emergency Departments (#)	Community Clinics (#)	Geographic Coverage: State Name(s)
Intermountain	*Not reported*	*33*	*3,800*	*many*	*33*	*385*	UT, ID, WY, NV*, CO*, KS*, MT*

**The CDM currently does not include patients seen in the 9 hospitals and 170 clinics in these states, but as Intermountain moves to EPIC for its EHR by mid-2025, data from all hospitals and clinics will become available to include in the CDM.*

CLINICAL RESEARCH NETWORK SITES

Summary of CRN Site Care Settings: University of Kansas Medical Center (KUMC) has over 100 clinical sites in the University of Kansas Health System (UKHS) including 1 hospital, 11 primary care practices, 86 specialty care practices, and 1 federally qualified health center. The UKHS serves patients from every Kansas county, most Missouri counties, 50 U.S. states and several countries. While the services described here are provided by our facilities in the Kansas City area, the health system includes hospital and clinic locations in Great Bend, Olathe, and Topeka, Kansas. KUMC is one of only 53 National Cancer Institute-designated comprehensive cancer centers in the nation. Comprehensive designation is the highest level of recognition awarded by the NCI, granted only to cancer centers with the deepest and broadest knowledge of cancer.

Summary of CRN Site participation in PCORnet® Studies: University of Kansas Medical Center has participated in several PCORNet studies like ADAPTABLE, PREVENTABLE, PROVIDE-HF, PaCR, NEXT-D (Natural Experiments in Diabetes Translation), COVID Healthcare Data Initiative, HERO Registry and Trial, Cancer Rapid Cycle Research, BP Track, NET-PRO, DS Determined, RECOVER, ODYSSEY, and DROOL. Under the guidance of Duke's ADAPTABLE team, we learned several invaluable recruitment lessons and we stood 4th in the overall CDRN enrollments by site where we recruited 738 patients into the trial. Additionally, our site leveraged the PCORnet CDM to deliver data to the National COVID Cohort Collaborative (N3C) and PCORNET CDC COVID-19 Healthcare Data Initiative in 2020.

We put our best foot forward to adhere to the pragmatic approach of the trial and obtained the most yield by low touch approaches like emails. We applied the same approaches to other PCORNet trials that followed ADAPTABLE like DS-DETERMINED and had good success. Currently, we are successfully enrolling in the NET-PRO study and will continue these diligent enrollment efforts.

Table 1 University of Kansas Health System Population	
Number of Unique Patients	*1,621,029*
Demographics	
Age	
• Mean Age	*48.63*
• 0-19	*171509 (11.00%)*
• 20-44	*522429 (33.50%)*
• 45-64	*437262 (28.04%)*
• 65-74	*233704 (14.99%)*
• Older than 75	*194600 (12.48%)*
Sex	
• Female	*871071 (53.74%)*
• Male	*748893 (46.20%)*
• Other	*1065 (0.07%)*
Race	
• American Indian or Alaska Native	*25876 (1.60%)*
• Asian	*72 (0.00%)*
• Black or African American	*145186 (8.96%)*
• Native Hawaiian or Other Pacific Islander	*4725 (0.29%)*
• White	*1005156 (62.01%)*
• Multiple Race	*9098 (0.56%)*
• Refuse to answer	*2237 (0.14%)*
• Unknown	*2768 (0.17%)*
• other	*425911 (26.27%)*
Hispanic	
• Yes	*118001 (7.28%)*
• No	*1180681 (72.84%)*
• Other	*322,345 (19.89)*

Sravani Chandaka (KUMC site PI) has wide experience in delivering complex informatics/analytics solutions in healthcare delivery and clinical research settings. At KUMC, she has been heavily involved in collaborative medical research through Greater Plains Collaborative (GPC) since its inception. **Diego R. Mazzotti, PhD (Co-investigator)** will

facilitate the utilization of GPC resources by investigators at the University of Kansas Medical Center. With his collaborative approach to research, he will play a pivotal role in advancing our scientific initiatives. **Lav Patel (Datamart Liaison)** has efficiently worked on optimizing CDM ETL, GROUSE implementation and COVID CDC instance development at KUMC. Mr. Patel will support the ongoing common data model refreshes, record linkage and other technical requirements as needed.

Data:
Our data sources include but are not limited to Epic (the hospital electronic medical record), Cardiovascular registry (NCDR), Cystic Fibrosis registry, IDX, KU Cancer registry, KU biospecimen repository, REDCap, Social security death index data, Trauma registry and Vizient. Our site is one of the very few sites that have used machine learning/NLP methodologies to de-identify notes at a large scale. As of now, we have de-identified all our physician notes, progress notes, radiology/cytology/pathology notes and smart elements. We are currently in the process of incorporating structured notes and NLP-extracted clinical concepts from unstructured notes. KUMC has also made PCORnet CDM available for researchers on our analytic server Green HERON and Databricks platform in Microsoft Azure to engage the broader scientific community and catalyze research collaborations using PCORNet infrastructure. This initiative will be a great asset for PCORNet Phase 4 as we aim to increase the utilization of GPC resources by local researchers.

KUMC received 80 percent or more of Phase 3 data curation approvals by the deadline. We continue to improve the quality of our data with each refresh resulting in less than 3 data check exceptions. We aim to improve the Primary Dx data in the Cycle 16 Refresh 1. We mapped at least 80 percent of medications (by frequency to the appropriate Tier 1 Preferred RxNorm CUI codes. We mapped the top 80 percent (by frequency) of labs to LOINC, fully specifying the result and result unit. We have reduced our data latency to <=15 days. KUMC has less than a 5 percent decrease in the number of patients and records in a CDM table between refreshes. KUMC has successfully responded to at least 80 percent of Phase 3 Front Door queries by the deadline.

Table 2. KUMC Characteristics

Site Name	Medical Institutions (#)	Hospitals (#)	Physicians (#)	Primary Care Practices (#)	Emergency Departments (#)	Community Clinics (#)	Geographic Coverage: State Name(S)
KUMC	*1*	*4*	*>1,000*	*11*	*4*	*>100*	*Kansas Missouri*

KUMC PCORnet-enabled Research
KUMC researchers have collaborated with PCORNET and GPC investigators on multiple research projects including but not limited to cancer, intellectual and developmental disabilities, and rare diseases. These efforts have led to publications, as well as national and international presentations, including topics regarding obesity with sleep apnea[1,2], and hypertension[3]. KUMC is also participating in the actively enrolling NET-PRO led by University of Iowa[4].

CLINICAL RESEARCH NETWORK SITES

Table 1. Marshfield Clinic Research Institute Site Population	
Number of Unique Patients 1,183,559	*Total number of unique patients (% of patients)*
Demographics	
Age	
• Mean Age	*48.4*
• 0-19	182,666 (15%)
• 20-44	366,857 (31%)
• 45-64	281,363 (24%)
• 65-74	159,361 (14%)
• Older than 75	193,155 (16%)
Sex	
• Female	600,064 (51%)
• Male	583,344 (49%)
• Other	151 (0%)
Race	
• American Indian or Alaska Native	9,344 (1%)
• Asian	15,175 (1%)
• Black or African American	9,766 (1%)
• Native Hawaiian or Other Pacific Islander	1,264 (0%)
• White	742,497 (63%)
• Multiple Race	65,563 (6%)
• Refuse to answer	24,672 (2%)
• Unknown	301,789 (26%)
• Other	13,489 (1%)
Hispanic	
• Yes	2,8417 (2%)
• No	784,960 (66%)
• Other	370,182 (31%)

Summary of CRN Site Care Settings

The Marshfield Clinic Research Institute (MCRI) is the research 'arm' of the Marshfield Clinic Health System (MCHS). MCHS is a large multispecialty integrated care system serving the rural region of northern, central, and western Wisconsin. As outlined in the summary table below, MCHS is comprised of 65 clinics, 10 dental centers, 19 pharmacies, 36 clinical laboratories, and 11 hospitals in multiple communities, serving over 300,000 unique patients annually. Scientific staff at MCRI, which includes approximately 30 PhD and MD level investigators, plus over 200 staff and 124 current clinician-researchers, has a close relationship with MCHS. MCHS currently operates the Cerner electronic health records system, with computerized diagnostic files dating back to 1963 and ICD coded data since 1979. In addition to usual care and billing data, MCRI routinely accesses claims data from their affiliated health plan (Security Health Plan of Wisconsin) and CMS claims using the GPC GROUSE environment. CRN-level data elements are better described in the full application, but MCRI can contribute observations from millions of patient-years of follow-up.

PRINCIPAL INVESTIGATOR (MCCLAY, JAMES, C.):

Site Name	Medical Institutions (#)	Hospitals (#)	Physicians (#)	Primary Care Practices (#)	Emergency Departments (#)	Community Clinics (#)	Geographic Coverage: State Name(s)
MCRI	*76*	*11*	*1,600*	*65*	*11*	*65*	*Wisconsin, Michigan*

Summary of CRN Site participation in PCORnet® Studies

MCRI has been a very active partner in the Greater Plains Collaborative (GPC) and PCORnet phases I, II, and III, bringing an extensive history of participation in prior national research consortiums such as the Healthcare Systems Research Network, Vaccine Safety Datalink, All of Us, CTSA partnership with the University of Wisconsin, and the FDA Sentinel initiative. Our collaboration with GPC partners is an institutional hallmark of success in multisite, interdisciplinary research. As part of the GPC, MCRI has actively participated in several PCORnet, including the ADAPTABLE trial[1], Antibiotics and Childhood Growth cohort, Bariatric, and GPC Acute Kidney Injury studies in phases I and II. MCRI ranked in the top half of recruiting sites in ADAPTABLE and served as an early model of pragmatic electronic recruitment approaches that have assisted other sites. In phase III, MCRI has been the leading GPC recruiting site for the PREVENTABLE trial (and in the top 4 nationally), including the CAC sub-study. MCRI also participated in several other phase III PCORnet studies, including the HERO trial and registry, BP Control, Characterization of Patients with Heart Failure and Patients with Atrial Fibrillation and Atrial Flutter, BESTMED, and is planned to be included the latter phase of the BASICS study. One of our main goals in future phase IV PCORnet studies is to engage clinicians and patients in our network of satellite clinics in more remote areas of our north-central Wisconsin service area. This approach has worked particularly well in the PREVENTABL trial, which has enrolled many rural residents. Dr. Jeffrey VanWormer, the MCRI site lead for the GPC, has been a co-author on several ADAPTABLE trial and other GPC study publications[2].

Data and Technology

MCRI has been successful in returning results during our Phase 3 participation in GPC. As a CRN site and participating sites for the Cycle 15 (First Refresh), Cycle 15 (Second Refresh), and Cycle 16 (First Refresh) we received 80 percent or more of Phase 3 data curation approvals by the deadline. Our site received 80 percent or more of Phase 3 data curation approvals by the deadline and reported eight or fewer data site exceptions in the past nine out of ten refreshes. Our site has mapped at least 80 percent of medications (by frequency) to the appropriate Tier 1 preferred RxNorm CUI codes as stated in the CDM Implementation Guidance, and successfully mapped the top 80 percent of labs (by frequency) to LOINC. Our site has successfully responded to at least 80 percent of Phase 3 Front Door queries by the deadline with results included in the final query report. Specifically, our site's query fulfillment received 27 queries and completed 26 of those queries by the due date. The average response time was 4.6 days.

While our site has had a few refreshes where we had a five percent decrease in patients/records for a select number of CMD tables between refreshes, these changes have all tied back to efforts to de-duplicate encounters and improve data accuracy. Staff has confirmed at each refresh that we were not truly losing five percent of records or patients. Research staff has recently teamed up with the Marshfield Clinic Health System main IT staff to work together on data governance and join forces to resolve issues with data at the source.

Some EDC reports have indicated latency in a small number of CDM tables. This latency is an artefact of the MCHS switch to Cerner in January 2023. Prior to the transition, we had more records per encounter, which were being factored into the 24-month average. As these records begin to fall off our EDC report, we expect these data checks to resolve. Our obs_clin table continues to be identified as a table with latency, however that table was populated on a one-time basis for a study and can be readily populated for future data elements that are requested.

PRINCIPAL INVESTIGATOR (MCCLAY, JAMES, C.):

CLINICAL RESEARCH NETWORK SITES

Summary of CRN Site Care Settings:

The Medical College of Wisconsin (MCW) is an integral partner within the Froedtert & Medical College of Wisconsin (F&MCW) Health Network, providing primary, specialty, tertiary, and quaternary level patient care by physician and advanced practice providers to the Southeastern Wisconsin catchment area.

Site Name	Medical Institutions (#)	Hospitals (#)	Physicians (#)	Primary Care Practices (#)	Emergency Departments (#)	Community Clinics (#)	Geographic Coverage: State Name(s)
MCW(1)(2)	*1*	*5*	*1,815*	*57*	*9*	*57*	*Wisconsin*

This highly integrated partnership creates synergies between our academic and community clinical practices, hospital care partners, community partners, and innovative research teams. These powerful collaborations fuel and fortify enterprise investment in national research initiatives like All of Us and NCAA-DOD CARE Consortium as well as highly competitive awards including our NCATS CTSA Program award which funds the Clinical and Translational Science Institute (CTSI). MCW was awarded a 3rd round of CTSA funding in 2020 and will be reapplying for a 4th round in 2024.

In addition to our main catchment area, the F&MCW regional health network provides academic and clinical outreach in Northeastern and Central Wisconsin counties. As a member of the Greater Plains Collaborative (GPC), the Medical College of Wisconsin contributes longitudinal health records for over 1.8 million patients in the PCORnet Common Data Model (CDM) curated from our multi-sourced Clinical Research Data Warehouse (CRDW.) (**Table 1**)

Table 1. Clinical Research Network (CRN) Site Population	
Number of Unique Patients	*1,835,304*
Demographics	
Age (% of patients)	
• Mean Age	*50*
• 0-19	*11.5%*
• 20-44	*31.9%*
• 45-64	*27.3%*
• 65-74	*13.8%*
• Older than 75	*15.5%*
Sex (% of patients)	
• Female	*53.2%*
• Male	*46.6%*
• Other	*0.2%*
Race (% of patients)	
• American Indian/Alaska Native	*0.34%*
• Asian	*2.22%*
• Black or African American	*13.24%*
• Native Hawaiian/Other Pacific Islander	*0.08%*
• White	*66.41%*
• Multiple Race	*0.45%*
• Refuse to Answer	*0.28%*
• Unknown	*13.05%*
• Other	*3.93%*
Hispanic (% of patients)	
• Yes	*5.4%*
• No	*81.3%*
• Other	*13.4%*

The F&MCW health care network includes hospitals, an adult Level 1 trauma center, ambulatory surgery centers, transplant surgery, urgent care, cancer centers, labs, pharmacies, eye care, ambulatory clinics, virtual clinics, translational research units, and stand-alone diagnostic imaging centers located primarily in Southeastern WI.

Summary of CRN Site participation in PCORnet-enabled Research:

MCW is ranked in the top 25% of NIH funded academic medical centers, a national leader in biomedical research, and a highly collaborative and engaged PCORnet partner in Phases 1 through 3. In response to the COVID-19 pandemic, MCW demonstrated data engineering agility by quickly increasing the frequency of CRDW refreshes from monthly to weekly without sacrificing data quality or completeness. This accomplishment has allowed MCW to reduce the latency of our quarterly CDM data and participate in important initiatives such as the CDC COVID-19 Data Project.

MCW has participated in PCORnet demonstration studies and numerous PCORnet designated studies. The most notable include ADAPTABLE as a top 10 recruiting site, PREVENTABLE as a top 10 recruiting site, PRECIDENTD as a vanguard site, and NET-PRO as a top 3 recruiting site. MCW has also contributed to Using PCORnet to Compare Blood Pressure Control Strategies (BP Control-7), COVID-19 Evidence Accelerator (Coagulopathy), CDC COVID-19 EHD, Cancer CRG, Pediatric CRG, Kidney Health CRG, Natural Experiments in Diabetes Translation (NEXT-D2 & NEXT-D3), ODYSSEY RCC, BESTMED, ILD Care, RECOVER/PASC-Adults, PKIDS, and PRESERVE. MCW plans to participate in USD OASIS and NOTIFY as well as Comparative Effectiveness of Extending Postpartum Medicaid Coverage on Maternal Outcomes.

Tools and methods development: MCW is an active collaborator within the GPC research community, sharing our tools, code, and methods with partner sites via the GPC GitHub platform. In addition, MCW maintains a public code repository on GitHub to share de-identification methods and algorithms for interrogating unstructured clinical documentation. The MCW team shared these methods with the NCATS National Center for Data to Health (CD2H) teams and was the first hub to upload de-identified data to the NIH/CD2H cloud infrastructure.

MCW's site PI, Bradley Taylor, is an active, proven leader within the NIH and PCORnet data communities. He has engaged MCW in many national research informatics initiatives including ENACT, N3C, FDA Sentinel, and 4CE.

MCW was an early adopter of privacy preserving record linkage (PPRL) technology, engaging with Datavant and other Wisconsin CTSA hubs in the 2018 All of Us/EHR demonstration project, to identify overlap between academic centers. MCW has engaged in several other funded projects (RADx-UP, etc.) that take advantage of PPRL methods to enhance knowledge of patients' healthcare journeys. We continue to explore new data sources and novel methods for connecting disparate data to expand and enrich our instance of the PCORnet CDM. MCW is committed to implementing future table expansions and maintaining the highest level of data quality.

Data: MCW's CDM tables are curated from EHR and billing data. Our quarterly EDC reports consistently show excellent compliance with PCORnet guidance, highlighting the following statistics in Cycle 15 Refresh1/Refresh2:

- 100% data curation approvals on or before the deadline
- No red investigative checks, and only 2 irremediable blue data checks due to source data limitations
- 89.1%/91.53% medications mapped to Tier 1 Preferred RxNorm CUI codes
- 99.36%/99.37% labs mapped to LOINC with known result and result unit
- One data latency <90 days in Dispensing table caused by lag in our EHR Surescripts data
- 3.3-day query response time and 95.5% of QF queries responded on time/data included in report

CLINICAL RESEARCH NETWORK SITES

Summary of CRN Site Care Settings:

University of California, Davis Health System: (UCDHS): UCDHS is a self-supporting non-profit organization, owned and operated by the Regents of the University of California. it supports the clinical and research activities of the professional schools of medicine and nursing, the UC Davis Comprehensive Cancer Center, and multiple research centers. UC Davis Health serves over 65,000 square miles in Central and Northern California, UCDHS supports 642 beds, admits over 30,000 patients, and manages over 1M outpatient visits annually. It is the only Level 1 Trauma Center in the region with the ER seeing an average of 210 patients per day. The Health System employs 1,212 faculty, 1,007 residents, 3,364 Nurses, 1,081 students, and 10,155 staff and is a major employer in the region.

UC Davis Health System includes the UC Davis NCI-designated Comprehensive Cancer Center which sees over 100,000 encounters annually and the NCATS Clinical and Translational Science Center. UC Davis research centers include the UC Davis MIND Institute (Medical Investigation of Neurodevelopmental Disorders), UC Davis Alzheimer Disease Research Center, USDA Western Human Nutrition Research Center, and affiliations with Shriners Hospital for Children in Sacramento, Veterans Affairs Northern California Health Care System, USDA Western Human Nutrition Research Center, Lawrence Livermore National Laboratory, California Department of Public Heath, and the David Grant Medical Center at Travis Air Force Base.

Table 1. University of California, Davis Health System Site Population		
Number of Unique Patients	Total number of unique patients (% of patients)	1,379,252
Demographics		
Age		
• Mean Age	45	
• 0-19	243,618	17.7%
• 20-44	457,149	33.1%
• 45-64	319,171	23.1%
• 65-74	172,998	12.5%
• Older than 74	186,316	13.5%
Sex		
• Female	716,307	52.18%
• Male	652,868	47.56%
• Other	3,613	0.26%
Race		
• American Indian or Alaska Native	5,624	0.41%
• Asian	76,155	5.55%
• Black or African American	78,330	5.71%
• Native Hawaiian or Other Pacific Islander	7,951	0.58%
• White	472,727	34.44%
• Multiple Race	27,692	2.02%
• Refuse to answer		
• Unknown		
• other	182,128	13.27%
Hispanic		
• Yes	164,823	12.01%
• No	681,719	49.66%
• Other	526,246	38.33%

The UCDH patient population of nearly 1.4 million includes an active population of 305,019 seen in 2023-2024. 37% of the patient population speak a non-English language at home which reflects the broad and diverse population in the UCDH service area, which covers over 5M residents in 33 predominantly rural counties, and 28% of California's total land in farming (i.e., cropland, pastureland, woodland). This includes one of the largest Middle Eastern and Native American populations in the U.S. with the 2020 Census reaffirming Sacramento as one of the most diverse cities in the nation.

Sacramento's Diversity Index – or the calculated "probability that two people chosen at random will be from different race and ethnic groups" – increased from 75% to 77% between 2010 and 2020, according to U.S. Census Bureau data.

Site Name	Medical Institutions (#)	Hospitals (#)	Physicians (#)	Primary Care Practices (#)	Emergency Departments (#)	Community Clinics (#)	Geographic Coverage: State Name(S)
UC Davis Health	1	1	1007	17	1	17	California

Summary of CRN Site participation in PCORnet® Studies:
UC Davis has been an active technology and informatics partner in multiple collaborative networks, including being an initial partner with the ACT and now ENACT network, as well as *All of Us*, N3C, and multiple regional or national disease-focused networks. Dr. Nicholas Anderson is Professor and Chief of the Division of Health Informatics in the Department of Public Health Sciences and was the Co-PI of the PCORI-supported Community Engaged Network for All (CENA, PI: Sharon Terry). UC Davis is also poised for active leverage and participation in the GPC network. Dr. Brad Pollock (Chair, Department of Public Health Sciences), is an epidemiologist and biostatistician, was the original GPC PCORnet site PI for UT Health San Antonio, served on the PCORnet Clinical Trials Task Force, and has been engaged in clinical/translational technology infrastructure development for decades. He served as the Chair of the CTSA Biostatistics/Epidemiology/Research Design (BERD) Key Function Committee and has continuously served as the PI of the NCI Community Oncology Research Program (NCORP) Research Base for the Children's Oncology Group for 30 years. Dr. Courtney Lyles, Professor in the Department of Public Health Sciences leads the Center for Health Care Policy Research at UC Davis and is Co-PI of the PCORI CHARMED study. Through the UC Davis Health System, the UC Davis CTSC, and the Department of Public Health Sciences there is significant infrastructure, expertise, and training resources that will expand novel PCORNET research on local and national populations.

Tools and methods development:
UC Davis (UCD) has developed a mature set of OMOP databases refreshed and curated to serve both quality and research needs. UC Health supports the Center for Data Driven Insights and Innovation (CDI2), which is a centralized repository of OMOP data collected from the 5 separate health systems into a secure enclave. A key component of this system is the regular data quality and improvement processes involved in the ETL, which includes a growing suite of use-cases and formalized algorithms for improved mapping and loading support. Locally UC Davis supports the richer "DataPATH" repository, which includes access to both clinical structured data and unstructured clinical notes. This repository supports the ATLAS interface as well as Jupyter-level notebook access.

These tools and ecosystems describe the more recent examples of UC Davis history of collaborative research network development, which started with the development of UC Rex (University of California Research Exchange) in 2011. UC-Rex leveraged o the i2b2/SHRINE architecture and initially federated within the 5 academic medical centers of the University of California health system. UC Rex was an early participant in the NCATS supported ACT network and is now an active participant in the successor ENACT network which uses an OMOP CDM. Other infrastructure includes ongoing participation in the ATHENA breast health network, the NIH Precision Medicine All of Us as both a data site and collaborator, and collaboration with the N3C centralized research platform.

PRINCIPAL INVESTIGATOR (MCCLAY, JAMES, C.):

CLINICAL RESEARCH NETWORK SITES

Summary of CRN Site Care Settings: The University of California, Los Angeles (UCLA) is a self-supporting non-profit organization, owned and operated by the Regents of the University of California, to support the clinical activities of the professional schools of dentistry, medicine, nursing and public health.

UCLA represents a highly collaborative partnership between UCLA Health (including our hospitals and numerous clinics), our research centers, the UCLA Faculty Group, and the David Geffen School of Medicine. This combination allows us to achieve our interrelated clinical, educational, and research missions and powers our investment in major research initiatives, such as our Clinical and Translational Sciences Institute (CTSI).

UCLA provides tertiary and quaternary-level patient care primarily to the state of California residents but also serves patients nationally and internationally while being a leader in biomedical research. For the GPC partnership, UCLA Healthcare represents 5 hospitals, 280 clinic sites and 3.4 million patients having data in their EMR (**Table 1**). The institution has a medical staff of 1,142 primary care providers and 12,958 specialty providers. The University of California is both a CTSA site and is an NCI Designated Cancer Center. UCLA also provides quaternary care for Southern California and the nation with particular focus on patients with rare diseases, organ transplants, and independent investigator-initiated research (UCLA's NIH funding is the tenth highest among schools of medicine, approaching half a billion in 2022).

Our geographic and demographic reach throughout Los Angeles and surrounding counties enables us to bring enhanced diversity to our research and to PCORnet. UCLA represents geographic expansion for GPC and PCORnet into California and into the second largest metropolitan area in the US. Highlights include our large Asian patient population, who are underrepresented in the GPC.

Table 1. UCLA Site Population

Number of Unique Patients	*3,372,583*
Demographics	
Age	
• Mean Age	*49.6*
• 0-19	378,298 (11%)
• 20-44	1,117,420(33%)
• 45-64	895,656(27%)
• 65-74	432,964(13%)
• Older than 75	*548,245(16%)*
Sex	
• Female	1,800,625(53.4%)
• Male	1,566,542(46.4%)
• Other	5,416(0.2%)
Race	
• American Indian or Alaska Native	18,050 (0.5%)
• Asian	227,603 (6.7%)
• Black or African American	146,709 (4.4%)
• Native Hawaiian or Other Pacific Islander	5,579 (0.2%)
• White	1,259,849 (37.4%)
• Multiple Race	62,309 (1.8%)
• Refuse to answer	*210,850 (6.3%)*
• Unknown	*1,061,254 (31.5%)*
• other	*380,380 (11.3%)*
Hispanic	
• Yes	*440,952 (13.1%)*
• No	*1,718,825 (51.4%)*
• Other	1,212,806 (36%)

Summary of CRN Site Care Settings:
UCLA, as a health care provider and a research institution, provides care to patients in our hospitals and clinics.

PRINCIPAL INVESTIGATOR (MCCLAY, JAMES, C.):

Site Name	Medical Institutions (#)	Hospitals (#)	Physicians (#)	Primary Care Practices (#)	Emergency Departments (#)	Community Clinics (#)	Geographic Coverage: State Name(S)
UCLA	*1*	*5*	*14,100*	*280*	*2*	*None*	*California*

Summary of CRN Site participation in PCORnet® Studies: UCLA has been a highly active and responsive partner to PCORnet studies through its prior participation in the pSCANNER network. UCLA is resuming its participation in PCORnet through GPC. UCLA now refreshes its CDM instance quarterly in conformance with PCORnet standards. UCLA has now led or participated in several PCORI-funded projects, including:

- ADAPTABLE, PCORnet's first pragmatic study, PCORI 20163102
  Roe (PI); Bell: UCLA site PI
  Aspirin Dosing[2]: A Patient—Centric Trial Assessing Benefits and Long-term Effectiveness (ADAPTABLE) was a pragmatic clinical trial aimed at identifying the optimal dose of aspirin for secondary prevention of ischemic events among 20,000 patients with ASCVD at high risk. Patients were randomly assigned in a 1:1 ratio to receive an aspirin dose of 81 mg/day vs. 325 mg/day. Patients interacted with the study primarily through a web portal and their electronic health record data was extracted for analysis. Final results were published 5/27/2021 in the New England Journal of Medicine.
- Pediatric KIDney Stone (PKIDS) Care Improvement Network[1]
  Tasian (PI); Sturm: UCLA author
- The PCORnet Bariatric Study (PBS)[3]
  Arterburn (PI); Bell: UCLA site PI
- Community-Based Palliative Care Delivery for Adult Patients with Advanced Illnesses and their Caregivers
  Walling, Wenger: UCLA site PIs; Bell: Co-Investigator
- Comparative Efficacy of Advanced Practice Provider vs. Electronic Co-Management in a Diverse Population of Aging Women with Urinary Incontinence
  Anger (PI); Bell: Co-Investigator

Data: UCLA has access to data from 3.3 million patients for research purposes. This includes information from various sources such as:

- EPIC, which serves as both the hospital electronic health record and the clinical and hospital billing system.
- CNeXT hospital tumor registry.
- The ATLAS Community Health Initiative, covering 115,000 patients.
- REDCap, which includes selected projects involving patient reported outcomes.
- Data from the UCLA Neuroscience Genomics Core (UNGC) and UCLA Precision Health Biobank, totaling 200k patients.
- The California Death Registry.

Furthermore, UCLA is actively pursuing access to Medicare/Medicaid Claims in the GPC GROUSE environment. We are committed to implementing future expansions of our Clinical Data Mart (CDM).
UCLA EDC showed strong indicators of high quality data/process:

- The first EDC report only receive five investigative data check exceptions. One of which we are expecting to clear in the next cycle (IVE table since it was off only 0.01%)
- It mapped more than 80 percent of medications (by frequency) to the appropriate Tier 1 Preferred RxNorm CUI codes as specified in the CDM Implementation Guidance
- It mapped the top 80 percent (by frequency) of labs to LOINC, fully specifying the result and result unit as per CDM.

PRINCIPAL INVESTIGATOR (MCCLAY, JAMES, C.):

CLINICAL RESEARCH NETWORK SITES

Summary of University of Iowa (UIowa) Care Settings: University of Iowa Health Care (UIHC) represents a highly integrated partnership of the University of Iowa Hospitals and Clinics, University of Iowa Physicians, and the Carver College of Medicine that is led by the Vice President for Medical Affairs. This close integration creates synergies between our clinical, educational, and research missions and enables joint investment in major research initiatives, such as the Institute for Clinical and Translational Science (ICTS), which houses our CTSA.

UIHC provides tertiary and quaternary-level patient care to the state of Iowa and the surrounding region and is a national leader in biomedical research. The University of Iowa is both a CTSA site and a NCI Designated Cancer Center. **Table 1** displays UIHC population characteristics.

Table 1. University of Iowa Health Care Site Population

Number of Unique Patients	1376413
Demographics	
Age (% of patients)	
• Mean Age	44.25
• 0-19	19.46 (267833)
• 20-44	34.07 (469008)
• 45-64	20.85 (286997)
• 65-74	11.62 (160000)
• Older than 74	13.99 (192575)
Sex (% of patients)	
• Female	52.04 (716284)
• Male	47.90 (659249)
• Other	.06 (880)
Race (% of patients)	
• American Indian or Alaska Native	0.25 (3451)
• Asian	2.57 (35368)
• Black or African American	5.20 (71518)
• Native Hawaiian or Other Pacific Islander	0.12 (1687)
• White	77.33 (1064389)
• Multiple Race	2.05 (28189)
• Refuse to answer	1.75 (24155)
• Unknown	7.1 (98051)
• Other	3.06 (49605)
Hispanic (% of patients)	
• Yes	4.38 (60315)
• No	79.78 (1098090)
• Other	15.84 (218008)

Summary of UIowa participation in PCORnet-enabled Research:

The UIowa has been a collaborative and responsive partner in the GPC and PCORnet in Phase 1-3. Ulowa continues to refresh its CDM instance quarterly in conformance with PCORnet specifications and, since the COVID-19 pandemic, maintains a weekly whole-CDM refresh. We have been highly responsive to applicable Front Door Collaborator data requests, requests submitted to and approved by the GPC Data Request Oversite Committee (DROC) in support of feasibility analyses and research proposals, and data requests for prep to research and active research projects (N=377 total requests from 2018 onward). UIowa has participated aggressively in completed studies (e.g. ADAPTABLE, COVID CDC. FDA Sentinel Using PCORnet, NEXT-D) and is **participating in 12 currently active PCORnet® - Designated studies**: BACK-OFF JSpA, BASICS, cvMOBIUS2, HERO Registry & Trial, NET-PRO, ODYSSEY RCC, PRESERVE, PREVENTABLE, NEXT-D, RECOVER EHR (peds), Using PCORnet to Compare Blood Pressure Control Strategies, and most recently, we have joined CODA, PRECIDENTD, RESTORE, and Understanding the Short- and Long-term Effects of the COVID-19 Pandemic on the Opioid Overdose. We are **lead site on one active PCORnet-designated study** and one 2024 cycle 1 PCORnet-designated study submission in review and are a named collaborating site on 22 pending studies with Front Door study IDs.

Data: UIowa has access to data from nearly 2 million patients for research purposes (**Table 2**): 1) EPIC (the hospital electronic health record); 2) EPIC (the clinical and hospital billing system); 3) UIHC hospital tumor registry; 4) UI Bioshare

(biospecimen data – 520,798 samples from 52,067 subjects); 5) REDCap (selected projects including patient reported outcomes); 6) AXIUM (225,000 dental patients); 7) Social Security Death Index; and additionally 8) Medicare/Medicaid Claims in the GPC GROUSE environment. Our average query response time is 4.8 days and we are compliant with the top 30 lab groups and our 89% of RxNorm terms in prescribing records are Tier 1 terms. We are committed to implementing future CDM expansions. Over time we have between 2 and 4 exceptions that we address promptly.

Table 2. UI Health Care System Characteristics

Site Name	Medical Institutions(#)	Hospitals(#)	Physicians (#)	Primary Care Practices (#)	Emergency Departments(#)	Community Clinics (#)	Geographic Coverage: States)
UI Health Care	1	1	1403	11	1	43	Iowa, W. Illinois

UIowa PCORnet personnel have been highly engaged in **PCORnet Workgroups, Coordinating Center, and infrastructure innovations**:

- COVID CDM Research Workgroup (Ryan Carnahan); COVID Research Workgroup (Elizabeth Chrischilles); Workgroup to evaluate the PCORnet Coordinating Center (Brian Gryzlak); Innovations Workgroup (Ryan Carnahan); Query Fulfillment site in PCORnet Coordinating Center (Ryan Carnahan and Rhonda DeCook)
- Cancer Research leadership:
    - Dr. Bradley McDowell led PCORnet CDM TUMOR table development published in PCORnet iMeetCentral;
    - In Phase 2, UIowa co-led the 100-member Cancer Collaborative Research Group (CRG)(1) and also led a 3-CRN rapid cycle research initiative on Molecular Testing and Targeted Therapies. In Phase 3, the Iowa-led NET-PRO designated study and NCI-funded BASICS study are cancer studies enabled by this work.
    - UIowa cancer molecular epidemiologist, Dr. Michael O'Rorke, is the PI for an ongoing PCORnet Rare Disease proposal, "Neuroendocrine Tumors – Patient Reported Outcomes" (NET-PRO).
- In 2020, our site leveraged the PCORnet CDM to deliver data to the National COVID Cohort Collaborative (N3C). We continue weekly whole-CDM refreshes in support of RECOVER and to provide computable phenotype-based lists for pragmatic study recruitment across several studies.

Tools and methods development: UIowa is open in sharing tools, code and methods through the GPC TRAC wiki software. We are interested in contributing to user-centered design and usability methods for patient-facing tools. Designed with patients as partners, UIowa maintains a secure online system (Iowa Personal Health Record, Iowa PHR) for capturing patient-reported outcomes for pragmatic trials and prospective observational studies. Open-source code for the PHR has been made available on GitHub and an adaptation of the PHR to rare diseases is featured in the PCORnet NET-PRO project. We are part of the PCORnet Coordinating Center (Scope 2) where, in addition to developing queries, we have beta-tested all queries on our own CDM as a service to PCORnet.

UIowa PCORnet-enabled Research Publications and Presentations at National Meetings: Selected publications from UIowa-led studies include the *Share Thoughts on Breast Cancer Study* (the GPC Phase 1 common disease cohort characterization activity (1-4) and the ongoing Iowa-led NET-PRO study (5). Iowa site investigators have contributed also to methodology studies of PCORnet infrastructure including: the ability of PCORnet data resources to investigate molecular-guided cancer treatment (6), evaluating number of visits as a criterion for determining which patients have sufficient EHR information to be included in a study sample, and lessons learned in ADAPTABLE. UIowa investigators have made national presentations about molecular testing in PCORnet research at the PCORI annual meeting and the North American Association of Central Cancer Registries annual meeting, and about breast cancer patient-reported outcomes at the San Antonio Breast Cancer Symposium, the Society of Surgical Oncology and the American Society of Preventive Oncology. Presentations from NET-PRO have been featured nationally and internationally. As part of UIowa's role in the PCORnet Coordinating Center, Scope 2, we have contributed to researcher engagement in a national workshop for investigators.

CLINICAL RESEARCH NETWORK SITES

Summary of CRN Site Care Settings: University of Nebraska Medical Center (UNMC) represents an integrated partnership of the Nebraska Medicine (NM) Hospitals, Children's Nebraska (CN), each of their physicians and clinics, and UNMC College of Medicine. This closely integrated academic medical center creates synergies among our clinical, educational, research and community health missions. Close collaboration between the University and the community enables large scale joint investments such as the Fred & Pamela Buffett Cancer Center, a National Cancer Institute (NCI)-designated cancer center; the Davis Global Center for Health Security and the Great Plains IDeA Clinical and Translational Research Network (GPC-CTR), our regional IDeA-CTR program.

Although UNMC is the academic partner for both NM and CN, the two have independent clinical systems. NM provides primary through quaternary-level patient care to patients from Nebraska and surrounding regions. The NM provider network offers primary and specialty care in our rural counties. The UNMC campus supports 80 residency programs with over 700 house officers. In addition, through the NM Community Connect program, two rural health systems have opted to include their data in the PCORnet CDM:

- Mary Lanning Hospital, a 183-bed hospital and health system in Hastings, NE
- Great Plains Health, a 116-bed hospital with 72 clinical locations centered in North Platte, NE

NM contributes electronic health record (EHR) data on 1.2 million patients in UNMC's PCORnet CDM (Table 1).

All approvals have been obtained to include CN data in the UNMC PCORnet CDM. The technical build is underway and we anticipate data inclusion this calendar year. CN is the only freestanding full service pediatric specialty healthcare center in Nebraska and has a Level II Pediatric Trauma Center, PICU, a 40-bed Level IV NICU and operates a regional network of primary care clinics and urgent care centers. See Table 1 for CN patient counts. Historically, one-third of CN are also seen at NM. Therefore, we do not anticipate these counts to be entirely additive. However, we do anticipate more complete records for a substantial number of patients.

Table 1. Nebraska Medicine (NM) Site Population		**Children's Nebraska (CN) Site Population**	
Number of Unique Patients 1,219,844	*Total number of unique patients (% of patients)*	**Number of Unique Patients** 490,358	*Total number of unique patients (% of patients)*
Demographics		**Demographics**	
Age		Age	
Mean Age	*45.7*	Mean Age	*14.2*
0-19	*(15.8% of patients) 192,305*	0-19	*(75.2% of patients) 368,998*
20-44	*(35.0% of patients) 426,430*	20-44	*(23.4% of patients) 114,719*
45-64	*(23.2% of patients) 283,032*	45-64	*(1.0% of patients) 5,032*
65-74	*(12.3% of patients) 149,957*	65-74	*(0.2% of patients) 1,039*
Older than 75	*(13.8% of patients) 168,120*	Older than 75	*(0.1% of patients) 570*
Sex		Sex	
Female	*(53.1% of patients) 647,282*	Female	*(50.2% of patients) 245,922*
Male	*(46.8% of patients) 570,430*	Male	*(49.8% of patients) 244,219*
Other	*(0.2% of patients) 2,132*	Other	*(0.04% of patients) 217*
Race		Race	
American Indian or Alaska Native	*(0.6% of patients) 6,787*	American Indian or Alaska Native	*(0.8% of patients) 3,702*
Asian	*(2.0% of patients) 24,321*	Asian	*(2.5% of patients) 12,218*
Black or African American	*(6.9% of patients) 84,621*	Black or African American	*(7.0% of patients) 34,305*
Native Hawaiian or Other Pacific Islander	*(0.2% of patients) 2,658*	Native Hawaiian or Other Pacific Islander	*(0.1% of patients) 534*
White	*(71.8% of patients) 875,823*	White	*(63.6% of patients) 312,006*
Multiple Race	*(0.01% of patients) 92*	Multiple Race	*(7.1% of patients) 34,798*

Refuse to answer	*(0.2% of patients) 2,911*	Refuse to answer	
Unknown	*(11.7% of patients) 142,284*	Unknown	*(2.6% of patients) 12,521*
other	*(6.6% of patients) 80,347*	other	*(16.4% of patients) 80,274*
Hispanic			
Yes	*(8.1% of patients) 98,544*	Yes	*(13.9% of patients) 68,027*
No	*(79.8% of patients) 972,831*	No	*(76.9% of patients) 377,082*
Other	*(12.2% of patients) 148,469*	Other	*(9.2% of patients) 45,249*

Site Name	Medical Institutions (4)	Hospitals (5)	Physicians (2075)	Primary Care Practices (35)	Emergency Departments (6)	Community Clinics (131)	Geographic Coverage: State Name(S)
UNMC	Nebraska Medicine	2	1,400	16	3	70	NE, IA, KS, MO
	Children's Nebraska	1	500	15	1	32	NE, IA, KS, MO
	Mary Lanning	1	75	1	1	16	NE
	Great Plains Health	1	100	3	1	13	NE, KS, CO

Data: UNMC Data is derived from: 1) EHR data (EPIC) from hospital partners, 2) hospital cancer tumor registry, 3) Nebraska state vaccine registry, 4) mediation dispense records from Surescripts integrated into the EHR, 5) Social Security Death Index, 6) anatomic pathology data from Cerner CoPath, and 7) Community-level social determinants of health data from sources such as, but not limited to, the American Community Survey. UNMC continues to refine and expand its CDM instance in conformance with PCORnet specifications. Our data is 99.2% mapped to LOINC for quantitative lab results which fully specify the result unit. Our response rate to Front Door Collaboration queries is 100% complete and on time, with an average response time of 4.8 days, and 100% on-time approved data curations. UNMC's data latency is 2 weeks.

UNMC PCORnet Personnel have been highly engaged with PCORnet and GPC leadership and innovations leveraging GPC-wide distributed expertise and capabilities:

- UNMC supported development and participates in the GPC Rapid Community and Engagement (Rapid PACE) resource to support researchers' in including patients in research proposal development and review. For the past three years, we have hosted a local patient advisory that meets monthly to consult local researchers in planning and implementing research projects. In addition, Dr. Geary continues advancement of engagement [1, 2].
- Drs. Geary and Anzalone co-led incorporation of SDOH into the CDM to provide a privacy-preserving method for incorporating community-level SDOH in studies. Nebraska maintains the International Nebraska Lexicon, a regular release of the latest SNOMED CT and LOINC terminologies mapped to the PCORnet CDM and for use by EPIC Corporation sites to standardize EHR data. The Nebraska Lexicon includes standardized mappings for cancer and biomarker encoding increasing the richness of EHR data. Drs. Geary and Anzalone are also actively working to advance potential for rural entities to participate in pragmatic trials. UNMC routinely supports PCORnet query development and testing as an alpha or beta site.
- Dr. Geary co-chaired the national PCORnet Research Committee during the first 19 months of its activity. Caroline Hoedemaker served as the GPC Stakeholder Representative on the national Engagement Committee. Dr. Brandy Clarke serves as an SME on the national workgroup, A Roadmap for Accelerating Research to Improve Mental and Behavioral Health in PCORnet®.

Summary of CRN Site participation in PCORnet® Studies: UNMC has participated in multiple retrospective observational studies and pragmatic clinical trials. We are currently involved in retrospective observational studies including COVID-19 Electronic Health Data Initiative, RECOVER Post-Acute Sequelae of SARS-CoV-2 (PASC) Electronic Health Record (EHR) Cohort Study [3, 4] and Understanding the Short- and Long-term Effects of the COVID-19 Pandemic on the Overdose Crisis. Study participation includes PREVENTABLE and the now completed ADAPTABLE, among others [5,6]. We are the national leader for a multi-site implementation trial using the PCORnet CDM: BEST-ICU (Michele Balas, PI 4UH3HL165740-02). This study, in collaboration with 3 health centers, expands the CDM to include necessary ICU data.

PRINCIPAL INVESTIGATOR (MCCLAY, JAMES, C.):

CLINICAL RESEARCH NETWORK SITES

Summary of CRN Site Care Settings: Houston is the largest city in Texas with growth over 10% (2010-2019) and some areas of Houston (e.g., Sugar Land) with growth over 50%. Houston is the **fourth largest and most ethnically diverse city** in the US. Unfortunately, Houston (Harris county) was also **an epicenter for the COVID-19 pandemic** with 359,948 confirmed cases (as of 3/10/21, 6th most cases of any US county, data no longer tracked). Houston's Texas Medical Center (TMC) has 49 member institutions that collectively support over 120,000 employees, 9200 hospital beds, and manage over 10M patient encounters per year. Thus, we have a **large and diverse population**. In addition to ethnic diversity, because there are no zoning laws and due to extreme variation in income and health care access and coverage there are very wide ranges of environmental exposures and variations in behaviors and deprivation that contribute to disease risk and severity.

The University of Texas Health Science Center at Houston (UTH) has a large and rapidly growing network of outpatient clinics across a range of specialties. In addition, clinical activities include two local hospital networks: 1) Memorial Hermann Hospital System (MHHS), a non-profit hospital system with 6,600 affiliated physicians, 33,000 employees and 260 care delivery sites. 2) Harris Health System is a county-funded safety-net health care provider with a population that is over 80% underserved minority; primarily Black and Hispanic patients.

Table 1. University of Texas Health Science Center at Houston Site Population	
Number of Unique Patients	*4,112,034 (100%)*
Demographics	
Age	
• Mean Age	*44.12*
• 0-19	*770,887 (18.78%)*
• 20-44	*1,376,831 (33.53%)*
• 45-64	*1,037,457 (25.27%)*
• 65-74	*470,410 (11.46%)*
• Older than 75	*450,226 (10.97%)*
Sex	
• Female	*2,280,932 (55.47%)*
• Male	*1,823,884 (44.35%)*
• Other	*7,218 (0.17%)*
Race	
• American Indian or Alaska Native	*11,981 (0.29%)*
• Asian	*88,640 (2.16%)*
• Black or African American	*692,372 (16.84%)*
• Native Hawaiian or Other Pacific Islander	*2 (0%)*
• White	*1,310,838 (31.88%)*
• Multiple Race	*0 (0%)*
• Refuse to answer	*85,392 (0.49%)*
• Unknown	*296,114 (7.20%)*
• other	*1,606,628 (39.07%)*
Hispanic	
• Yes	*680,802 (16.56%)*
• No	*3,184,410 (77.44%)*
• Other	*246,822 (6%)*

UTH provides primary, tertiary and quaternary-level patient care to Houston and the surrounding region and is a national leader in biomedical research. For the GPC partnership, UTH represents 5 hospitals, over 60 clinic sites and over

6 million patients with administrative data (e.g., demographics, billing codes, insurance status), over 3.5 million patients with EHR (clinical) data. The UTH is a CTSA site.

Site Name	Medical Institutions (#)	Hospitals (#)	Physicians (#)	Primary Care Practices (#)	Emergency Departments (#)	Community Clinics (#)	Geographic Coverage: State Name(S)
UT-Houston	*2*	*5*	*2600*	*14*	*1*	*100*	*Texas*

Summary of CRN Site participation in PCORnet-enabled Research:
UTH is relatively new to GPC but has been a member of PCORNet since the beginning of the program. Our site was a founding member of PCORNet Clinical Data Research Network called ARCH (previously Shared Collaborative Infrastructure for a Learning Healthcare System, SCILHS) with Harvard as the lead site.

UTH has greatly improved its EDC results during its Phase III participation in GPC. While UTH's most recent EDC report did show a total of 9 investigative data check exceptions, that is an all-time low. Over the past 2 years, hard work has decreased this tally from a high of 23 investigative data check exceptions. Among others, Houston has resolved an RXNorm mapping issue, problems with records appearing in incorrect tables, and issues with extreme measurements. The remaining checks include one for a single lab test with an extreme median value, which will be depreciated according to DRNOC, and one for a single month (May 2021) with unusual record volumes, which is due to an EHR transition (i.e., the data check has been investigated and was determined to reflect source data, likely due to the transition from an Allscripts to Epic EHR in May 2021; thus, this check cannot and should not be "resolved" by changing the data). In short, 7 data checks remain to be addressed. Continued work from the Houston team should be able to resolve the remaining issues and further reduce the number of investigative data check exceptions.

As far as deadlines and incompleteness on both Cycle Refreshes and Front Door queries, issues present at the beginning have improved, not only the data but the process. Infrastructure issues have since been resolved, and moving forward, checks are in place to ensure prompt responses to alleviate delays or inconsistencies in returned data.

Tools and methods development: UTH is open in sharing tools, code and methods through the GPC TRAC wiki software. In support of expanding use of natural language processing (NLP) for a variety of purposes including improved phenotyping for cohort discovery.

Data: UTH has access to data from over 4 million patients for research purposes: 1) Allscripts transitioned to EPIC in May 2021 (outpatient EHR); 3) axiUm (>467,000 dental patients); 4) REDCap (selected projects including patient reported outcomes); 5) Cerner (MHHS >870,000 patients tested for COVID); and additionally 6) Medicare/Medicaid Claims in the GPC GROUSE environment. We are committed to implementing future CDM expansions. These data are updated nightly.

Summary of CRN Site participation in PCORnet® Studies:
In addition to participating in network activities including previous CDRNs described above, during Phase 3 the UT Houston site supported (and continues to support) the Pragmatic evaluation of events and benefits of lipid lowering in older adults (PREVENTABLE) trial that has recruited 75 subjects at our site (including four subjects in Brownsville in South Texas that was approved as another location for our site) as of May 2024.

CLINICAL RESEARCH NETWORK SITES

Table 1. University of Texas Southwestern (UTSW) Site Population	
Number of Unique Patients 5,138,125	*Total number of unique patients (% of patients)*
Demographics	
Age	
● Mean Age	*40*
● 0-19	*1317843 (26%)*
● 20-44	*1668792 (32%)*
● 45-64	*1214985 (24%)*
● 65-74	*490599 (10%)*
● Older than 75	*437419 (8%)*
Sex	
● Female	*2741178 (53%)*
● Male	*2350318 (46%)*
● Other	*46629 (1%)*
Race	
● American Indian or Alaska Native	*11925 (0.23%)*
● Asian	*187026 (3.64%)*
● Black or African American	*652019 (12.69%)*
● Native Hawaiian or Other Pacific Islander	*7167 (0.14)*
● White	*2370517 (46.14%)*
● Multiple Race	*unknown*
● Refuse to answer	*unknown*
● Unknown	*876082 (17.05%)*
● other	*1022243 (19.90%)*
● No Information	*11146 (0.22%)*
Hispanic	
● Yes	*1288311 (25%)*
● No	*2153210 (42%)*
● Unknown	*1269596 (25%)*
● No information	*427008 (8%)*

Summary of CRN Site Care Settings: UTSW contributes clinical data from our healthcare system which includes two University Hospitals (William P. Clements Jr. University Hospital and Zale Lipshy Pavilion) and 55 clinics which provide care to >120,000 hospitalized patients, nearly 370,000 ER visits, and ~5 million outpatient visits each year. Together these facilities include hospitals, ambulatory surgery centers, hospital-based clinics, physician-based clinics, virtual clinics, and stand-alone diagnostic imaging centers. They provide care in ~80 specialties, including specialty areas in which we have invested heavily to establish large enterprises advancing clinical and translational research alongside patient care, such as the Harold C. Simmons Comprehensive Cancer Center and the Peter O'Donnell Jr. Brain Institute.

UTSW implemented the Epic Electronic Health Record system in 2001, and it is used across all these care settings. In addition, we contribute billing data from Parkland Health and Hospital System and Children's Health, which are staffed by UTSW physicians. Our clinical data warehouse established for research purposes currently contains data from ~9.7 million patients with clinical and demographic data, ~206.6 million clinical encounters, and ~373.7 million clinical procedures. These data form the basis of the data warehouse we established for our participation in the GPC utilizing the PCORnet Common Data Model. The PCORnet CDM, which includes data on all patients with at least one encounter since 2010, contributes data for >5,000,000 patients from a diverse population that is 27% non-White among those reporting a race and 25% Hispanic (Table 1).

Site Name	Medical Institutions (#)	Hospitals (#)	Physicians (#)	Primary Care Practices (#)	Emergency Departments (#)	Community Clinics (#)	Geographic Coverage: State Name(S)
UTSW	*1*	*2*	*3,259*	*12*	*1*	*43*	*Texas*

PRINCIPAL INVESTIGATOR (MCCLAY, JAMES, C.):

Summary of CRN Site participation in PCORnet® Studies: UTSW is a very active member of the Greater Plains Collaborative. We refresh our CDM instance quarterly in compliance with PCORnet specifications and refresh study-specific tables more frequently, as needed (e.g., for the CDC COVID-19 project). We have been highly responsive to Front Door Collaborator data requests and network-level requests submitted to and approved by the GPC Data Request Oversight Committee (DROC), responding to 143 and 26, respectively, during the Phase 3 period (January, 2021, through April, 2024). In addition to responding to data requests, we have participated in a large number of studies, including demonstration studies and studies that involve patient recruitment. Some of the studies we have participated in include the GPC breast cancer, ALS, and childhood obesity demonstration projects and the ADAPTABLE, PREVENTABLE, Natural Experiments in Diabetes Translation (NEXT-D), Bariatric, GPC Acute Kidney Injury, Burden of Imaging of Renal Cysts, cvMOBIUS, COVID-19 Electronic Health Data Initiative, RECOVER, and NET-PRO studies. We also participated in the HERO registry and trial. We have initiated several studies from UTSW, including most recently the submission of "**P**olypill for imp**r**oving **A**dheren**C**e **T**o card**I**oprote**C**tive therapies in Heart Failure: PRACTICE-HF" in January 2024. We look forward to initiating more studies in Phase 4.

From January 2021 through April 2024, we had 8 data checks on the last refresh. We mapped the appropriate Tier 1, preferred RX Norm CUI codes as specified in the CDM Implementation Guidance and met the 80% RX norm data check at 94%. We met the LOINC data check of 94 % mapped to known LONIC codes. We had less than a 5 percent decrease in the number of patients and records in the CDM table between refreshes and are usually good on this data check, however, we did have an issue with a large number of records falling off due to a change in data flows/workflow, but that has now fallen out of the 5-year window and didn't show up on the last refresh. Quarterly refreshes with a less than 90-day data latency-only dispensing, which comes from Surescripts, shows up with latency. It's a known issue across all sites that use Surescripts. We have responded to virtually all front-door queries and will continue to do so.

UTSW personnel have been highly engaged at both the GPC and PCORnet levels and are committed to even more engagement in Phase 4. Notable examples include:

- Dr. Cowell (site PI) is the GPC representative on the PCORnet CDC COVID-19 Scientific Advisory Group and on the RECOVER Steering Committee.
- Dr. Cowell has participated in manuscript writing for multiple studies, including the Bariatric, NEXT-D, Renal Cyst, RECOVER, CDC COVID-19, and NET-PRO studies.
- Mr. Reeder (technical lead) contributed to the development of the terminology structures for incorporating medications, labs, and many other data types into the GPC i2b2 data warehouse. The UTSW PCORnet team has participated in testing, evaluating, and providing feedback for multiple new terminologies, including the document ontology, and we have shared tools, code, and/or methods with our GPC collaborators.
- We have set up FHIR infrastructure for real-time integration of computable phenotypes with Epic and we have integrated REDCap and Epic via FHIR.
- Mr. Reeder made early contributions to standardization efforts for incorporating notes into the GPC i2b2 data warehouse. We have implemented de-identification of notes with TiDE for RECOVER. Additionally, we have explored NLP on notes. Incorporation of notes and/or data extracted from notes is an area we are excited to contribute to in Phase 4.
- We have patient-reported outcomes (PRO) questions, including PROMIS, incorporated into Epic and have the capability to integrate these into the CDM for future studies.
- We have integrated genomic data, including germline and tumor, on the clinical side and are excited to pursue extending that to the research side under Phase 4.

PRINCIPAL INVESTIGATOR (MCCLAY, JAMES, C.):

CLINICAL RESEARCH NETWORK SITES

Table 1. Clinical Research Network (CRN) Site Population - UofUtah	
Number of Unique Patients: 1,682,863	*Total number of unique patients (% of patients)*
Demographics	
Age	
• Mean Age	*42.6569*
• 0-19	*17.34%*
• 20-44	*38.96%*
• 45-64	*22.85%*
• 65-74	*10.4% (10.397%)*
• Older than 75	*10.45% (10.445%)*
Sex	
• Female	*51.9% (51.895%)*
• Male	*48.08% (48.079%)*
• Other	*00.03% (00.025%)*
Race	
• American Indian or Alaska Native	*00.9% (00.898%)*
• Asian	*2.73% (02.726%)*
• Black or African American	*2.02%*
• Native Hawaiian or Other Pacific Islander	*0.71% (00.709%)*
• White	*68.3%*
• Multiple Race	*0%*
• Refuse to answer	*0%*
• Unknown	*4% (3.9868%)*
• other	*16.97%*
Hispanic	
• Yes	*12.46%*
• No	*68.94% (68.9376%)*
• Other	*2.73% (2.72785%)*

Site Name	**Medical Institutions (#)**	**Hospitals (#)**	**Physicians (#)**	**Primary Care Practices (#)**	**Emergency Departments (#)**	**Community Clinis (#)**	**Geographic Coverage: State Name(S)**
University of Utah	*1*	*5*	*3,200*	*12*	*2*	*12*	*Idaho, Montana, Wyoming, Utah, Colorado, Nevada*

PRINCIPAL INVESTIGATOR (MCCLAY, JAMES, C.):

Summary of CRN Site Care Settings: *Describe the care setting(s) for the CRN participating site (e.g., hospital, federally qualified health center, community practice, care facility) and complete the below table.* University of Utah Health (U of U Health) is the Intermountain West's only academic health care system, combining excellence in patient care with the latest in medical research and teaching. For 10 consecutive years, Vizient Inc., has ranked U of U Health in the nation's top 10 for quality health care among leading academic medical centers. U of U Health includes five hospitals: University of Utah Hospital, Huntsman Cancer Institute, University Orthopedic Center, Huntsman Mental Health Institute, and the Craig H. Neilsen Rehabilitation Hospital; 12 community clinics; and several specialty centers including the John A. Moran Eye Center, the Cardiovascular Center, the Clinical Neurosciences Center, and the Utah Diabetes Center. Collectively, U of U Health has 748 inpatient beds and provides care for 1.2 million Utahns and residents of five surrounding states in a referral area encompassing more than 10% of the continental United States. U of U Health is staffed by over 1,700 board-certified physicians representing 200 medical specialties and over 650 subspecialties, with over 5,000 practicing clinicians staffing hospitals and clinics. U of U Health is also one of the largest providers of ambulatory services in Utah, with connections to more than 50 general and specialty outpatient clinics and logging 2 million patient visits per year. As part of an academic health care system, U of U Health leverages its ties to the U of U Health Schools of Medicine and Dentistry, and Colleges of Nursing, Pharmacy, and Health, to advance translational research projects to transform patient care.

Summary of CRN Site participation in PCORnet® Studies: ***Describe the CRN participating site's prior participation in PCORnet® Studies.*** The University of Utah has participated in PCORnet since 2015 and has responded to over 150 queries, partnered on 10 pragmatic clinical studies, and 6 randomized controlled trials. U of U has been a high enrolling site in the PCORnet ADAPTABLE, INVESTED, and PROVIDE-HF trials and is participating in NET-PRO and thus has intimate knowledge of pragmatic recruitment and enrollment approaches and tools. We partnered with Intermountain Healthcare and the Utah Department of Health on a PCORnet surveillance pilot project – Using PCORnet for Comprehensive Hypertension Surveillance during 2018-19. The University of Utah led a local pilot initiative in 2019 to engage junior investigators in PCORnet and Greater Plains Collaborative data. The U of U maintained an up-to-date Common Data Model instance during both Phase 1, 2, and Phase 3 of PCORnet, including making COVID-related enhancements in 2020. We have received institutional and IRB approval for the implementation of the PCORnet Datavant initiative. The University of Utah site received 90% or more of the phase 3 data curation approved by the deadline with fewer than eight data check exceptions. The site has at least 80% of medications by frequency to appropriate Tier 1 Preferred RxNorm CUI codes mapped in the CDM (specified in the CDM Guidance). In terms of mapping the top 80% of labs to LOINC (by frequency), The University's current EDC indicates levels of 77% (all years) and 78% (most recent 5 years) have been mapped. This is one of only three exceptions evidenced in the University of Utah's most recent refreshes. The team has prioritized this benchmark and will resolve the issue by the subsequent curation cycle. There was no less than a 5 percent decrease in the number of patients and records within a CDM table in the Cycle 15 refresh. All refreshes have data within 90 days. The site refreshes its local development CDM every Tuesday and Friday with new data from the EMR.

CLINICAL RESEARCH NETWORK SITES

Table 1.Washington University and BJC HealthCare Site Population	
Number of Unique Patients	*5,500,133*
Demographics	
Age	
• Mean Age	*49*
• 0-19	*848,923 (15.6%)*
• 20-44	*1,644,731 (30.2%)*
• 45-64	*1,292,515 (23.7%)*
• 65-74	*701,174 (12.9%)*
• Older than 75	*966,952 (17.7%)*
Sex	
• Female	*2,881,753 (52.4%)*
• Male	*2,590,594 (47.1%)*
• Other	*27,586 (0.5%)*
Race	
• American Indian or Alaska Native	*8,100 (0.2%)*
• Asian	*70,343 (1.3%)*
• Black or African American	*808,712 (14.7%)*
• Native Hawaiian or Other Pacific Islander	*7,429 (0.1%)*
• White	*3,409,604 (62.0%)*
• Multiple Race	*48 (0.0%)*
• Refuse to answer	*13,141 (0.2%)*
• Unknown	*953,877 (17.3%)*
• other	*228,788 (4.2%)*
Hispanic	
• Yes	*63,206 (1.2%)*
• No	*2,480,815 (45.1%)*
• Other	*2,956,112 (53.7%)*

Summary of CRN Site Care Settings: We are a network of hospitals and clinics across Washington University in St. Louis (WashU) and BJC HealthCare, located throughout Missouri and Illinois. This includes the combined academic health center, which includes Barnes-Jewish Hospital, St. Louis Children's Hospital, and Washington University Physicians (WUP). WUP are members of the medical school's full-time faculty and ranks as one of the largest academic clinical practice groups in the nation, with 1,593 physicians who represent 76 specialties and subspecialties. BJC HealthCare is one of the largest nonprofit health care organizations in the United States and is focused on delivering services to residents primarily in the greater St. Louis, southern Illinois and mid-Missouri regions. In addition to academic facilities, there are 12 other community hospitals as well as BJC's outpatient community practice, the BJC Medical Group. Services include inpatient and outpatient care, primary care, community health and wellness, workplace health, home health, community mental health, rehabilitation, long-term care and hospice. For the GPC Partnership, WashU represents WUP, all hospitals of BJC HealthCare, and the BJC Medical Group, with 7,325,065 distinct patients. Of those, 5,550,133 meet inclusion criteria. WashU/BJC is both a CTSA hub and is an NCI Designated Cancer Center.

PRINCIPAL INVESTIGATOR (MCCLAY, JAMES, C.):

Site Name	Medical Institutions (#)	Hospitals (#)	Physicians (#)	Primary Care Practices (#)	Emergency Departments (#)	Community Clinics (#)	Geographic Coverage: State Name(S)
WashU/BJC	*15*	*14*	*6500*	*7*	*14*	*0*	*MO, IL*

Summary of CRN Site participation in PCORnet-enabled Research:
Washington University in St. Louis and BJC HealthCare has participated in all previous phases of PCORnet, previously participating in the SCILHS and PEDSnet CDRNs, and currently in the GPC. Site co-investigator, Joyce Balls-Berry, currently serves as GPC's lead engagement officer. We have a strong history of PCORnet participation, with on time data curation approvals, being highly responsive to Front Door Collaborator data requests and network-level requests. We have consistently strived for more comprehensive and continuously improving the data quality of our submissions. Recently, as part of our efforts to improve the comprehensiveness and quality of our data, we made some changes to our ETL that resulted in 9 investigative checks in our most recent refresh. This was due to populating the MED_ADMIN table and the splitting of telehealth (TH) visits away from being classified as ambulatory visits (AV). With these changes, some new medications without proper dosing information and encounters without diagnoses are now found in our CDM. We anticipate being able to reduce our investigative checks in the Cycle 16 first refresh (July 2024) down to 6 and will continue to diligently improve our data quality. Specifically, we will be able to address DC 2.01, DC 2.06, and DC 3.01 by 1) Setting source-system future outpatient prescription end dates to OHDSI-consortium recommended values, 2) locally correcting incorrectly-coded LOINC code mappings from source systems, and 3) adding diagnosis information for TH encounters.
We have a strong history of being engaged in studies. Notable examples include the following:

- We received an award to participate in the PRESERVE study (on preserving kidney function in children with chronic kidney disease), locally led by Dr. Vikas Dharnidharka who also leads a new multi-network NIH R01 CISTEM2[1] that is a newly designated PCORnet Study
- We participated in the COVID-19 Electronic Health Data Initiative as well as COVID-19 research, leading to several publications, including JAMA Pediatrics
- We have participated in the PREVENTABLE study (on helping older adults live well for longer by preventing dementia, disability, or heart disease)

Tools and methods development: Washington University in St. Louis has been heavily involved in sharing tools and code to support the PCORnet network. Previously, in our participation in the SCILHS network, which had an i2b2 backbone, our team was able to contribute PostgreSQL-specific code some of which is now also part of the mainstream i2b2 metadata scripts. In addition, we did a lot of the PostgreSQL-specific application and ETL and metadata code testing and identified and resolved many bugs, as we were among the first few sites to implement i2b2 on PostgreSQL.

Data: The Institute for Informatics, Data Science, and Biostatistics at Washington University in St. Louis operates the Washington University School of Medicine (WUSM) Data Lake, which serves as the single source of truth for WUSM and contains over 5500 data tables from over 40 sources. The data lake supports all WUSM data domains, including clinical operations, education, research, finance, and administration. The data lake is built on top of Azure Databricks, which supplies a fully modern and scalable architecture. A component within the data lake is the Research Data Core (RDC), upon which the GPC infrastructure will be deployed, and provides access to clinical data to researchers at WU/BJC HealthCare. The RDC is an OMOP-based comprehensive research data warehouse that is fed by enterprise-wide clinical information systems and optimized for secondary use purposes. The RDC includes data from various EHR domains, including, but not limited to demographics, visits, lab tests, medication orders, vitals, documents, illicit drug use, current census, and allergies. These electronic clinical data date back to 1992, collected during inpatient and outpatient clinical visits under the umbrella of the Washington University Physicians and BJC HealthCare.