2017 ANNUAL REPORT OF HHS PROJECTS TO BUILD DATA CAPACITY FOR PATIENT-CENTERED OUTCOMES RESEARCH

Office of the Secretary's Patient-Centered Outcomes Research Trust Fund (OS-PCORTF) Portfolio Report

Office of Health Policy
Assistant Secretary for Planning and Evaluation
U.S. Department of Health and Human Services

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Executive Summary

The Office of the Assistant Secretary for Planning and Evaluation (ASPE) is responsible for administering the Office of the Secretary Patient-Centered Outcomes Research Trust Fund (OS-PCORTF) to fund Department of Health and Human Services (HHS) projects that help to strengthen national data capacity and infrastructure for the conduct of patient-centered outcomes research (PCOR).

The projects that make up the OS-PCORTF portfolio span a diverse set of topics that include data standardization at the point of care; improving the utility of disease registries and public health surveillance systems; empowering patients with improved access to health data and the ability to direct it towards research; and leveraging national standards to develop new applications to link data systems.

Investments in PCOR data infrastructure are informed by a strategic framework, which was developed in consultation with HHS agency representatives. The strategic framework describes five research functionalities critical to realizing a sustainable interoperable data network to collect, link, and analyze data on outcomes and effectiveness from multiple sources.[i] Each funded project focuses on research that advances at least one of the core research functionalities critical to a robust PCOR data infrastructure, with many projects spanning multiple functionalities. A 2017 formative evaluation of the OS-PCORTF portfolio, Building Data Capacity for Patient-Centered Outcomes Research in HHS: A Formative Evaluation of 2012-2016 Projects, reported significant progress across all five functionalities.[ii]

The five core research functionalities are:

- Collection of Participant-Provided Information
- Standardized Collection of Standardized Clinical Data
- Linking of Clinical and Other Data for Research
- Use of Clinical Data for Research
- Use of Enhanced Publicly-Funded Data Systems for Research

In this Annual Report, we provide project descriptions for each of the OS-PCORTF portfolio's 21 projects that were active in calendar year 2017. Each project description provides an overview of the **project goals and objectives**, highlights major **project accomplishments**, describes **dissemination activities** intended to raise awareness of the project's work to the larger PCOR community, summarizes the core **research functionalities** the project addresses, identified **potential applications** of the project products, and illustrates **interagency collaborations** that seek to leverage project products and lessons learned. The project work performed in the past year contributes in a substantial way to HHS' activities to build data capacity for PCOR.

I. Introduction

The goal of the Office of the Secretary Patient-Centered Outcomes Research Trust Fund (OS-PCORTF) is to strengthen national data capacity and infrastructure for patient-centered outcomes research (PCOR) in order to advance a patient-centered health care system that is characterized by evidence-based care and integrated decision-making between providers, patients, and caregivers.

This Portfolio Report provides a synopsis of the 21 OS-PCORTF projects active in calendar year 2017. These 21 projects, many of which are cross-agency project collaborations, represent 34 individual project awards. The report details project goals, objectives, major accomplishments, draws connections between the projects and potential contributions to Department of Health and Human Services (HHS) initiatives (e.g., the *All of Us* Research Program) and relevant laws and initiatives (e.g., 21st Century Cures). It also illustrates how the projects contribute to the five core PCOR data research functionalities, identifies opportunities to leverage project products amongst OS-PCORTF awardees, and highlights cross-agency collaborations across HHS more broadly.

The products being developed within the OS-PCORTF portfolio encompass standards, tools, services, and resources to support PCOR. These products are in various stages of maturity—ranging from those in the planning stages to fully developed products available for implementation in real-world research settings. As such, the Portfolio Report is a key resource for monitoring ongoing progress and identifying future PCOR data infrastructure needs.

II. Background and Context

HHS agencies routinely collect, link, and analyze data that can be used to generate new scientific evidence that further expands knowledge about the outcomes and effectiveness of health care treatments and interventions. The OS-PCORTF was created to help build and enable national data capacity and infrastructure that successfully leverages federal data for the conduct of PCOR. These goals and data infrastructure investments support the mission, statutory authorities, and annual priorities of each HHS agency and the Department as a whole.

The Office of the Secretary (OS) of HHS delegated authority to the Office of the Assistant Secretary for Planning and Evaluation (ASPE) to coordinate and invest OS-PCORTF funds to build data capacity for PCOR. Specifically, the Secretary is charged, through OS-PCORTF funding, to:

> … provide for the coordination of relevant Federal health programs to build data capacity for comparative clinical effectiveness research, including the development and use of clinical registries and health outcomes research networks, in order to develop and maintain a comprehensive, interoperable data network to collect, link, and analyze data on outcomes and effectiveness from multiple sources including electronic health records.[iii]

In keeping with this charge, since 2011, ASPE has supported a large portfolio of HHS agency projects that are designed to build data capacity for research on patient outcomes. A common cross-agency interest in a robust data infrastructure for patient-centered research brings together the expertise of HHS agency leaders, informaticians, technologists, and researchers to solve data governance, policy, and technical challenges and achieve the goals described for PCOR. The topics of these projects simultaneously respond to the Secretary's priorities, major federal initiatives, and HHS agency priorities.

Supporting Data Infrastructure for Patient-Centered Care

Investments in PCOR data infrastructure are informed by a strategic framework, which was developed in consultation with HHS agency representatives. The strategic framework describes five research functionalities critical to realizing a ***sustainable interoperable data network to collect, link, and analyze data on outcomes and effectiveness from multiple sources***.[iv]

These functionalities are:

- **Standardized Collection of Standardized Clinical Data.** Supports the use of common data elements to enable more effective and efficient linking and aggregation across data sources.
- **Collection of Participant-Provided Information.** New data collection technologies, facilitate the collection of patient-generated information critical to PCOR.
- **Linking of Clinical and Other Data for Research.** Allows researchers to collect longitudinal patient information and to link data sets with other relevant information for research.
- **Use of Clinical Data for Research.** There are multiple sources of clinical data available for research (e.g., electronic health records (EHRs), patient portals, registries); work in this area is focused on improving access and interoperability of clinical data for query and analysis.
- **Use of Enhanced Publicly Funded Data Systems for Research.** Focuses on efforts to leverage current investments in infrastructure to inform future infrastructure development.

OS-PCORTF Evaluation

Collectively, investments in these functionalities have begun to lay the foundation for data capacity and an infrastructure that can be leveraged for patient-centered research by users across the Federal government and PCOR data networks (e.g., PCORnet, Sentinel, and *All of Us* Research Program). To assess the progress of the OS-PCORTF portfolio in building data capacity, ASPE initiated a formative evaluation of the active or completed projects between 2012 and 2016.

The evaluation addressed three overarching research questions:[v]

- What contributions has the OS-PCORTF portfolio of projects made to strengthening standards, services, policies, and governance needed to effectively conduct PCOR?
- To what extent has the OS-PCORTF portfolio of projects enabled the five functionalities to improve data capacity?
- Is ASPE's strategic framework sufficiently comprehensive to build clinical data capacity for PCOR and advance researchers' ability to capture, store, access, link, exchange, and analyze data securely and efficiently?

The evaluation, which was completed in 2017, found that progress has been made in each of the five functionalities for data capacity with the most significant gains in the standardized collection of standardized clinical data. The evaluation findings also indicated several strategic areas within each research functionality that would benefit from OS-PCORTF investment—data quality, standards implementation, data linkages, governance, privacy and security, and the collection of patient-generated health data (PGHD). In partnership with HHS agencies, ASPE continues to address these gaps areas with the pursuit of new projects to achieve the ultimate goal of building an interoperable, sustainable infrastructure for PCOR.

Leveraging OS-PCORTF Project Products for HHS Policy Initiatives

As it focuses on core data infrastructure functionalities for PCOR, ASPE is actively pursuing opportunities to align its portfolio with key HHS priorities and initiatives. One such example is the *All of Us* Research Program, described in detail below, for which a robust data infrastructure is essential. In this Annual Report, we highlight the potential for OS-PCORTF products to support five specific HHS initiatives: 1) the opioid crisis, 2) the *All of Us* Research Program, 3) the 21st Century Cures Act, 4) value-based purchasing (VBP), and 5) the Commission on Evidence-Based Policy Making Recommendations.

We begin by providing a synopsis of these key HHS initiatives and how their data infrastructure needs can be met by the OS-PCORTF (Exhibit 1).

Exhibit 1. Federal Priorities and Initiatives and Relevance to PCOR Data Infrastructure

Federal Initiatives	PCOR Data Infrastructure Needs
Opioids	The opioid epidemic is widely acknowledged as a public health crisis, requiring action by agencies across the government.[vi] One strategy is to address opioid over-prescription by clinicians, misuse by patients, and support patient treatment and recovery, which involves providing stakeholders with accurate timely, and actionable information on how to decrease overdoses by using clinical, pharmaceutical, and mortality data. [vii] This aim underscores the utility of multiple data infrastructure innovations: faster and more complete data access and linkages between data sources to facilitate opioid-targeted PCOR.
***All of Us* Research Program**	The NIH *All of Us* Research Program is an historic effort to gather longitudinal data from one million people in the U.S. to accelerate health care innovations. The program will rely on patients to donate various forms of data, which must be supported by patient consent protocols, data infrastructure, and the governance structure to support privacy and security of these sensitive data. Given the program's intent to collect and analyze genetic variables, the program will benefit from data standards for genomic data. The richness and robustness of the collected data will be dependent upon the successful linking of diverse data sets to clinical data. Finally, the program will need a sustainable architecture that allows researchers to access data from a cloud-based environment.[viii]
21st Century Cures Act	The 21st Century Cures Act (the "Cures Act") focuses on enhancing access to clinical data to efficiently conduct outcomes research, with emphasis on harnessing data from diverse "real world" sources. The Cures Act calls for HHS agencies to support and enhance data sharing, especially with NIH, a goal for which multiple OS-PCORTF projects can be leveraged. Central to this charge is improving data interoperability and promoting data access and exchange through application programming interfaces (APIs).[ix] Further, it prioritizes increasing the privacy and security of patient-mediated data exchange and data donation, and enhancing patient access to protected health information.

Federal Initiatives	PCOR Data Infrastructure Needs
Value-Based Purchasing	VBP programs reward health care providers with incentive payments for quality and safety improvements in patient-centric care. Data reporting on key quality measures is central to these programs. To this end, VBP programs will require linking of data across the care continuum, data aggregation within individual health care systems, as well as the incorporation of patient-reported outcomes (PROs) into clinical data. VBP programs will need to rely on high quality EHR data, including structured data elements, to ensure accurate reporting of provider performance on quality measures and other indicators. In order to use EHR data for actionable clinical insights and decision making, health systems will need to improve interoperability of their clinical data systems to facilitate data sharing and analysis.
Commission on Evidence-Based Policy Making Recommendations	The Commission on Evidence-Based Policy Making (the Commission) was established to develop a strategy for increasing the availability and use of data in order to support evidence-based policy making in government programs.[x,xi] The Commission's recommendations have cross-cutting relevance to the OS-PCORTF portfolio's goal to build data capacity for PCOR. For example, a series of recommendations pertain to providing the data infrastructure for secure, private, and confidential access to data (e.g., rigorous privacy protections for linking Federal data assets, mechanisms to facilitate external researchers' access to data). The report also emphasizes the need for robust privacy protections for patient data, in terms of policy, governance, and infrastructure, all of which the OS-PCORTF project work informs.

Active OS-PCORTF Funded Projects

The goal of this report is to describe the OS-PCORTF projects active in the past calendar year (2017). Exhibit 2 tabulates the number of active awards for the 21 projects by their first Fiscal Year of funding.

Exhibit 2. OS-PCORTF Active Project Awards by their Fiscal Year of Funding

Federal Fiscal Funding Year	Number of Funded Project Awards
FY 2017	16
FY 2016	8
FY 2015	8
FY 2014	1
FY 2013	1
Total Active Awards in 2017	34

Note: For a complete list of active and closed projects reference Appendix A.

Below, we summarize each project's goals and objectives, highlight project accomplishments, draw connections between the projects and potential contributions to the HHS initiatives described above, illustrate how the projects contribute to the PCOR data research functionalities, identify opportunities to leverage project products amongst OS-PCORTF awardees, and underscore cross-agency collaborations.

The summaries that follow were constructed based on a review of the project statements of work, quarterly progress reports submitted by the awardees to ASPE, calls between project officer and awardees, submitted deliverables, and information publicly posted to HHS agency websites.

The projects are organized by the Federal agency responsible for administering the project. A number of projects are collaborations between one, or multiple, HHS agencies. Jointly funded projects are summarized collectively in the penultimate section of this report, "Cross-Agency Projects." This structure highlights the breadth of Federal partners involved and the applicability of building PCOR data capacity to each agency's core mission, as well as to the shared goals of improving research, quality, and patient outcomes through PCOR and the learning health system.

Exhibit 3 provides a brief summary of the 21 active projects described in this Annual Report,

Exhibit 3. OS-PCORTF 21 Active Projects

Active Project	Project Description
Advancing the Collection and Use of Patient-Reported Outcomes through Health Information Technology*	▪ Develop technical tools for collecting and integrating PRO assessments into EHRs or other health information technology products.
Collection of Patient-Provided Information through a Mobile Device Application for Use in Comparative Effectiveness and Drug Safety Research	▪ Create the infrastructure for collecting data from patients through a mobile device application, allowing patient-generated data to be linked with a single data partner that participates in the Food and Drug Administration's Sentinel distributed network. The project will develop and pilot a mobile application to capture data from pregnant women who volunteer to participate.
Conceptualization of a Data Infrastructure for the Capture and Use of Patient-Generated Health Data	▪ Develop a policy framework for the use of patient-generated data in research and care delivery that addresses data collection tools, data donation policies, regulatory gaps, combining data with medical record data, and interoperability of data across health information systems and devices.
Creating the Foundational Blocks for the Learning Health Care System: Data Access Framework	▪ Develop technical standards for how health care providers, researchers, and the public health community access and extract data from EHRs to conduct PCOR.
Creating the Foundational Blocks for the Learning Health Care System: Structured Data Capture	▪ Identify and develop the functional and technical specifications necessary to enable EHR systems to retrieve, display, and fill a structured form or template and store and submit the completed form to an external repository.
Creation of LOINC Equivalence Classes	▪ Create a flexible, extensible, and computable mechanism for rolling data into clinically relevant equivalence groups that enable more efficient processing aggregation of laboratory data and other data from diverse health information technology systems. The primary focus of this work will be on laboratory tests.
Cross-Network Directory Service	▪ Create an interoperable service that allows data partners to participate in multiple data research networks, query across the networks, and share analytic capabilities and knowledge across networks. The project will be piloted across two existing networks: Food and Drug Administration's Sentinel and PCORnet.

Active Project	Project Description
Development of a Natural Language Processing Web Service for Public Health Use*	▪ Develop a natural language processing service that will be accessible and publicly available to researchers on the Public Health Community Platform – a cooperative platform for sharing interoperable technologies to address public health priority areas aimed at improving population health outcomes and health equity (e.g., tobacco use).
Developing a Strategically Coordinated Registry Network to Support Research on Women's Health Technologies*	▪ Create a coordinated registry network for women's health technologies that will collect patient reported outcomes and employ structured data capture from EHRs for data collection and exchange.
Enhancing Data Resources for Researching Patterns of Mortality in Patient Centered Outcomes Research: Projects 1 - 4*	▪ Linkage of data on fact, cause, and manner of death from the National Death Index to several federal population-based health data platforms in order to demonstrate the feasibility of such linkage, enable PCOR on patterns and correlates of mortality via the resulting linked data; and to facilitate collaboration between federal partners regarding strengthening the infrastructure and methods for linking healthcare data to mortality outcomes and using such linked data for PCOR.
Harmonization of Clinical Data Element Definitions for Outcome Measures in Registries	▪ Convene clinical topic-specific working groups to discuss the data definitions currently in use and how these definitions can be harmonized to promote common definitions for outcome measures across systems. These common definitions are to be made publicly available to PCOR researchers and analysts
Harmonization of Various Common Data Models and Open Standards for Evidence Generation*	▪ Build data infrastructure for conducting PCOR using data from routine clinical settings. The sources of these data may include, but are not limited to, insurance billing claims, EHRs, and patient registries. This project intends to harmonize several existing common data models, potentially including PCORnet and other networks.
Improving Beneficiary Access to their Health Information through an Enhanced Blue Button Service	▪ Create an interface that enables CMS beneficiaries to connect their MyMedicare.gov data to applications and services they trust, including research platforms related to research studies in which the beneficiary may be interested in participating.
Improving the Mortality Data Infrastructure for Patient-Centered Outcomes Research	▪ Improve the infrastructure to support timely and complete mortality data collection through more timely delivery of state death records to the National Death Index database and by linking National Death Index database records with nationally collected hospital datasets to obtain a more complete picture of patient care.
Privacy and Security Blueprint, Legal Analysis and Ethics Framework for Data Use, and Use of Technology for Privacy*	▪ Develop a privacy and security data infrastructure blueprint, legal analysis, and ethical framework to address legal and privacy and security related policy issues that affect the use of data for various types of PCOR.
Security and Privacy Standards for Patient Matching, Linking, and Aggregation	▪ Identify the best patient attributes to address the challenge of linking patients' data across research, clinical, and claims data sets in order to support the PCOR data infrastructure that enables standardization and sharing of patient data across organizations.

Active Project	Project Description
Source Data Capture from Electronic Health Records: Using Standardized Clinical Research Data	▪ Create a single point data capture approach from the EHR to electronic data capture systems using the Retrieve Form for Data Capture standard. Stakeholders will be provided with a tool to seamlessly integrate electronic health record and electronic data capture systems.
Standardization and Querying of Data Quality Metrics and Characteristics for Electronic Health Data	▪ Create and implement a metadata standard data capture and querying system for data quality and characteristics, data source and institutional characteristics, and "fitness for use."
Technologies for Donating Medicare Beneficiary Claims Data to Research Studies*	▪ Leverage the Sync for Science and Blue Button application programming interface programs to enable Medicare beneficiaries to donate their medical claims data for scientific research studies.
Use of the ADAPTABLE Trial to Strengthen Methods to Collect and Integrate Patient-Reported Information with Other Data Sets and Assess Its Validity	▪ Generate tools and data standards that could be deployed in other comparative effectiveness research studies by leveraging the infrastructure of an existing research study called the ADAPTABLE trial (Aspirin Dosing: A Patient-Centric Trial Assessing Benefits and Long Term Effectiveness). This trial is the first major randomized comparative effectiveness trial to be conducted by PCORnet.
Utilizing Data from Various Data Partners in a Distributed Manner	▪ Develop and test the capability to conduct timely and secure distributed regression analysis in distributed data networks. Additionally, explore the feasibility of creating virtual linkage capabilities to utilize data from multiple data sources and data for one specific patient with information at different institutions.

*Denotes a cross-agency funded project that involves more than one federal agency.

III. Agency for Healthcare Research and Quality (AHRQ)

AHRQ is administering two active OS-PCORTF-funded projects, 1) Harmonization of Clinical Data Element Definitions for Outcome Measures in Registries; and 2) Advancing the Collection and Use of Patient-Reported Outcomes through Health Information Technology. The latter is a jointly funded project described in the "Cross-Agency Funded Projects" section.

Harmonization of Clinical Data Element Definitions for Outcome Measures in Registries

AHRQ is actively working with registry owners to set up a common group of outcome measures, in a standardized vocabulary, and get the registries' outcome measures harmonized so the data can be combined and analyzed together.

EHRs and registries contain a variety of rich clinical information including demographics, diagnoses, medications, allergies, and laboratory values. These data have the potential to support hypothesis generation and large scale clinical research studies. To this end, vocabulary and standardization of electronic formats and methods to electronically exchange information have been a priority for EHRs and registries. Less focus has been placed on differences in clinical definitions across institutions and on efforts to harmonize these definitions; however, and it is essential to address the variability in clinical definitions in order to meaningfully interpret results of studies and use the results to improve patient outcomes. One example is variability within quality measures and public reporting

requirements related to care processes, use of medications, mortality, and readmission rates after myocardial infarction. While existing measures provide standard definitions for the process and outcomes, they do not address the variability in the definition of myocardial infarction used by individual health care institutions. For example, one study investigating the impact of differing clinical definitions on study findings showed that in one registry, the rate of reported myocardial infarction was 7.2 percent when using the biomarker CKMB as the criteria, compared to 24.3 percent when using the biomarker troponin as the criteria, representing a three-fold difference in ascertainment.[xii]

This project supports the creation of harmonized outcome measures and the AHRQ Outcome Measures Framework—a conceptual model for developing standard outcome measures. Together, these activities will harmonize clinical data element definitions thereby supporting the comparison of data across registries housed in the AHRQ Registry of Patient Registries, and will create a model for future harmonization efforts.[xiii]

Project Purpose and Goals: The purpose of this project is to convene a series of clinical topic-specific working groups to discuss the various definitions for outcome measures currently in use and how these definitions can be harmonized into a common set to be used across data collection and reporting systems. The working groups will solicit input from a broad stakeholder community, including registry holders, informaticists, and clinical subject matter experts; policymakers developing quality measures and other types of mandatory reporting measures; as well as clinicians, health systems, industry representatives, federal health and human service agencies, and patients.

The project objectives are to:

- Develop a consensus set of clinical data element definitions that can be consistently used to represent specific outcome measures for each of five clinical topic areas: atrial fibrillation (AF), lumbar spondylisthesis (lower back pain), lung cancer, asthma, and depression
- Develop best practices for governance of data element definition libraries and harmonization between registries. The definitions and best practices will be made publicly available for use by registry owners and PCOR researchers.

Contributions to the PCOR Data Infrastructure Functionalities:

- *Linking of Clinical and Other Data for Research.* There is significant variation in both the types and definitions of outcome measures used in patient registries, even within the same clinical area. These heterogeneous data reduce the utility of registries to collect, link, and aggregate data. By using the AHRQ libraries, the information captured in one registry will have the same clinical meaning as another and so that it becomes easier to aggregate data collected for varying primary purposes. In the OS-PCORTF evaluation, issues of data quality were identified as an area for future work, which will be will addressed here in the form of reducing data heterogeneity to increase the availability of consistent quality data for PCOR.
- *Standardized Collection of Standardized Clinical Data.* This project is also aimed at standardizing clinical data collection. By adopting the core common outcome measures/data element sets, the data available for research will be standardized and comparable across different registries and health care organizations that collect the information.

Accomplishments and Deliverables: The five clinical topic focus areas this project addresses were selected because they represent different clinical conditions and a wide variety of patient populations. In addition to the active clinical working groups advising the project, a stakeholder group of payers, patient representatives, and health system leaders has been assembled to discuss challenges and provide feedback on the harmonization effort.

- A draft library of clinical definitions for the first three topics: atrial fibrillation, depression and asthma is complete. These libraries contain not only the clinical definitions of the outcome measures, but also the value sets, which are critical to implementation and interoperability. Value sets use standard clinical coding terminologies (i.e., RxNorm, ICD-10, LOINC, and SNOMED) to define the clinical concepts (in this context, the outcome measure itself).
- AHRQ is working with relevant professional societies (e.g., Heart Rhythm Society, the American Medical Association) to publish and seek endorsement for the AHRQ definitions in these organizations' registries. Some professional societies have expressed interest in seeing the clinical data elements and value sets submitted to the NIH's National Library of Medicine (NLM) Value Set Authority Center, a repository of publicly created value sets.

Disseminated Products:

- AHRQ publicly posts each clinical definition in a library on their website for peer review. These libraries are available here: https://effectivehealthcare.ahrq.gov/topics/registry-of-patient-registries/outcome-measures-framework.
- AHRQ presented a panel titled "Harmonizing Outcome Measures to Increase the Utility of Patient Registries: A Case Study in Atrial Fibrillation" at the American Medical Informatics Association (AMIA) Joint Summits on Translational Science in 2017.

Coordination with Other Federal Agencies: AHRQ is working with the NIH/NLM to add the AHRQ-developed clinical data elements, when complete, to the NIH's Common Data Element (CDE) Repository. The NIH CDE Repository is a platform that contains data element definitions to use in research and other purposes. The NIH CDE Repository definitions include "machine-readable" definitions (i.e., those that can be interpreted by an EHR). Adapting the AHRQ clinical data elements in machine-readable format will facilitate standard data collection at the point of care.

Leveraging Project Products: VBP programs rely on the collection and aggregation of clinical quality measures across providers and health systems for payment and reimbursement. However, there is considerable variability in the measures used to assess clinical outcomes, analogous to the data heterogeneity in outcome measures reported to registries. The lessons learned from this project have the potential to inform efforts to standardize and harmonize quality measures, and importantly the associated outcome, for VBP programs.

The real-world implementation of these harmonized outcome measures could be accelerated with the standardized collection of standardized data. To address this challenge, AHRQ is exploring opportunities to leverage existing standards that will ease the process of extracting data from EHRs to populate clinical registries. Specifically, ASPE is reviewing the ONC's Structured Data Capture and Health Level 7 (HL7) Fast Healthcare Interoperability Resources (FHIR) standards to pilot the AHRQ clinical element definitions into point of care data collection within an EHR.

Period of Performance:
4/29/16 – 4/28/18

Federal Point of Contact:
Elise Berliner

IV. Centers for Disease Control and Prevention (CDC)

The CDC is administering four active OS-PCORTF-funded projects: 1) Improving the Mortality Data Infrastructure for Patient-Centered Outcomes Research; 2) Privacy and Security Blueprint, Legal Analysis and Ethics Framework for Data Use, and Use of Technology for Privacy; 3) Development of a Natural Language Processing Web Service for Public Health Use; and 4) Enhancing Data Resources for Researching Patterns of Mortality in PCOR. The Improving Mortality Data Infrastructure for Patient-Centered Outcomes project is described in this section. The remaining projects are jointly funded and are therefore summarized in the Cross-Agency Funded Projects section.

Improving the Mortality Data Infrastructure for Patient-Centered Outcomes Research

The timely reporting of death information is critical for public health surveillance and patient-centered outcomes research (PCOR). Comprised of all U.S. mortality events since 1979, the National Death Index (NDI) database allows researchers to match death entries in the NDI with their research populations (e.g., those participating in longitudinal clinical and epidemiologic studies) to determine both death "status" and cause of death. A significant challenge with the NDI is the lag between the occurrence of an individual's death and the availability of their record for matching purposes. This has limited the NDI's utility for timely patient follow-up and survival outcomes determination.

Project Purpose and Goals: The CDC's National Center for Health Statistics (NCHS) is working to improve the mortality data infrastructure on multiple fronts, including improving the timeliness of state death records (which provide cause of death) being incorporated into the NDI database, and obtaining a more complete picture of patient care by linking NDI records with nationally collected hospital datasets.[xiv]

The CDC is engaged in three inter-related tasks to enhance the national mortality system:

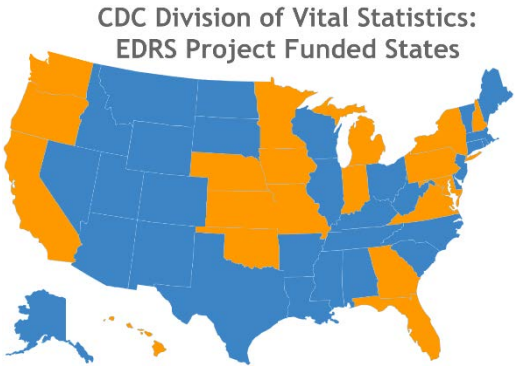
- *Strengthening existing state mortality data collection infrastructure.* Currently, 48 jurisdictions have Electronic Death Registration Systems (EDRS); however, not all are statewide and they do not cover all death events in a given region. This project is forging a comprehensive EDRS network from existing EDRS and enabling electronic data transfer. The intended outcome is for states to report 80 percent of deaths electronically within 10 days of event to NCHS, which will enable more timely availability of clinical data for research.
- *Piloting draft national standards for the exchange of relevant electronic death data from EHRs to EDRS.* Integrating EHR systems with vital records systems provides another opportunity to improve quality and timeliness of mortality data collection and distribution through standardization and reduction of duplicate data entry. The CDC will pilot the Health Level Seven International (HL7) standards pilot, to support the bi-directional exchange of mortality data from to state EDRS to NCHS. The exchange of data in this format supports improvement in the quality and timeliness of mortality data, clinical care assessments, and PCOR.
- *Piloting the linkage of the National Hospital Care Survey (NCHS) in-patient and emergency department data with the NDI.* The pilot will assess the feasibility, validity, and reliability of measuring in-patient and post-discharge mortality. This linkage will provide additional information on patient survival after hospitalization and emergency care and eventually allow identification of patterns of care, as well as individual and provider charateristics associated with in-hospital and post-discharge mortality.

Contributions to PCOR Data Infrastructure Functionalities:

- *Standardized Collection of Standardized Clinical Data.* The project is modifying systems to enable the use of HL7 messages and piloting standards to govern the transmission of death-related information from EDRS to the NDI. The result will be better quality data from state-level systems, better electronic reporting, and therefore more complete mortality data that allows researchers to easily utilize standardized components. This includes publishing HL7 death reporting standards and Clinical Document Architecture (CDA) Death Reporting implementation guide to enhance standardization.
- *Linking of Clinical and Other Data for Research.* CDC's work is supporting the enhancement of strategic publicly-funded data systems—linking National Hospital Care Survey data (inpatient and emergency department) with NDI data to facilitate analysis of trends in hospital mortality. In addition, the improved linkage between state-level EDRS to the NDI will improve mortality reporting and the data's completeness data for research purposes.

Accomplishments and Deliverables: The CDC has made significant progress as it enters into the final year of the project.

- CDC funded 19 states (depicted in orange), to improve the timeliness of reporting. Some states are using the funding to update their EDRS to remove manual steps, while others are promoting physicians and medical provider community trainings to increase participation in local EDRS. Twelve states have concluded their improvement activities; the remaining states in the second cohort will complete their funded activities in early 2018.



- HL7 standards have been developed and a new implementation guide drafted, the "HL7 v2.6 Vital Records Death Reporting Implementation Guide."[xv] NCHS and California have successfully exchanged "live" mortality records using the HL7 draft standards. An HL7 Pilot Project debriefing was held among collaborating partners on July 17, 2017. The forum was intended to share experiences, lesson learned and reflect on project outcomes that will inform future HL7 projects. Overall consensus by pilot partners confirmed the pilot successfully demonstrated HL7 format as an effective modality for mortality reporting.
- The pilot linkage of the NHCS in-patient and emergency department data with the NDI has been completed. CDC has prepared a report describing the methods and preliminary results of the data linkage project.

Disseminated Products:

- HL7 Implementation Guide for CDA® Release 2: Vital Records Death Reporting, Release 1 STU 2 - US Realm) is available here: http://www.hl7.org/implement/standards/product_brief.cfm?product_id=386.
- Published the "Electronic Death Reporting System Online Reference Manual" as a resource guide for jurisdictions to support development and sustainability of EDRS; the online guide is available here: https://www.cdc.gov/nchs/data/dvs/edrs-online-reference-manual.pdf.

Leveraging Project Products for HHS Initiatives: The overarching significance of this project is to strengthen mortality-related data infrastructure across states. It successfully conducted inter-system exchanges between EHRs and EDRS in states by using draft national HL7 standards; and linked the NCHS inpatient and emergency department data with the NDI data to measure within and post-hospital mortality.

Period of Performance:
4/3/2015 - 7/1/2018

Federal Point of Contact:
H. Mac McCraw

V. Centers for Medicare and Medicaid Services (CMS)

CMS is administering three OS-PCORTF-funded projects: 1) Improving Beneficiary Access to Their Health Information through an Enhanced Blue Button Service; 2) Technologies for Donating Medicare Beneficiary Claims Data to Research Studies; and 3) Enhancing Data Resources for Researching Patterns of Mortality in Patient Centered Outcomes Research. The first project, Improving Beneficiary Access to Their Health Information through an Enhanced Blue Button Service, is described in this section. The remaining two projects, Technologies for Donating Medicare Beneficiary Claims Data, and Enhancing Data Resources for Research Patterns of Mortality in Patient Centered Outcomes Research, are jointly funded projects summarized in the Cross-Agency Funded Projects section.

Improving Beneficiary Access to Their Health Information through an Enhanced Blue Button Service

The original CMS Blue Button service was established in 2010 to allow CMS beneficiaries to download their data via MyMedicare.gov. However, the current download functionality supported in the Blue Button beneficiary portal presents patient data in formats (e.g., plain text and PDF) that make it difficult for patients to use and share their data with applications, researchers, and other service providers they trust.

CMS has undertaken a conceptual redesign of Blue Button to be a “data as a service” platform, allowing data to be accessed on demand. To accomplish this redesign, CMS is utilizing the HL7 FHIR standard. FHIR is an HL7 standard for exchanging health information electronically designed to simplify implementation without sacrificing information integrity.

Project Purpose and Goals: The enhanced Blue Button service, Blue Button 2.0, is an application programming interface (API) that enables CMS beneficiaries to connect their Medicare Parts A, B and D claims data to applications and services they trust, including research platforms. CMS is utilizing the FHIR framework for BlueButton 2.0 to ensure data is in a structured format that can be accepted by a wide range of applications. Research study investigators can direct interested beneficiaries to a web page or app that guides the beneficiary through the process of granting permission to investigators to access their Medicare Parts A, B, and D data. This dramatically simplifies acquisition of beneficiary claims information to support participation in clinical research studies. The Blue Button API allows researchers to selectively pull individual beneficiaries’ data for specific research needs.

> *“CMS has recruited more than 100 organizations – including some of the most notable names in technological innovation – to join CMS’ Medicare Blue Button 2.0 developer preview program… the program provides a “sandbox” environment that allows applications to be tested with the Blue Button 2.0 API and a dataset of synthetic beneficiary and claims data.”*

For example, queries could be constructed to access all Part D medication claims or all claims occurring since the last data request.

The project objectives are to:

- Develop a Blue Button API 2.0 and publish the code as open source software;
- Launch full production of the Blue Button 2.0 API; and
- Promote the availability of Blue Button 2.0 API to external sources.

Contributions to PCOR Data Infrastructure Functionalities

- *Use of Enhanced Publically-Funded Data Systems for Research.* This project's focus on facilitating the access, use, and retrieval of CMS data by beneficiaries to support their participation in research.

Accomplishments and Deliverables: CMS had successfully completed the majority of the deliverables for this project.

- The Blue Button API, Blue Button 2.0, has launched. Open source code has been published to the Blue Button Repositories on GitHub. A working prototype of the service was implemented in August 2016. Since April 2016, a prototype API with dummy data has been available. This data was replaced in December 2017 with de-identified synthetic data that represents 30,000 beneficiaries with realistic claims information. A pilot Code-a-thon was hosted in April 2016, and a report was delivered to ASPE in August 2016 for public posting. The team has also participated in HL7 FHIR Connectathons in 2016 and 2017.
- A CMS Blue Button API developer sandbox environment was created using the front-end development system and backend sandbox server in the HHS IDEALab cloud. This developer preview was announced to developers at the HL7 Connect-a-thon as part of a consumer mediated exchange track at the event. The developer preview is open to all interested parties and can be accessed via the webpage at http://go.cms.gov/bluebutton. As of Apr 13, 2018, 240 organizations had joined the Developer Sandbox.
- CMS Administrator Seema Verma announced the launch of Blue Button 2.0 during her keynote presentation at the Healthcare Information and Management Systems Society (HIMSS) conference on March 6, 2018. Organizations are now able to request access to the production API, which will allow Medicare beneficiaries to connect their claims data to the health applications they choose to trust.

Disseminated Products:

- Project team members participated in a series of HL7 FHIR Connect-a-thons and Health Datapalooza code-a-thons to advance the development work of the Blue Button API.
- The project team presented "The Power of Consumer-Directed Data" at Health Datapalooza in Washington, D.C. (April 2017).
- The CMS Blue Button API developer environment is open to all interested parties and can be accessed via the CMS webpage at https://bluebutton.cms.gov.

Leveraging Project Products: CMS is supporting the *All of Us* Research Program through this project by making it easier for CMS beneficiaries to donate their data for research. The focus on improving the data's extractability and readability for researchers will further the 21st Century Cures Act's goal of improving data interoperability.

Period of Performance:
4/30/16 – 4/29/18

Federal Point of Contact:
Carly Medosch

VI. Food and Drug Administration (FDA)

The FDA has nine active OS-PCORTF projects: 1) Collection of Patient-Provided Information through a Mobile Device Application for Use in Comparative Effectiveness and Drug Safety Research; 2) Cross-Network Directory Service; 3) Source Data Capture from Electronic Health Records: Using Standardized Clinical Research Data; 4) Standardization and Querying of Data Quality Metrics and Characteristics for Electronic Health Data; 5) Utilizing Data from Various Data Partners in a Distributed Manner; 6) Development of a Natural Language Processing Web Service for Public Health Use; 7) Developing a Strategically Coordinated Registry Network to Support Research on Women's Health Technologies; 8) Harmonization of Various Common Data Models and Open Standards for Evidence Generation; and 9) Enhancing Data Resources for Researching Patterns of Mortality in Patient-Centered Outcomes Research.

The five FDA-funded projects will be described below, while the four cooperatively funded projects—Development of a Natural Language Processing Web Service for Public Health Use; Developing a Strategically Coordinated Registry Network to Support Research on Women's Health Technologies; Harmonization of Various Common Data Models and Open Standards for Evidence Generation; and Enhancing Data Resources for Researching Patterns of Mortality in Patient Centered Outcomes Research—are summarized jointly in the section on Cross-Agency Funded Projects.

Collection of Patient-Provided Information through a Mobile Device Application for Use in Comparative Effectiveness and Drug Safety Research

A critical component of the FDA's mission is to monitor the safety and effectiveness of the products it regulates. The FDA has developed a robust national electronic surveillance system, Sentinel, for monitoring FDA regulated medical products and devices. Sentinel is a distributed research network, using existing electronic health care data from multiple sources to support FDA surveillance activities. In a distributed network, data is held locally at each data partner site and queried for information on a specific research question. Currently, Sentinel is comprised largely of administrative and claims data from health insurance plans and the Clinical Research Network component of the Patient-Centered Outcomes Research Institute's (PCORI) PCORnet.[xvi] The FDA has identified a need for patient-provided data to fill gaps and mitigate the impact of potential biases in existing data, and is targeting mobile devices as a viable option that is significantly less time and resource intensive than traditional data collection with research cohorts.

Project Purpose and Goals: This project will create the infrastructure for collecting data from patients on medical product exposures, outcomes, risk factors and confounders through a mobile device application, allowing patient generated data to be linked with a single data partner that participates in the Sentinel and

PCORnet distributed networks. The project will develop and pilot a mobile application to capture these types of data from pregnant women, who represent a traditionally understudied population and for whom significant gaps in research on drug safety exist. As a result, researchers will be able to query Sentinel for both the new patient generated health data (PGHD) (also known as patient provided information, PPI) and the data routinely captured by the Sentinel data partner.

The project objectives are to:

- Leverage existing electronic medical record algorithms to identify pregnant women in one collaborating health plan ("data partner");
- Develop a generalizable HHS/FDA/Sentinel Operations Center mobile device application that can be transmitted to the pregnant women identified by the data partner;
- Develop Medical/Epidemiological data elements and interface to capture pregnancy exposures, outcomes, confounders, and risk factors, as well as a programming and hosting component; and
- Link data provided by patients through the app with data from the health plan (data partner).

This effort will serve as a pilot for future applications. For example, the web-based interface has a customizable design; therefore, the mobile application could be re-configured to collect information from another patient population or a disease cohort so that other researchers or HHS agencies could answer other research questions of interest.

Contributions to PCOR Data Infrastructure Functionalities:

- *Collection of Participant-Provided Information.* This project will support the collection of PPI functionality by creating a secure mobile application to collect PPI from pregnant women that has potential for expansion to other patient populations.
- *Linking of Clinical and Other Data for Research.* This project will support this functionality through supporting the further development of Sentinel by integrating PPI information into the Sentinel research network of administrative and clinical data.

Accomplishments and Deliverables: The project has made significant progress in developing the mobile device application.

- The FDA has developed data transmission and storage procedures, as well as a secure patient data storage environment.
- An integrated health care delivery system, Kaiser Permanente Washington Health Research Institute, was selected to pilot test the mobile application among pregnant women and to conduct analyses of the resulting data. The pilot cohort enrollment goal was reached, and the project's questionnaires and research protocol received IRB approval.
- Data collection was completed as of December 26, 2017 and data analysis is underway. This includes a descriptive analysis of exposures and health outcomes of the pilot cohort using crosswalk-matched data from both the mobile application and existing electronic health data formatted in the Sentinel Common Data Model or available within the Kaiser Permanente EHR system.
- The FDA launched its mobile application on the Google Play store and the Apple Store. Prior to the launch, a prototype application had been built for testing and feedback.

FDA is exploring a potential real world use case to support value-based care: A company that acts as an intermediary between health insurance and pharmaceutical companies has expressed interest in using the mobile app to measure PROs related to covered medical drug and device products.

- The team produced two reports for this project. One is a report on procedures used to obtain participant contact information and the other describes patient feedback on the mobile application.

Disseminated Products:

- Presented "Developing a Mobile App for Studies of Medication Safety" at the International Conference on Pharmacoepidemiology & Therapeutic Risk Management (August 2017). The presentation is available here: https://www.sentinelinitiative.org/sites/default/files/Sentinel-ICPE-2017-Presentation-Mobile-App.pdf.
- Presented "Engaging Patients in Evidence Generation" at the National Academy of Medicine's Clinical Effectiveness Research Innovation Collaborative (April 20, 2017). The presentation is available here: https://nam.edu/wp-content/uploads/2017/04/Martin-NAS-042917.pdf.
- A poster presentation at the AMIA Joint Summits on Translational Science titled, "Collection of Patient Provided Information through a Mobile Device Application for Use in Medical Product Safety Surveillance." (March 2017).

Leveraging Project Products: There are several national distributed database systems including PCORnet, Sentinel, the NIH Collaboratory, the CDC Vaccine Safety Data Link, and the FDA Foundation Innovation in Medical Evidence Development and Surveillance system that could potentially use the mobile application and associated patient data storage environment. This project could support the *All of Us* Research Program through linking diverse data (e.g., PPI information with the existing Sentinel data system) and paves the way for increased ease of patient data donation through PPI-collecting mobile device applications. In alignment with the 21st Century Cures Act, it generates "real world" data and takes important steps toward improving data interoperability through inclusion of mobile application data into the Sentinel and PCORI research network. For example, the Center for Biologics Evaluation and Research is working with the Sentinel Operations Center to identify a condition to potentially study using this project's mobile application and FDA, CDER, and PCORI are working to identify a joint pragmatic trial candidate that could use mobile patient reports.

Finally, VBP programs could benefit from this project as it enables incorporation of patient-reported-outcomes into clinical data, both of which are being used to assess patient outcomes and quality of care in order to determine appropriate levels of payment.

Period of Performance:
7/15/2018 – 6/30/2018

Federal Point of Contact:
David Martin

Cross-Network Directory Service

The FDA is tasked with developing and implementing a Cross-Network Directory Service (CNDS) that addresses the stand-alone nature of existing distributed research networks and barriers to working across these networks. Distributed research networks facilitate large scale comparative and effectiveness studies by allowing researchers to send data queries to multiple organizations and networks, while those organizations being queried maintain possession and protection over the data they house. This product will enhance network scalability and allow each data partner to determine their own level of participation and governance rules.

Project Purpose and Goals: This project will create an open source interoperable service that allows data partners to participate in multiple data research networks, query across the networks, and share analytic capabilities and knowledge across networks. The project will be piloted across two existing networks: FDA's Sentinel System and PCORI's National Patient-Centered Clinical Research Network (PCORnet).

The project objectives are to:

- Identify the key functionalities and an overarching technical design for a CNDS;
- Develop and test a detailed design for the CNDS with at least two existing distributed research networks; and
- Conduct additional analyses of the robustness of the CNDS and produce user materials.

This project will produce the following deliverables: a CNDS Software and Source Code; a report on the Failure Mode and Effects Analysis; technical documentation; and user documentation. Additionally, the information gained from the CNDS will help inform additional FDA projects, including the Standardization and Querying of Data Quality Metrics and Characteristics for Electronic Health Data.

Contributions to the PCOR Data Infrastructure Functionalities:

- *Use of Enhanced Publically-Funded Data Systems for Research.* This project aims to build and implement a CNDS that will support a scalable data network infrastructure to allow integration of HHS investments in health data networks. This project proposes to extend PopMedNet to support query creation and execution for cross-network queries. The resulting CNDS will enable data partners to participate in multiple data research networks, seamless querying across networks, and sharing of analytic capabilities and knowledge across networks. Ultimately, the knowledge gleaned and tools developed from this project will inform other FDA initiatives and research.

Accomplishments and Deliverables: All deliverables for this project have been successfully completed.

- The design phase of the project—which included identifying business and technical requirements, determining and describing key functionalities—was completed in 2016 and detailed in a Use Case Summary report.
- The CNDS software application has been designed, built, released, and tested. In early 2018, the project team prepared the technical and user documentation for the CNDS. "The ASPE CNDS User Documentation" will be posted to the Sentinel Initiative website. Beta testing of the software application was performed by a Sentinel and a PCORnet data partner. In the first round of beta testing, the data partners successfully registered and entered their metadata. In the second and final round of testing, the data partners successfully completed a round trip through Discovery (search data sources) and Communication (send and receive queries). Further, data partners were not able to discover data that the other partner did not actively make available.
- The source code and documentation on how to implement the code in an existing instance of PopMedNet is publicly available on GitHub here: https://github.com/PopMedNet-Team/cnds.

Disseminated Products:

- "Cross Network Directory Service: A Socio-technical Platform to Enable Meaningful Collaboration across Organizations" was accepted as an oral presentation at the Health Care Systems Research Networks Conference in Minneapolis (April 12, 2018).

- A project poster was accepted for the AMIA 2018 Informatics Summit in San Francisco (March 12-15, 2018).

Leveraging Project Products: The CNDS software and source code, along with technical and user documentation, can be leveraged across HHS initiatives. Specifically, the infrastructure will enable better data access for researchers, allowing data partners to engage with multiple networks as research needs dictate. This product is in alignment with the 21st Century Cures Act and would be particularly helpful for the Opioids initiative, as well as other public health surveillance activities.

Period of Performance:
7/15/15 – 6/30/18

Federal Point of Contact:
Michael Nguyen

Source Data Capture from Electronic Health Records: Using Standardized Clinical Research Data

The current information systems and data models that define both clinical care and clinical research are disparate in many ways. Thus, using data from EHRs and electronic data capture (EDC) systems necessitates a detailed understanding of each data source. Moreover, even data sources within the same database can have extensive differences in coding, schema, format, and usage.[xvii] Given that clinical data are mostly collected through EHRs, a guideline or protocol for the use of health care data use in clinical research and trials could be helpful to enable PCOR studies. In 2013, FDA published guidance on Electronic Source Data in Clinical Investigations,[xviii] which provides recommendations on the capture, review, and retention of electronic data in FDA-regulated clinical trials. To provide a working example of the FDA's recommended approach, the FDA has initiated this project, which will provide a real world demonstration of their guidelines and commitment to EHR-to-EDC in clinical research environments.

Project Purpose and Goals: This project will create a single point data capture approach from the EHR to EDC systems using the Retrieve Form for Data Capture (RFD) standard, and the HL7 Continuity of Care Document (CCD) and FHIR standards. PCOR stakeholders will be provided with a cloud-based Health Insurance Portability and Accountability Act (HIPAA)-compliant and 21 C.F.R. Part 11-compliant tool to seamlessly integrate EHR and EDC systems.

The project objectives are to:

- Demonstrate an end-to-end, EHR-EDC, standards-based technology solution, OneSource, for the capture and transmission of regulated clinical research data. The pilot will be conducted with the University of California San Francisco (UCSF) as part of a phase 3 breast cancer trail that includes the capture of PROs (via "I-SPY");
- Assess the utility of the standards-based technology solution processes to facilitate FDA activities related to inspection, reconstruction, and evaluation of the trial/clinical investigation;
- Assess the impact of the standards-based technology solution on current workflow processes at the sites, and on FDA's remote monitoring of studies;
- Develop guidelines for future implementations in both health care and clinical research;
- Provide recommendations for the improvement of existing standards and implementation guides to standards-development organizations; and
- Develop a general framework (technologies, processes, policies, governance, and standards) for the capture and use of electronic structured data in regulated clinical trials.

Accomplishments and Deliverables: The FDA has made significant progress towards demonstrating the EHR to EDR data capture.

- The RFD and CCD technical standards to capture EHR data have been piloted
- The standards and reference materials (above) were maintained through regular updates. Maintenance activities included updates to the technical standards, Implementation Guides, reference implementation documentation, testing documentations, and any other artifacts during the period of performance

Disseminated Products:

- A presentation to the Digital Data & Health Therapeutics Group for Production implementation.
- A presentation to the University of California Office of the President, demonstrating how OneSource could serve as a platform across the University of California System.
- OneSource was presented as part of the University of California San Francisco (UCSF) Share Case IT Symposium "Data Integration Real World Impact & USCF – Integration Overview" on October 12, 2017.
- At the annual DIA conference on June 20th, 2017 in Chicago as part of a session on academic collaborations with the FDA and eSource solutions
- A presentation to the UCSF Orthopedics group as part of the Health Innovation & Technology in Ortho Committee (HITO) on June 14th, 2017.
- At I-SPY consortium's workshop/retreat (which focus on innovation in breast cancer clinical trials) with FDA participation (March 7-8, 2017)

Contributions to PCOR Data Infrastructure Functionalities:

- *Standardized Collection of Standardized Clinical Data.* The project supported standardization through: the development of a set of research CDEs in specific gaps areas and the development of a governance structure for CDEs; and the development of a core set of standards for the collection and integration of prevalent use cases of PPI for PCOR.
- *Use of Clinical Data for Research.* The project also supports the use of EHR and PRO through the implementation of standards for the collection and use of this data in FDA-regulated clinical trials.

Coordination with Other Federal Agencies: The team collaborated on a report detailing recommendations in collaboration with CDISC (Clinical Data Interchange Standards Consortium) for the improvement of existing standards. The team also provided project presentations to the CERSI and the Center for Drug Evaluation and Research (CDER) Health IT Board.

Leveraging Project Products for HHS Initiatives: The services, standards, and tools created can be widely leveraged across the federal government to support electronic data query, linkages, and exchange of information. This has potential for numerous federal and non-federal initiatives.

Period of Performance:
9/1/16 – 12/30/18

Federal Point of Contact:
Mitra Rocca

Standardization and Querying of Data Quality Metrics and Characteristics for Electronic Health Data

Currently, limited standards exist for describing and characterizing the quality and completeness of electronic health data. In order to best utilize data, it is imperative that researchers and investigators know the fitness-for-use and reliability of data. In order to address this gap, the FDA will build upon the connections and knowledge gained from the FDA CNDS to discover and design data quality metrics for metadata "data about data" standards. These data standards will enable users to tag, structure, format, and code data according to its categorization and fitness.[xix] Researchers affiliated with research networks will be the primary audience for this system; however, researchers (outside distributed research networks) with access to clinical data partners will also be able to utilize the CNDS to describe their data sources in a standardized format. The standardized format will include a way for researchers to describe data sources, domains, attributes and other critical data characteristics, enabling cross-data partner comparisons that will help researchers identify and use fitting data sources, matching data to the needs of the research team.

Project Purpose and Goals: This project will create and implement a metadata standards data capture and querying system for: 1) data quality and characteristics; 2) data source and institutional characteristics; and 3) "fitness for use".

The project objectives are to:

- Develop metadata standards and technical specifications for implementation;
- Develop and test the metadata standards data capture and querying approach;
- Implement the new metadata standards in at least two distributed networks; and
- Incorporation of the standards in an open source software release.

Contributions to PCOR Data Infrastructure Functionalities

- *Use of Clinical Data for Research.* This project supports the development and testing of metadata standards that describe data quality to determine fitness of use for particular research purposes.
- *Use of Enhanced Publically-Funded Data Systems for Research.* The project will create an open source tool that can be implemented with any data model ensuring broad applicability. With this work, the FDA team aims to provide a harmonized approach to data characterization across multiple sources so we can better understand candidate data sources before analyzing them. This will increase research planning efficiency through enhanced understanding of a data source before putting resources into conducting study, asking a question, or distributing complex analytic programs. Additionally, the work will help improve the interpretability of analytic results across agencies and research teams.

Accomplishments and Deliverables:

- Created first draft of documents that describe: the ideal end-state of the system; the proposed set of metadata standards; use cases describing likely points of leverage; each metadata element (i.e. data dictionary); the data model and systems diagram that illustrate how the data and information will be managed once the system is implemented.
- The project team has started background research on existing data quality methods and frameworks.

- The team has started to define and document the ideal end-state; the proposed set of metadata standards; use cases describing likely points of leverage; each metadata element (i.e. data dictionary); and the data model and systems diagram that illustrate how the data and information will be managed once the system is implemented. The team is on track to complete this Discovery and Design phase in early 2018.
- Confirmed project workgroup participants and held project kickoff meeting.

Coordination with Other Federal Agencies: Because of the close relationship between this project and the CNDS project, the two share team members within the FDA to improve collaboration and cross-fertilization.

Leveraging Project Products: Effective use of the growing number of electronic health data sources and distributed data networks—by researchers and across the federal government—will require adoption of a standardized approach to describing the quality and general characteristics of these data, as well as the information related to how such data are captured, stored, and maintained.

This project focuses on creating a system that operationalizes existing data quality parameters across multiple CDMs. The project will provide a flexible data quality collation system that captures data directly from established CDMs within and external to HHS, such as Sentinel, PCORnet, and the Electronic Medical Record Support for Public Health. The system will be designed to apply calculated data quality metrics to data sets and to enable flexible exploration of data quality characteristics for multiple data sources at the same time. Importantly, the project will provide an open source, web based platform for exploring and describing the quality, completeness, and stability of data sources, which will benefit multiple agencies and non-federal teams conducting PCOR (e.g., *All of Us* and other National Institutes of Health (NIH) initiatives, in alignment with the 21st Century Cures Act).

Period of Performance:
8/20/2016 - 9/30/2019

FDA Federal Point of Contact:
Michael Nguyen

Utilizing Data from Various Data Partners in a Distributed Manner

Currently information on patients' health care is captured across various data sources held across institutions. Distributed research networks enable researcher access to significantly larger study populations by providing the infrastructure to centrally query and aggregate data controlled and stored locally by network participants. In a distributed network, data are held at different institutions (*horizontally partitioned*), or information about a single person is held at different institutions (*vertically partitioned*). Distributed regression analysis enables sites to maintain control of patient-level data while generating valid regression estimates across the network without the need to transfer protected health information. This kind of system provides a balance between analytic requirements, patient privacy and confidentiality, and proprietary considerations. This FDA project builds upon previous work on distributed linear regression analysis to develop and test a new analytic capability that automates distributed regression analysis in horizontally partitioned data, a previously resource intensive task.

Distributed Regression Analysis has been fully integrated into the 2017 PopMedNet release and is publicly available for download.

Project Purpose and Goals: This project will develop and test the functionality to conduct timely and secure distributed regression analysis in distributed data networks. The identified use case for this pilot test is a comparison of bariatric surgery survival outcomes (e.g., body mass index change and

hospitalization one year post-surgery). Additionally, it will explore the feasibility of creating virtual linkage capabilities to: utilize data for one specific patient with information at different institutions (*vertically partitioned data*) through a unique key used to identify the patient.

The project objectives are to:

- Develop a new open-source software application that will use PopMedNet™, an open source software application that enables the creation, operation, and governance of distributed health networks, to automate distributed regression analysis on horizontally-partitioned data; develop this software application so that it can be supported by PopMedNet™ and can be modified and adopted for non-PopMedNet™ applications;
- Test the new, distributed regression application in an actual distributed research network;
- Provide technical and user documentation to accompany the new software and allow for its widespread adoption; and
- Explore the feasibility of conducting distributed regression analyses in which data from the same people are held at different institutions (vertically-partitioned data).

This project will produce the following deliverables for horizontally partitioned data: 1) develop and test code for multiple regression analyses; software prototype and source code; and 2) a technical report. After completing those deliverables, additional deliverables will be produced for vertically partitioned data: 1) develop and test code for distributed linear regression and 2) a technical report.

Contributions to PCOR Data Infrastructure Functionalities:

- *Use of Clinical Data for Research.* The ability to link clinical data across health care organizations' databases provides more robust cross-sectional or longitudinal patient profiles, enhancing secondary uses of electronic health care information for research purposes, and improving access to information that would not be present in a single data source (e.g., claims, registry, or EHR data).
- *Use of Enhanced Publicly-Funded Data Systems for Research.* By developing this solution to work with PopMedNet, it has the potential to affect the way research is conducted across disparate research networks (e.g., PCORnet, Sentinel), many of which use PopMedNet as their platform, to apply a consistent approach to these types of analytics.

Accomplishments and Deliverables: The FDA has achieved significant milestone progress towards completion of each of the project deliverables.

- Development of the open source code to perform the distributed regression analysis is complete.
- The integration of PopMedNet™ query workflow and analytic code allowing users to specify automated DRA is complete. Notably, the distributed regression analysis code was integrated into the December 2017 PopMedNet™ release.
- FDA continues to work on additional PopMedNet™ enhancements.

Pilot testing of the analytic code is currently ongoing in two PCORnet studies: the PCORnet Bariatric Study and the PCORnet Antibiotics and Childhood Growth Study. The final report describing the testing methods used to validate the software in the horizontally partitioned data systems and results of the tests is in progress. FDA plans to publicly post the final report on its website.

Disseminated Products:

- The distributed regression analysis SAS code is available on FDA's Sentinel website here: https://www.sentinelinitiative.org.
- The distributed regression analysis was fully integrated into the 2017 PopMedNet™ release; the new version of the software is available here: https://www.popmednet.org. The service supports automated file transfers within the network.

Leveraging Project Products. The implementation of distributed regression analysis has the potential to support efforts like the *All of Us* Research Program and other longitudinal studies. Using this service will allow PCOR researchers to perform real-world distributed regression to answer specific study questions for pre-defined cohorts, creating more effective data for PCOR.

Period of Performance:
7/15/15 – 6/30/18

Federal Point of Contact:
Michael Nguyen

VII. National Institutes of Health (NIH)

NIH has seven active projects: 1) Creation of LOINC Equivalence Classes; 2) Use of the ADAPTABLE Trial to Strengthen Methods to Collect and Integrate Patient-Reported Information with Other Data Sets and Assess Its Validity; 3) Technologies for Donating Medicare Beneficiary Claims Data to Research Studies; 4) Developing a Strategically Coordinated Registry Network to Support Research on Women's Health Technologies; and 5-7) Three projects are funded under the umbrella of Harmonization of Various Common Data Models and Open Standards for Evidence Generation. The LOINC and ADAPTABLE projects are described below while the remaining NIH-funded projects are jointly funded projects described in the Cross-Agency Funded Projects section.

Creation of LOINC Equivalence Classes

Interoperability relies in part on common vocabulary standards that allow disparate systems to interpret and exchange information with the same clinical meanings. Logical Observation Identifiers Names and Codes (LOINC©), developed by the Regenstrief Institute, Inc., is a universal coding system for laboratory tests and other clinical observations. LOINC is a national standard with widespread adoption and recognition of its utility; for example, LOINC is required under the CMS EHR Incentive Program, state and national public health reporting mandates, and in research networks like PCORnet.

Mapping local terms to LOINC codes can be complex and resource intensive. This complexity can lead to differences in mapping granularity and specificity that limit interoperability. Furthermore, not all important data uses require the full granularity of detailed LOINC names; for some purposes, "equivalencing" LOINC codes may be sufficient. "Equivalencing," or rolling-up a hierarchy, groups similar LOINC codes together in clinically relevant and similar groups. This project's efforts to create equivalencing classes addresses the important interoperability barriers created when clinical and laboratory terms are mapped to LOINC terms with different levels of granularity.

The LOINC Equivalence Class release contains 21 Parent Groups and 4,100+ Groups that aggregate more than 17,500 unique LOINC terms.

Project Purpose and Goals: The goal of this project is to create a flexible, extensible, and computable mechanism for rolling LOINC codes into clinically relevant equivalence groups that enable more efficient processing aggregation of data from diverse health IT systems. The primary focus of this work will be on laboratory tests.

The project objectives are to:

- Identify high priority and clinically relevant content subsets for representation in the new LOINC hierarchy. To support this work, the Regenstrief LOINC team will develop an enhanced software tool that searches the LOINC database and stores subsets for later retrieval. Input on the high priority subsets will be gathered from an expert advisory group and the global LOINC user community;
- Develop a clinically relevant roll-up hierarchy for LOINC terms. The Regenstrief LOINC team will review the candidate subsets to identify "equivalence groups" and define the term attributes necessary to create the group. The goal is to create rule-based group definitions and save them so that they can be updated and re-executed over time and in subsequent LOINC releases; and
- Disseminate the aggregation hierarchy within the main LOINC release distribution. The new hierarchy will be published with each bi-annual LOINC release and available publicly at no cost.

Contributions to PCOR Data Infrastructure Functionalities:

- *Standardized Collection of Standardized Clinical Data.* This project supports the standard collection of data by developing a standard mechanism for assigning newly defined LOINC codes to represent clinically-relevant hierarchies. The application of these hierarchies by LOINC users will help address issues of variability in LOINC mappings and will allow for more consistent comparisons of data across institutions.

Accomplishments and Deliverables: The project has nearly completed all of its deliverables.

- To date, the team has created two releases of the LOINC Equivalence Class artifact. The first release, LOINC Groups Alpha 1, contained new artifacts and documentation based on significant input from the LOINC user community; it was released on June 23, 2017. The publication represented the culmination of ten months of implementation work to create and deploy grouping rules/queries within the dynamic LOINC development infrastructure. These infrastructure enhancements enable: 1) the creation and persistence of the classes; 2) automatic rule processing to execute the rules each night; and 3) automatic creation of the new LOINC Group codes assigned to each group. These enhancements enable the Groups to be dynamically updated as the underlying LOINC terminology continues to be developed.
- The second iteration of the LOINC Groups Alpha was released on December 15, 2017. The project team will continue to collect feedback from the stakeholder community in preparation for a June 2018 LOINC release.
- To support this initiative, the team has created a webpage/portal for submitting LOINC equivalence groups and allowing users to share groups of LOINC codes they are using and to submit new groups for addition to LOINC. The portal was demonstrated to the LOINC Committee on December 7, 2017 and is now publically available.
- The NIH project team began meeting with representatives from the FHIR community to create FHIR value set representations of the LOINC Groups. Making the LOINC Groups available as FHIR value sets will support their uptake and availability within the broader health IT community.

Disseminated Products:

- LOINC Groups Alpha 1 released in June 2017; the artifact was published on the LOINC website along with LOINC version 2.61.https://loinc.org/groups/.
- LOINC Groups Alpha 2 released in December 2017 the artifact was published along with LOINC version 2.63 and is available here: https://loinc.org/groups/

The project team presented at the public meetings of the LOINC Committee (both Laboratory and Clinical Committees).

Leveraging Project Products: This project will contribute to building data capacity for PCOR by improving the use of standardized data for various purposes, which is key for facilitating linkage and aggregation of data across sources and between research projects. Specifically, the resulting User's Guide of data policies and standards will inform work across HHS initiatives, especially Opioids, the *All of Us* Research Program, 21st Century Cures, and VBP, all of which demand standardized, high quality data for optimal effectiveness.

Period of Performance:
8/31/16 –4/30/18

Federal Point of Contact:
H. Timothy Hsiao

Use of the ADAPTABLE Trial to Strengthen Methods to Collect and Integrate Patient-Reported Information with Other Data Sets and Assess Its Validity

The ADAPTABLE (Aspirin Dosing: A Patient-centric Trial Assessing Benefits and Long-Term Effectiveness) trial is the first major randomized comparative effectiveness trial to be conducted by PCORnet. This pragmatic clinical trial will compare the efficacy and safety of two different daily doses of aspirin widely recommended to patients with chronic cardiovascular disease.[xx] As part of this new type of comparative effectiveness trial, ADAPTABLE is notable in several key features, including its enrollment of 20,000 patients across six large health care systems; use of an internet portal to consent patients and collect patient-reported information regarding risk factors, medications, and experiences; and its user of existing EHR data sources for baseline characteristics and outcomes follow-up data.

Integration of patient-reported information and EHR-derived data has the potential to both enhance evaluation of outcomes that are meaningful to patients and to improve data quality and validity for PCOR.

Project Purpose and Goals: Because ADAPTABLE will rely on patients to report key information at baseline and throughout follow-up, it represents a unique opportunity to develop, pilot, and evaluate methods to validate and integrate patient-reported information with data obtained from EHRs. The project will generate tools and data standards that could be deployed in other PCOR studies beyond the ADAPTABLE trial.

The project objectives are to:

- Develop, test, and validate metadata standards for patient-reported information to describe the completeness, consistency, and fitness-for-use of patient-reported data in EHR research;
- Evaluate the validity of patient reported data through systematic comparison with EHR data. The project will develop a Patient-Reported Data Assessment Tool to quickly and efficiently evaluate concordance of patient-reported data and EHR data; and

- Develop approaches to resolve inconsistencies between patient-reported data and EHR-derived data.

This project will inform future efforts to synthesize potentially inconsistent data from patient-reported and EHR sources, to identify opportunities to streamline data capture, and to facilitate enrollment in study-specific target populations within larger health systems.

Contributions to PCOR Data Infrastructure Functionalities:

- *Standardized Collection of Standardized Clinical Data.* This project focuses on methods to streamline and standardize data capture from the EHR. Baseline and follow-up data will be obtained from the PCORnet CDM, which serves as the foundation of the PCORnet distributed research network.
- *Collection of Participant-Provided Information.* This project utilizes the ADAPTABLE web portal to consent patients and collect patient-reported information regarding risk factors, medications, and experiences. Specifically, patients will provide information for four domains in the portal: 1) PROs for general domains of health; 2) specific information about medications they take; 3) specific details about reasons for stopping aspirin when this occurs; and 4) hospitalizations.
- *Linking of Clinical and Other Data for Research.* After vetting data for quality and appropriateness with patient stakeholders, patient-reported data elements from ADAPTABLE (i.e., symptoms, side effects and quality of life) will be submitted for inclusion into LOINC so that they may be readily accessible for use in future research studies. Data elements will also be submitted to the REDCap shared library to support implementation of patient-reported elements in future studies conducted at REDCap partner institutions.
- *Use of Clinical Data for Research.* The trial will leverage data from the EHR to identify the optimal dose of aspirin therapy for secondary prevention in atherosclerotic cardiovascular disease.

Accomplishments and Deliverables: The project team has made notable progress towards stated project aims.

- For the peer-reviewed manuscript, the team completed a literature review on data and metadata standards for patient-reported data in EHR-based trials to inform their development of a priority list of metadata standards. After discussing initial findings, the project leadership recommended that elements also be connected to the NIH CDE browser. The project team also finalized their concordance plan (statistical analysis plan) and explored smoking status categories in the CDM for mapping.
- As a result of the ADAPATABLE Supplement Roundtable Meeting held on September 14, 2017, the project team is in the process of producing a jointly-authored white paper on available resources for best practices, key challenges, information gaps, and future research needs for promoting best practices in the use of patient-reported health data in pragmatic studies.
- Related to the Patient-Reported Data Assessment Tool developed on the PopMedNet platform: The team has developed a statistical analysis plan that has been vetted internally with leadership, statisticians, and informaticists, as well as with ASPE and the sub awardees. The team has refined elements to be included in menu-driven query tool, refined the tool development plan/timeline and completed a preliminary assessment of patient-reported data.
- Through collaboration with its sub-awardees, the project team has determined that patient-reported data elements will be submitted to LOINC. They will also be published on the PCORnet website and submitted for inclusion in the NIH/NLM CDE Resource Portal and the REDCap shared library to support implementation of patient-reported data elements in future studies.

Coordination with Other Federal Agencies: The NIH held a Roundtable Meeting that included attendees from the informatics and patient-reported outcomes communities, as well as ASPE, ONC and FDA, to review study progress and dissemination plans.

Leveraging Project Products: This project will generate tools and data standards that could be deployed in other PCOR studies beyond the ADAPTABLE trial, and benefit other HHS initiatives. The project will contribute to building data capacity for PCOR by further enabling the collection and use of patient-provided information for PCOR.

The project team will produce a peer-reviewed manuscript focusing on patterns of validity between data sources and by relevant patient and health system characteristics, with comparison to population norms to contextualize results. The patient engagement process and portal-based tool for patient consent and data collection developed for the ADAPTABLE trial could inform the *All of Us* Research Program, which involves collecting patient-donated information, and aligns with 21st Century Cures, which calls for increasing privacy and security of patient-mediated data exchange and data donation. The developed patient-reported data assessment tool can also inform the *All of Us* and Value-Based Purchasing initiatives, which rely on valid measures and high quality data.

Period of Performance:
8/31/16 – 9/30/17; NCE: 8/31/18

Federal Point of Contact:
Wendy Weber

VIII. Office of the National Coordinator for Health Information Technology (ONC)

ONC has eight OS-PCORTF projects, six of which are active as of April 2018 and two of which have ended: 1) Conceptualization of a Data Infrastructure for the Capture and Use of Patient-Generated Health Data; 2) Creating the Foundational Blocks for the Learning Health Care System: Structured Data Capture which ended in 2016; 3) Security and Privacy Standards for Patient Matching, Linking, and Aggregation; 4) Creating the Foundational Blocks for the Learning Health Care System: Data Access Framework, which ended in 2017; 5) Advancing the Collection and use of Patient-Reported Outcomes through Health IT; 6) Privacy and Security Blueprint, Legal Analysis and Ethics Framework for Data Use, and Use of Technology for Privacy; 7) Developing a Strategically Coordinated Registry Network to Support Research on Women's Health Technologies; and 8) Harmonization of Various Common Data Models and Open Standards for Evidence Generation.

The four projects that are cooperatively funded are summarized in the section on Cross-Agency Funded Projects: Advancing the Collection and use of Patient-Reported Outcomes through Health IT; the Privacy and Security Blueprint, Legal Analysis and Ethics Framework for Data Use, and Use of Technology for Privacy; Developing a Strategically Coordinated Registry Network to Support Research on Women's Health Technologies, Harmonization of Various Common Data Models and Open Standards for Evidence Generation.

Conceptualizing a Data Infrastructure for the Capture and Use of Patient-Generated Health Data

PGHD are "health-related data created, recorded, or gathered by or from patients (or family members or other caregivers) to help address a health concern."[xxi] PGHD are different from data gathered in clinical

settings and through provider encounters in two ways: 1) patients are responsible for capturing the data; and 2) patients decide how to share or distribute the data with clinicians in other health care settings and others in their care team. Examples of PGHD include blood glucose readings using a home blood glucose monitor, data generated by mobile fitness tracking apps, and survey data collected from patient questionnaires in both paper and electronic format. The use of PGHD offers a unique opportunity to fill in gaps in information and provide a more comprehensive picture of ongoing patient health for use during care, resulting in potential cost savings and improvements in health care quality and outcomes, care coordination, and patient safety.

Understanding the potential benefits and concerns surrounding PGHD, ONC began a series of activities in 2012 to increase the capture and use of PGHD to meet the needs of patients, researchers, and providers. Lessons learned from those activities informed this project, which aims to identify best practices, gaps, and opportunities for progress in these seven PGHD topic areas:

1. Collection and validation of data and tools, including mobile health applications and wearable technologies
2. Data donation- consent management/patient preferences and patient expectations
3. Legislative and regulatory gaps
4. Ability to combine PGHD data with medical record data in multiple ways
5. Patient recruitment
6. Data interoperability
7. Big data analysis.

Project Purpose and Goals: This project is developing a white paper that describes the current policy landscape, challenges and opportunities for the use of PGHD in research and care delivery through 2024. The white paper addresses seven topics areas: 1) patient recruitment for research studies and trials; 2) collection and validation of data and tools; 3) data donation; 4) ability to combine PGHD with medical record data in multiple ways; 5) data interoperability; 6) big data analysis; 7) regulatory overview. Additionally, the project conducted pilots that tested the concepts discussed in the white paper.

The project objectives are to improve the collection and use of PGHD in research and care delivery by:

- Identifying challenges and opportunities that support the capture, use, and sharing of PGHD; and
- Conducting pilots to test the concepts discussed in the white paper.

Conducting pilots to test the concepts and implementation of Policy Framework

Contributions to PCOR Data Infrastructure Functionalities:

- *Collection of Participant-Provided Information.* The white paper and practical guide support the sharing and use of PGHD. The increased use of tools and applications to collect PGHD (e.g., from mobile devices, PRO assessments, remote monitoring devices) offers an opportunity for patients to be more engaged in their health care and can facilitate joint patient-clinician decision-making.[xxii] The white paper provides useful insights that describe the current policy landscape, challenges, and opportunities that can be used by a variety of stakeholders to support the capture, use, and sharing of PGHD. The practical guide offers suggested practices and questions for stakeholders to consider when implementing the capture, use, and sharing of PGHD in the clinical and research settings.

- *Standardized Collection of Standardized Clinical Data.* The insights from the project deliverables can be used to inform future policies and guidance that promote standardized data collection of PGHD, increase its consistency and utility for research, clinical uses, and other analytic activities.

Accomplishments and Deliverables: This PGHD project has concluded and ONC has successfully accomplished the following:

- The white paper was completed and shared publicly on HealthIT.gov along with a supporting infographic.
- The two pilot demonstrations concluded at the end of 2017. In one pilot demonstration, Validic and Sutter Health partnered to test personalized care that leveraged remotely-collected PGHD across patients participating in a diabetes-focused research study. In the other pilot demonstration, TapCloud, worked with AMITA Health, to gather PGHD across several medical conditions, such as orthopedic surgery, stroke, behavioral health, and kidney transplant.
- The pilot demonstrations informed the development of the practical guide, which offers suggested practices for implementing of the capture, use, and sharing of PGHD in clinical and research settings. The guide and a supporting infographic are publicly available and published on ONC's website.

Disseminated Products:

- The final version of the white paper is called Conceptualizing a Data Infrastructure for the Capture, Use, and Sharing of Patient-Generated Health Data in Care Delivery and Research through 2024. The white paper was published in January 2017 and is available here: https://www.healthit.gov/sites/default/files/onc_pghd_final_white_paper.pdf.
- The white paper Infographic is available here: https://www.healthit.gov/sites/default/files/onc_pghd_final_white_paper_infographic.pdf.
- Funded by an FDA grant, the Duke-Margolis Center for Health Policy, convened a workgroup to create an action plan for accelerating the use of PGHD in research. The working group used the draft white paper to inform their discussions and was referred to in the Duke-Margolis Center action plan as a resource to readers, which is available here: https://healthpolicy.duke.edu/sites/default/files/atoms/files/mobilizing_mhealth_innovation_for_real-world_evidence_generation.pdf
- Conceptualizing a Data Infrastructure for the Capture, Use, and Sharing of Patient-Generated Health Data in Care Delivery and Research through 2024 (Practical Guide) was published in January 2018. The Practical Guide is available here: https://www.healthit.gov/sites/default/files/onc_pghd_practical_guide.pdf.
- The Practical Guide infographic is available here: https://www.healthit.gov/sites/default/files/onc_pghd_pilot_demonstrations_infographic.pdf.

Leveraging Project Products: This project confirms there is strong potential for the use of PGHD to supplement research data and support programs like the *All of Us* Research Program, which envisions patient-led data donation and harnessing data from mobile applications and wearable technology. The white paper includes information about the current and future states of the use and sharing of PGHD as it relates to the 21st Century Cures Act's stated priority areas of achieving interoperability and promoting and protecting the privacy and security of health information while facilitating its secure access.

Period of Performance:
6/16/15 – 6/30/18

Federal Point of Contact:
Michelle Murray & Caroline Coy

Creating the Foundational Blocks for the Learning Health Care System: Structured Data Capture

Many PCOR studies rely on patients' clinical information collected and stored in EHRs. The use of this information for PCOR would be increased if relevant patient data (e.g., lab-test results) were defined and collected in a common way, using structured data definitions (i.e., CDEs) that comply with the consensus-derived health data standards (e.g., LOINC, Systematized Nomenclature of Medicine (SNOMED)) that were included under the Meaningful Use and MACRA. Development and adoption of CDE standards will enable interoperability in real-world settings to support PCOR.

Project Purpose and Goals: This project sought to develop the functional and technical specifications necessary to enable an EHR system to retrieve, display, and fill a structured form or template, and store and submit the completed form to an external repository. The goal of this project is to develop, pilot, and ballot technical data standards for CDEs, and to develop an electronic template for use in case reporting. Electronic case reporting refers to the ability of an EHR to automatically identify and report specific cases of interest, and submit this information in a particular format or template to an end-point (e.g., clinical research, public health registry surveillance system).

The project objectives were to:

- Conduct an environmental scan of existing technical standards and current use of data elements in research settings;
- Create a detailed use case document to guide the standards development process;
- Prepare a reference implementation guide for each of the technical standards;
- Develop, select, validate, and ballot standards for CDEs and the electronic case-reporting template. This includes CDE standards for the data elements for the form, the structure and design of the form, a standard for how the EHR interacts with the form, and a standard to enable these forms to auto-populate with data extracted from the EHR;
- Develop, select, validate, and ballot CDE standards for use in PCOR funded by HHS and other entities that use standard health IT terminologies;
- Coordinate with the NIH/NLM's efforts to develop a repository for CDEs and eCRFs that use standard health IT terminology, or value sets; and
- Ensure widespread adoption of standards by engaging vendors and the user community in the development and validation processes.

The standard balloting process improves the proposed standards and is necessary to ensure buy-in from the vendor and user communities, and hence, widespread use of the standards.

Contributions to PCOR Data Infrastructure Functionalities:

- *Use of Clinical Data for Research.* This project aimed to more easily enable use of structured data within EHRs to supplement data collected for other purposes, such as clinical research, patient safety and event reporting, adverse event reporting, public health reporting, and determination of coverage. This work has the potential to improve clinical research by leveraging data already in EHRs, improve comparability of data to better inform research, quality reporting

and ultimately, improve patient care. The project also contributes to the public health, patient safety reporting, adverse event reporting, and clinical research communities by identifying trends, predicting outcomes, influencing patient care, drug development, and therapy choices.

- *Standardized Collection of Standardized Clinical Data.* This project aims to streamline and reduce the data collection burden on health care providers and implement published interoperability standards. This initiative has adopted and enhanced existing standards for forms, data elements, form auto-population, and form transport.

Accomplishments and Deliverables: ONC successfully completed all deliverables for this project.

- The SDC Pilots Phase kicked off in October 2015 with a focus on testing and implementing the Integrating the Healthcare Enterprise (IHE) SDC Profile. The College of American Pathologists (CAP) and the University of California, San Francisco were selected as SDC's two pilot teams. The IHE SDC Profile was successfully tested and demonstrated at the IHE NA Connectathon in 2015, 2016 and 2017, and at HIMSS in 2017. Similarly, the FHIR SDC Profile was tested at multiple FHIR Connectathons. Both pilots demonstrated their work to the community and reported-out on their accomplishments, lessons learned and next steps in October 2016.
- ONC completed its environmental scan and resulting summary of the current landscape of available technical standards available to develop the electronic case reporting form. A detailed use case document was developed to provide the basis for further analysis of the technical standards needed to support practical interoperability for clinical data generated in the health care settings with research data.
- ONC also developed and balloted four standards for the CDE and eCRF through two standards organizations'—HL7 and IHE. The four standards are: 1) standards for common data elements; 2) template (form) for data entry; 3) methods for pre-population or auto-population; and 4) standards for transmission or movement of gathered information. ONC created reference implementation and testing tools for each of the standards that includes conformance testing for CDEs and templates, IHE profiles/functional standards for an EHR's interactions with templates and template auto-population.
- Lastly, the project team developed the SDC Standards Testing Environment and Tools, and corresponding code and documentation, which is being maintained in GitHub.

Disseminated Products:

- IHE SDC Profile (v2.1) successfully published through IHE Quality, Research and Public Health Domain as standard for Trial Implementation in October 2016; http://ihe.net/uploadedFiles/Documents/QRPH/IHE_QRPH_Suppl_SDC.pdf.
- FHIR SDC Profile through HL7. http://hl7.org/fhir/us/sdc/2016Sep/sdc.html.
- SOAP/SAML Implementation Guide: http://hl7.org/fhir/us/sdc/sdc-dataelement.html
- FHIR Data Element Profile: http://hl7.org/fhir/current/sdcde/sdcde.html
- SDC project artifacts are publicly posted and available on the ONC Tech Lab SDC home page here: https://oncprojectracking.healthit.gov/wiki/display/TechLabSC/SDC+Home. Example project artifacts include, the detailed SDC use case document and pilot site final reports of accomplishments and lessons learned,

Coordination for Other Federal Agencies: Since the project's inception, ONC has coordinated its efforts with the NIH/NLM's efforts to develop a repository for CDEs and eCRFs. ONC has completed the

mapping of the AHRQ Data Elements to the Structured Data Capture CDE standards format and has uploaded the format to the NIH/NLM repository.

Leveraging Project Products: Knowledge gleaned from the aforementioned products can inform VPB initiatives, which rely on high quality EHR data, including structured data elements, to ensure accurate reporting of provider performance on quality measures and other indicators. Project artifacts could also inform the initiative around opioids to enable linkages between data sources to facilitate opioid-targeted PCOR. Lastly, there is potential for leveraging the developed implementation and testing tools and testing environment by the *All of Us* Research Program to support standardized data collection from participating Health Care Provider Organizations.

Period of Performance:
7/15/13 – 9/30/17

Federal Point of Contact:
Farrah Darbouze

Security and Privacy Standards for Patient Matching, Linking, and Aggregation

Linking and aggregating patient data from disparate sources cannot be done without "matching" these data in a secure manner that protects patient privacy. Effective patient matching allows users of the data (whether patients, providers, or researchers) to draw correct inferences using the data that have been linked. Without accurate patient matching, stakeholders may inadvertently draw inaccurate conclusions that could significantly impair patient safety and privacy.[xxiii, xxiv] Challenges also arise when policies on data use and patient matching are in conflict.

It is critical to have the ability to uniquely match patients for any infrastructure building around data sharing.

Aggregating records requires strong and standardized methods (i.e., patient matching algorithms) to ensure that data on the same patient are kept together, and that data on different patients are kept separate. These patient matching algorithms rely on analyzing both unique identifiers and personal characteristics of the patient record (i.e., patient attributes) to match records. The accuracy and reliability of patient matching results vary widely due to inconsistent data quality and the variability of algorithms used in matching. For instance, one may believe "John Smith" and the likely misspelled "Jon Smtih" to be the same person. However, even small differences introduce the chance that two patient records do not correspond to the same patient. Measuring this risk and developing risk thresholds is challenging and dependent on the end use of the linked datasets. These issues may be further exacerbated when information collected in the EHR is incomplete making it more difficult to uniquely identify patients across data sources. While there are data exchange standards in place to electronically exchange information across health IT systems, there are no widely adopted standards that consistently address patient identity, authorization, and consent.

Project Purpose and Goals: This project identifies the best patient attributes to address the challenge of linking patients' data across research, clinical, and claims data sets in order to support the PCOR data infrastructure that enables standardization and sharing of patient data across organizations. This project involves work along five distinct tracks.

The project objectives are to:

- Standardize attributes and improve algorithm match rates. Use case(s), environmental scan, standards list, and a specifications/implementation guide will be developed for this portion of the

project. All the patient matching standards will be balloted through a recognized standards development organization (SDO) and piloted with a health IT vendor;

- Create an open source visual tool for patient matching and aggregation. ONC will repurpose an existing set of open source tools, developed for creating synthetic patient records for testing clinical quality measures, to create a patient matching toolkit. The toolkit will allow researchers to: 1) inspect patient match results; 2) quickly create test data for sharing; 3) incorporate results from clinical and claims feeds and PCORnet; and 4) model new patient attributes;
- Create a privacy and security API or PCOR infrastructure security "layer." This privacy and security "layer" (i.e., authentication, authorization, consent, and data provenance) will ensure that the data are being matched: 1) with the appropriate consents; 2) by a user who is authorized to do the matching; and 3) with authentication (i.e., validation that people are who they say they are) of those trying to access the data. The API work will provide the specifications for this layer along with corresponding implementation guides to manage the authentication, authorization, and consent policies necessary for all participants (patients, researchers, providers) to safely retrieve and contribute patient data to the PCOR infrastructure;
- Include clinical data research networks in the piloting and testing of the proposed standards and services; and
- Integrate the National Plan and Provider Enumeration System (NPPES) provider identification as an additional attribute to improve patient matching across sources.

Contributions to PCOR Data Infrastructure Functionalities:

- *Linking of Clinical and Other Data for Research.* Notably, PMAL addressed two potential gap areas identified in the OS-PCORTF evaluation: data quality and methods for facilitating and improving data linkages. PMAL seeks to improve data quality by standardizing patient attributes and algorithms that can be used to reliably perform patient matching across clinical and claims data sets to improve algorithm match rates. These algorithms, alongside the tools developed through this project (e.g., Patient Match Test Harness) enable researchers to more accurately link patient data from different sources, vastly increasing the availability of data for research.
- *Use of Clinical Data for Research.* By addressing issues of data provenance, which has a role in nearly all data use and exchange activities, has the potential to open up new data sources for inclusion in PCOR.[xxv]

Accomplishments and Deliverables: A number of open source tools and resources have been developed under this project.

- ONC secured a commitment of participation from a Community Health Applied Research Network (CHARN) partner to pilot all aspects of the algorithm, data management, and the privacy and security layer at six sites. Pilot testing is now complete; lessons learned will be documented in a series of key findings reports planned for release in June 2018. These reports describe key findings from the inter-related pilot activities to identify, test, and optimize a number of patient

Patient Match Algorithm Challenge

The goal of this prize challenge was to bring about greater transparency and data on the performance of existing patient matching algorithms, spur the adoption of performance metrics for patient data matching algorithm vendors, and positively impact other aspects of patient matching such as de-duplication and linking to clinical data.

matching algorithms against data sets previously identified as gold standards for testing purposes, and a Patient Match Algorithm Challenge.

- The Patient Test Match Harness development work has also concluded. This toolkit allows researchers to inspect patient match results, create test data for sharing, model new patient attributes, and incorporate results for claims, clinical, and research network data sources.
- Five final privacy and security profiles were delivered to the OpenID Foundation[xxvi] standards organization promoting the use of OpenID authentication protocols, and submitted to the broader community for public review in the summer of 2017.
- ONC is utilizing the Health Relationship Trust (HEART) Profile, an authentication and authorization protocol to facilitate more consistent user access management. In parallel with this effort, ONC is working to align SMART on FHIR profiles, geared toward provider worklows, with HEART profiles, focused on patient-mediated exchange.
- The API development work is being furthered by two open vendor challenges, the Move Health Data Forward (MHDC) Challenge and the Heath Data Provenance Challenge. The MHDF Challenge invited developers to use the HEART profiles to create an API to enable consumers to authorize the movement of their health data to destinations they choose. The Health Data Provenance Challenge seeks to address the challenges of data provenance and the lack of related meta-data standards.
- ONC has completed its deliverables for the NPPES work to support the provider directory integration of the NPPES. As a result, ONC and the Federal Health Archtecture have formed a collaborative, the Healthare Directory Technology Learning Community, to explore health care directory governance and sustainabiltiy issues.

Disseminated Products:

- The Patient Match Test Harness is publicly available for download from GitHub here: http://mitre.github.io/test-harness-interface/.
- The privacy and security reference implementation resources are available on GitHub here: https://github.com/mitreid-connect/OpenID-Connect-Java-Spring-Server/. The API profile specifications are available here: https://openid.bitbucket.io/HEART/.
- The Health Data Provenance Challenge is ongoing. Additional information can be found here: https://www.cccinnovationcenter.com/challenges/provenance-challenge/.
- The Move Health Data Forward Challenge has ended. Additional information can be found here: https://www.healthit.gov/buzz-blog/interoperability/announcing-winners-move-health-data-challenge/

Leveraging Project Products: The PMAL patient matching work is relevant to a number of HHS PCOR initiatives that link data sets together to make more informed decisions for patient care. For example, for VBP programs that rely on care coordination and population health management, it is necessary to match and link data on individual patients from both clinical and administration data. Researchers from Harvard University have been implementing a proof of concept that utilizes the patient match toolkit as integration to i2b2.

Period of Performance: 6/16/15 – 9/30/18
6/16/15 – 9/30/18

Federal Point of Contact:
Debbie Bucci

Creating the Foundational Blocks for the Learning Health Care System: Data Access Framework

EHRs have the potential to provide useful information for PCOR by aggregating patient data across disparate systems. Many current PCOR projects rely on patients' clinical data collected from site- or system-specific EHRs. While other ONC activities focus on standardizing the way the EHR data is collected within EHRs, building on near widespread adoption of EHRs utilizing standard data and vocabulary requirements as specified by Meaningful Use and Medicaid and CHIP Reauthorization Act (MACRA), researchers also need standardized ways to access that data. This project is a critical next step to enabling and simplifying data aggregation across widely distributed EHR systems (i.e., distributed population queries).[xxvii] To accomplish this goal, ONC developed an API that "connects" to a provider's EHR to extract data in a standard way. An API is a technology that allows one software program to access the services provided by another software program.[xxviii]

Project Purpose and Goals: The goal of this project was to develop technical standards for how health care providers, researchers, and the public health community access, query, and aggregate EHR data for multiple patients across multiple organizations using a standard mechanism in order to conduct PCOR. The project has three phases each building on the capacity developed in a prior phase.

ONC has balloted and pilot tested three implementation guides. These implementation guides make it easier for researchers and research networks to perform queries in a consistent and reproducible way.

The project objectives are:

- *Local DAF (DAF 1):* Intra-organizational query allows providers to access data in their own EHR in a standardized way. The API focuses on a standard way for providers and internal researchers to extract patient, practice, and outcomes data from the EHR. ONC developed use cases to develop a standard way to query an EHR and a standard format for how that data is returned.
- *Targeted DAF (DAF 2): Inter-organizational query* added a standardized interface to DAF 1 to allow outside researchers to remotely access another organization's EHR data. This phase focused on robust, secure authentication and authorization of the researcher for access to EHR data.
- *DAF for Research (DAF 3):* Leveraging both DAF 1 and DAF 2, ONC's work focused on the development of a capabilities to standardize distributed research queries. This phase built upon ONC's former Standards and Interoperability (S&I) Framework Query Health Initiative, aimed at identifying standards and services to support distributed population queries for large scale research.

In each of the phases, ONC established and balloted draft standards through an open and consensus-based standards organization tested and piloted the standards, and develop testing and certification tools to support consistent and interoperable implementations.

Contributions to PCOR Data Infrastructure Functionalities:

- *Use of Clinical Data for Research*. DAF addresses a number of challenges experienced by research network participants, such as barriers to extracting data from clinical data sources, complex data mappings, and the lack of standards for query and query results and specified modular standards for transport, security, query structure, query results, and information

models.[xxix] By creating standard query mechanisms, researchers can more easily compose and conduct research network queries, aggregating patient-level clinical data on multiple patients for PCOR.

Accomplishments and Deliverables: All three phases of the DAF initiative are complete. The first two phases (DAF 1 and DAF 2) were completed in Federal Fiscal Year 2014. Phase three, DAF for Research (DAF 3) standards and pilot testing, concluded in early 2017. The DAF initiative standards have been defined within three implementation guides, balloted through IHE or HL7. The DAF implementation guides are intended for vendors, SDOs, and researcher network IT teams.

Disseminated Products:

- Health Level Seven (HL7) FHIR® US Core Implementation Guide (IG) Release 1 (formerly known as DAF Core).[xxx] The US Core Implementation Guide specifies a set of core data elements (closely aligned with the common clinical data set) and APIs that can be used to extract those elements. The implementation guide is available here: http://hl7.org/fhir/us/core.
- The IHE Data Access Framework (DAF) Document Metadata Based Access Implementation Guide. [xxxi] This Implementation Guide specifies the metadata standards associated with the clinical information accessed using the US Core Implementation Guide The implementation guide is available here: http://ihe.net/uploadedFiles/Documents/PCC/IHE_PCC_IG_DAF_National-Extension.pdf.
- Health Level Seven (HL7) FHIR® DAF for Research Implementation Guide (IG) Release 1. [xxxii] The DAF for Research Implementation Guide specifies the standards to enable researchers to access data from multiple organizations. The DAF for Research implementation guide is available here: http://hl7.org/FHIR/us/daf/2016Sep/daf-research.html.
- The DAF Initiative artifacts and document resources are publicly available on an ONC-hosted wiki: https://oncprojectracking.healthit.gov/wiki/display/TechLabSC/DAF+Home. The artifacts hosted on the DAF wiki include a detailed overview of the initiative, access to past meeting materials, DAF SDO ballot artifacts and publications, and DAF for Research reference materials and pilot deliverables.
- The ONC project lead presented a poster at the 2017 AMIA Annual Symposium. The poster, titled, "Creating a Framework to Standardize Data Extraction from Electronic Health Record Systems for Researchers and to Support Distributed Queries" described the background, challenges, and methods used to address those challenges in order to successfully complete DAF for Research (DAF 3).

Leveraging Project Products. DAF has the potential to support efforts like the *All of Us* Research Program and other large-scale research studies. The DAF for Research query specifications were piloted using two common data models (i.e., the PCORnet and OMOP CDM) promoting more wide-spread implementation across research networks that use different CDMs.

Period of Performance:
11/1/13 – 9/30/17

Federal Point of Contact:
Farrah Darbouze

IX. Cross-Agency Funded Projects

Seven OS-PCORTF projects are jointly funded collaborations between federal agencies: 1) Privacy and Security Blueprint, Legal Analysis and Ethics Framework for Data Use, and Use of Technology for Privacy; 2) Development of a Natural Language Processing Web Service for Public Health Use; 3) Advancing the Collection and Use of Patient-Reported Outcomes through Health IT; 4) Technologies of Donating Medicare Beneficiary Claims Data to Research Studies; 5) Developing a Strategically Coordinated Registry Network to Support Research on Women's Health Technologies; 6) Harmonization of Various Common Data Models and Open Standards for Evidence Generation; and 7) Enhancing Data Resources for Researching Patterns of Mortality in PCOR: Projects 1 - 4. While working collaboratively to accomplish shared goals, the Federal agency awardees have distinct project activities.

Privacy and Security Blueprint, Legal Analysis and Ethics Framework for Data Use, and Use of Technology for Privacy

The Privacy and Security Blueprint, Legal Analysis and Ethics Framework for Data Use and Use of Technology for Privacy project is a joint project between the CDC and ONC. Patient-level data are essential to understanding and improving health outcomes. These data must be made available to researchers in a way that ensures the protection of patient privacy while providing sufficient granularity to allow meaningful research questions to be assessed. However, current laws and policies around the use of patient level data are nuanced and sometimes conflicting, creating confusion for researchers, providers, and patients.

Making PCOR data-sharing a reality requires addressing many privacy and security-related policy issues. This project is addressing these issues by: 1) conceptualizing and developing a privacy and security data infrastructure blueprint; 2) conceptualizing and developing the legal analysis and ethical frameworks needed to balance individual privacy rights with data use, sharing, and disclosure for PCOR; and 3) identifying, refining, harmonizing, validating, recommending, and piloting standards that support individual consent and preferences for research.

Project Purpose and Goals: ONC will develop a privacy and security data infrastructure blueprint, legal analysis, and ethical framework to address the many legal and privacy and security-related policy issues that affect the use of data for various types of PCOR. The CDC is leading the analysis of the public health legal and ethical analysis for use broadly and will supplement the overall privacy and security data infrastructure blueprint developed by ONC. In particular, the analysis will explore CDC's traditional data collection activities in the context of supporting individually identifiable data for PCOR.

The CDC project objectives are to:

- Conduct an "as-is" analysis of public health laws and ethical considerations that relate to the release and use of CDC public health and health surveillance data. These data include public health data generated or collected by the CDC and generated or collected by other agencies or organizations using CDC funds. The "as-is" analysis includes an environmental scan, analysis of findings, and gap analysis, each of which will result in a report;
- Convene a work group of public health legal and ethics experts to inform the "as-is" analysis and provide a "view" of agency wide data use and report of findings;

- Prepare a final white paper of findings and recommendations for best practice practices for data release beyond CDC, and provide guidance to researchers interested in using CDC data for PCOR; and

ONC project objectives are to:

- *Privacy and Security Data Infrastructure Blueprint:* This portion of the project will identify common PCOR use cases and diagram user scenarios/stories. These use cases will faciliate privacy and security analysis of the privacy and security requirements for PCOR infrastrcuture based on the identified user stories. ONC will engage with a braod spectrum of PCOR stakeholders to identify and diagram these use cases.
- *Legal Analysis and Ethical Framework:* The purpose of this framework is to enable PCOR researchers to analyze and evaluate their data needs against federal privacy, public health, and security laws. This will rely on a consistent understanding of the legal obligations related to privacy, confidentiality, and security of data to determine if and how PCOR can support those obligations. This framework will also include a legal and regulatory gap analysis of privacy and security protections, models of data flows mapping to privacy and security legal requirements, identification and definition of updates to policies and minimum requirements for de-identification and re-identification, and ethical implications (CDC lead) for PCOR data use.
- Conduct an enviornmental scan and gap analysis of consent management technologies for research.
- Develop and ballot standards for capturing and sharing patient consent for PCOR.

Contributions to PCOR Data Infrastructure Functionalities:

- *Standardized Collection of Standardized Clinical and Claims Data:* The project explored use cases focused on the collection and use of clinical and administrative data.
- *Collection of Participant-Provided Information.* The project explored several use cases focused on the collection and use of PPI for PCOR.
- *Linking and Use of Clinical and Other Data for Research.* The project explored use cases focused on the linking of clinical data with other data sets, held by different business entities.
- *Use of Clinical Data for Research.* The project explored use cases that highlight the privacy and ethical considerations of using clinical data for research. These are all gap areas identified in the OS-PCORTF portfolio evaluation.

CDC Accomplishments and Deliverables: The CDC is in the final stages of approval on the final White Paper, which will close out the project's deliverables.

- The environmental legal and ethical scan and analysis of findings reports are complete, having focused on data de-identification as a useful tool to further PCOR and the need for clarity surrounding the use of a single IRB versus multiple IRBs.
- CDC has also created a gap analysis to determine whether the current state of laws and ethical considerations that govern public health data release meet specific public health or health data release needs.
- Finally, CDC has created a final framework that analyzes hypothetical scenarios and provides assistive questions to guide readers through legal and ethical considerations

Disseminated Products:

- The final white paper is in clearance and has yet to be disseminated.
- Presented to external audience at the PRIM&R Advancing Ethical Research Conference in San Antonio on November 8, 2017. Audience included members from IRB's and other research institutions, as well as federal agencies. Title of panel presentation: The Boundaries of Privacy and Public Health Concerns.
- Presented on the Ethical Framework to an internal CDC audience on November 17, 2017 as the second speaker as part of an ethics seminar.

ONC Accomplishments and Deliverables: ONC's completed deliverables include the recently released "Legal and Ethical Architecture for PCOR Data ("Architecture").

- The development of the Architecture was informed by subject matter expert input and discussions on the development of PCOR data use scenarios, and an ensuing policy and legal and ethical gap assessment. The Architecture is a collection of tools and resources to help researchers navigate this complex legal and regulatory environment.
- For the technology-related components of the project, or The Patient Choice Technical Project, ONC completed the enviornmental scan and gap analysis of consent management technologies for research.
- Informed by its environmental scan, ONC completed the first round of 'Basic Consent' (Treatment, Payment, and Operations) use case pilot testing, and has developed a best practices implementation white paper based on the lessons learned from the pilot efforts. Pilot testing around two additional use cases (research consent leveraging FHIR specifications) and granular consent (in the context of HIE) is in progress.

Disseminated Products:

- ONC published the "Legal and Ethical Architecture for Patient-Centered Outcomes Research (PCOR) Data ("Architecture") available here: https://beta.healthit.gov/topic/legal-and-ethical-architecture-patient-centered-outcomes-research-pcor-data-architecture.
- Presented at HL7 Educational Session on June 29, 2017. This presentation reviewed the Phase 1: Basic Choice for TPO piloting efforts and outcomes as related to HL7 FHIR.
- Patient Choice Demo at HIMSS 2017
- Hosted HL7 FHIR Connectathon Consumer Centered Data Exchange demonstration in collaboration with project partners.

Coordination with Other Federal Agencies: The team held regular meetings with the ONC Patient Choice Technical Project, which was analyzing and developing standards to fulfill the technical capability for implementing and sharing individual consent (basic and granular choice) for health information exchange in healthcare and research settings.

CDC Period of Performance:
7/10/15 – 9/30/17

CDC Federal Point of Contact:
Carissa Holmes

ONC Period of Performance:
6/16/15 – 9/30/18

ONC Federal Point of Contact:
Rose-Marie Nsahlai

Development of a Natural Language Processing Web Service for Public Health Use

The Development of a Natural Language Processing (NLP) Web Service for Public Health Use is a joint project between the CDC and the FDA. NLP identifies and codes isolated clinical concepts in order to extract meaningful information and represent events from free-text.[xxxiii] The CDC and FDA are leveraging a recently developed NLP system to "translate" unstructured, free-text data submitted to existing agency surveillance systems into a structured form.

In the U.S., central cancer registries collect, manage, and analyze longitudinal data about cancer cases and cancer deaths. Cancer data are collected from multiple sources such as hospitals, laboratories, physician offices, and independent diagnostic and treatment centers. Hospital reporting of cancer cases has been standardized for over a decade; however, as the provision of cancer care has shifted away from the hospital, registries have had to expand their data collection efforts to include data from non-standard systems that contain large amounts of unstructured data. The CMS EHR Incentive Program, established under HITECH Act, established support for widespread adoption of EHRs and data and transmission standards to facilitate interoperable data exchange. The public health measures under Meaningful Use included specific cancer registry reporting requirements that facilitated the collection of structured cancer data from provider EHR systems. Additionally, over 90% of cancer cases are diagnosed using methods that generate pathology reports that are often documented in the form of unstructured text. The process of abstracting these crucial cancer data is very labor intensive and expensive.

This unstructured data limits the ability of researchers to analyze the information without manual review. Similarly, a considerable amount of clinical information submitted to the FDA Spontaneous Reporting Systems is unstructured. One of the FDA's major responsibilities is the post-marketing safety surveillance through the review of spontaneous reports submitted to the Vaccine Adverse Event Reporting Systems (VAERS) and the FDA Adverse Event Report System (FAERS). The adverse events description in VAERS and FAERS data are coded to the Medical Dictionary for Regulatory Activities (MedDRA) terms—a library of standardized medical terminology to facilitate sharing of regulatory information (e.g., registration, documentation, and safety monitoring) for medical products used by humans both before and after the product has been approved for use.[xxxiv] However, a considerable amount of clinical information in both systems is either not coded (e.g., medical and family history) or is not linked to the MedDRA codes (e.g., exact time information for each symptom). Additionally, there may be duplicate entries for the same event, a phenomenon that impacts the surveillance process, requiring manual review of submitted reports to trace the adverse event.

Project Purpose and Goals: This project proposes to develop an NLP service that will be accessible and publicly available to researchers on the Public Health Community Platform (PHCP)—a cooperative platform for sharing interoperable technologies to address public health priority areas aimed at improving population health outcomes and health equity (e.g., tobacco use).[xxxv] The NLP service will enable functionality that processes spontaneous report narratives, extracts clinical and temporal information from the text, formats the data for presentation, and maps unstructured medical concepts (e.g., cancer data and safety surveillance data) into structured and standardized data (i.e., International Classification of Diseases 10th Edition Clinical Modification (ICD-10-CM), LOINC, SNOMED, and Medical Dictionary for Regulatory Activities/MedDRA).

As a joint project, some project deliverables will be coordinated by a lead organization; as noted below.

The project objectives are to:

- Refine and/or harmonize health IT standards that can be used to support sharing of PRO data through APIs and Conduct an "as-is" environmental scan and literature review of exiting NLP algorithms, methods, and tools to inform the development of the NLP Web Service (FDA lead; CDC contributor);
- Design the NLP Web Service technical requirements (CDC lead; FDA contributor);
- Build structured datasets using CDC and FDA resources to capture data;
- Pilot the NLP Web Service on the PHCP;
- Evaluate the pilot; and release the final NLP Web Service.

Contributions to PCOR Data Infrastructure Functionalities:

- *Use of Clinical Data for Research*. This project will support the use of narrative text data captured in electronic health systems for research by converting the text to standardized coded data. This will also improve data quality for research.
- *Use of Publicly Funded Data Systems for Research.* This functionality was identified as a potential gap area in the OS-PCORTF portfolio evaluation and this project addresses the gap in using publicly-available repositories by working with cancer registries and safety surveillance domains. Cancer registries contain valuable information on cancer cases and deaths sent from various sources. Many parts of medical records, laboratory reports, and other clinical reports submitted to these registries remain in narrative text format. Similarly, the FDA Spontaneous Reporting Systems (SRS) receives a substantial amount of clinical information on vaccine, blood products, and drugs that are not coded or linked to the appropriate Medical Dictionary for Regulatory Activities (MedDRA) terms. This project aims to use the NLP Web Service to receive unstructured clinical information and return standardized data needed for CDC cancer surveillance and FDA safety surveillance domains.

Accomplishments and Deliverables: Since work on the project began in June 2016, the CDC and FDA project teams have completed several deliverables in support of the NLP web service.

- The project team completed an environmental scan of existing NLP tool algorithms and a literature review that identified existing clinical NLP systems that generate structured information from unstructured free text.
- The FDA team finalized the selection of the safety surveillance use cases for incorporation into the pilot version of the NLP Workbench Web Service and identified existing solutions to support these uses cases, and determined the required software development.
- The FDA also built the NLP Workbench prototype in the FDA's environment and shared knowledge and code with the CDC to support the development of the web-based NLP Workbench being developed by the CDC team.
- The CDC project team developed the high-level conceptual architectural design of the NLP Workbench Web Service, "Clinical Language Engineering Workbench (CLEW)". The CDC has designed initial web portal page content for the CLEW, installed the Language Application (LAPPS) Grid instance on the platform, and developed a draft technical web services technical report. The LAPPS Grid provides access to and deployment of language resources and processing functions available from servers around the globe.

- The eMaRC Plus application is used by central cancer registries to receive and process cancer pathology and biomarker data that are received in unstructured narrative text format. The CDC is further developing the eMaRC Plus application to interface with CLEW web services to process unstructured pathology data. The CDC completed a functional requirements document detailing enhancements of eMaRC Plus to interface with the CLEW web service titled "eMaRC Plus Functional Requirements."
- The CDC team received all of the de-identified pathology reports for their pathology pilot project, giving them a total of 2,000 pathology reports to train the pathology language model in the CLEW. The FDA completed annotation of 1,000 post-market vaccine reports.

The CDC has collected de-identified pathology data for four primary cancer sites (breast, lung, prostate, and colorectal) from three national labs and the Cancer Canada. They have used this data to create a language model which will be used to train the NLP web service to process pathology data.

Disseminated Products:

- The environmental scan resulted in literature review titled, "Natural language processing systems for capturing and standardizing unstructured clinical information: A systematic review"[xxxvi] and was published in the September 2017 issue of the Journal of Biomedical Informatics, and a manuscript submitted for potential presentation at the AMIA 2018 Summit.
- June 2017 North American Association of Central Cancer Registries (NAACCR) 2017 Annual Conference presentation: Development of Natural Language Processing (NLP) Workbench Web Services[xxxvii]
- Presented at the "Natural Language Processing and Machine Learning Workshop" organized by NIH/NCI in December 2016 and at an ASPE-organized webinar in April 2017
- A Conceptual Architectural Design of the CLEWNLP Workbench Web Services provides an overview of the Workbench, which includes user interfaces, web service components, NLP applications, and offline components

The FDA and CDC, in collaboration with NIH/NCI, hosted a Clinical Natural Language Processing Workshop on December 18-19, 2017 in Atlanta, Georgia. The workshop focused on structured data extraction, classification, and consolidation from heterogeneous free text documents.

Coordination with Other Federal Agencies: In April 2017, the CDC and FDA held a webinar, which was attended by over 60 participants from Federal agencies, state health departments, and universities who have expertise and/or an interest in NLP and machine learning. The insight gained during this webinar was used to further develop the design of the NLP Workbench Web Services. The FDA and CDC leads also met with the National Science Foundation to learn about their open source platform, LAPPS Grid, which is an interoperable web service platform for NLP research and development. They also discussed a possible collaboration with the National Science Foundation (NSF) to further expand the LAPPS Grid to incorporate clinical care and public health use cases. The CDC and FDA met with NIH/NCI several times throughout 2017 to continue their collaboration on this project.

The CDC and FDA submitted a Capstone proposal with National Library of Medicine to identify a permanent home for the CLEW, but unfortunately it was not funded. The CDC is talking with NCHS at CDC to share the CLEW with them to support their recently funded OS-PCORTF Opioid Project. They are interested in using CLEW to build their model and implement its use across public health and PCORI researchers.

Leveraging Project Products: The NLP Web Service has the potential to be useful for many HHS priority areas given that it will be a "generalized" open source service configured to meet NLP data needs in any research domain. This project supports the 21st Century Cures Act by helping researchers harness data from diverse "real world sources" that may be difficult or time-consuming to access and analyze because they are in unstructured formats. The web service will eventually also enhance data sharing by standardizing unstructured data, which will make it accessible to more researchers. The web service can also contribute to creating structured data elements for the use in quality reporting in VBP programs. VBP programs will need to rely on high quality EHR data, including structured data elements, to ensure accurate reporting of provider performance on quality measures and other indicators. Access to structured clinical and administrative data will also provide a wealth of information for clinicians and researchers focused on the opioid epidemic.

CDC Period of Performance:
6/1/16 – 5/31/18

CDC Federal Point of Contact:
Sandy Jones

FDA Period of Performance:
6/1/16 – 5/31/21

FDA Federal Point of Contact:
Mark Walderhaug

Advancing the Collection and Use of Patient-Reported Outcomes through Health Information Technology

The patient perspective is essential to health care decision making and health management, and can provide important data to inform PCOR. A patient-reported outcome (PRO) is "any report of the status of a patient's health condition that comes directly from the patient, without interpretation of the patient's response by a clinician or anyone else."[xxxviii] PROs provide complementary perspectives to those of providers and can provide insights into many health care facets, such as health status, symptom burden, health behaviors, and quality of life. Given the value of PROs, ONC and AHRQ are conducting a joint project focused Advancing the Collection and Use of PROs through Health IT.

The capacity of EHRs to capture PROs in standardized form is currently limited and underutilized. The Patient-Centered Outcomes Research Institute (PCORI) published a user guide on PRO and EHR integration, and detailed multiple challenges involved with integration options, from the technical and user perspectives (i.e., provider, patient, and researcher perspectives).[xxxix] Providers/health systems wishing to integrate PROs directly into EHR systems may need to work with EHR vendors or IT teams to properly customize and present the PRO questions to patients. Additionally, the EHRs may not be optimized to leverage the PRO data for clinical, research, or administrative needs. Patients may find logging into an EHR portal at home to record their PROs to be more burdensome than reporting their outcomes on paper handouts. Collecting paper PRO assessments and scanning them into EHRs is an option, but it creates its own unique challenges, such as extra manual processes and workflows, and reduced opportunity for user-friendly displays and automated clinical decision support. A separate system could be used to collect PRO data and then integrate the data into the EHR. However, utilizing two systems may be expensive, require additional IT expertise, and be less secure. The lack of standards for collecting and integrating PRO represents an additional hurdle. This project aims to widen the availability of PRO data for PCOR through supporting standardization and promoting the development of PRO collection applications.

Project Purpose and Goals: The purpose of this project is to develop user-friendly applications for standardized PRO data collection and integrate PRO data into an EHR or other health IT systems.

The PRO project objectives are:

- Refining and/or harmonizing health IT standards that can be used to support collecting and sharing of PRO data through relevant health IT products for clinical care and research;
- Supporting the development of user-friendly, PRO-collection applications that utilize the health IT standards; and
- Implementing private/public partnerships for pilot-testing these applications in a health system that supports both healthcare delivery and research.

Contributions to PCOR Data Infrastructure Functionalities:

- *Collection of Patient-Provided Information.* This project involves using standards which will enable easier sharing of PROs between patients, providers, and researchers. PRO data collection applications will be developed through a developer competition, and then pilot-tested in a health care system. The current state of PRO use will also be explored. Data capture standardization would improve the interoperable sharing of PRO data across providers.
- *Use of Clinical Data for Research.* This project will include developing implementation specifications that improve the standardization of the PRO data, thereby improving the potential usability of the data for research.

Accomplishments and Deliverables: Since the project commenced in January 2017, the project has made progress toward completing its first objective.

- ONC drafted a summary of key informant interviews regarding current PRO use for functional status assessments, standards for electronic capture and use of PROs, and research programs and networks that use functional status to study patient outcomes.

Coordination with Other Federal Agencies: The NIH, FDA, CMS, and HRSA are providing advice for this project. NIH is advising on work related to the Patient-Reported Outcomes Measurement Information System (PROMIS)[xl], whose PRO measures will be considered and tested for the standards refinement task. CMS and FDA will provide advice regarding how standards would be applied to their regulatory needs. HRSA is providing advice regarding the applicability of deliverables for the safety-net population.

Leveraging Project Products: This project has potential connections to three HHS initiatives. The *All of US* Research Program relies on the donation of patient lifestyle and environmental data, and therefore stands to benefit from more readily accessible PRO data. The 21st Century Cures Act emphasizes the use of diverse "real world" data, and this project's support for the sharing of PRO data through APIs will make the collection and use of "real world" data easier as well as diversify it by providing an alternative to provider-reported assessments. Lastly, value based programs will benefit from the incorporation of PROs with clinical data so that health care providers can provide "whole-person oriented" patient care and so that these data can be used for more complete quality reporting.

AHRQ Period of Performance:
1/15/17 to 4/15/19

AHRQ Federal Point of Contact:
Janey Hsiao

ONC Period of Performance:
1/15/17 to 4/15/19

ONC Federal Point of Contact:
Margeaux Akazawa

Technologies for Donating Medicare Beneficiary Claims Data to Research Studies

This project is a collaboration between NIH and the CMS to leverage the Sync for Science™ (S4S) and Blue Button® 2.0 programs to enable Medicare beneficiaries to donate their medical and prescription drug claims data for scientific research studies using the Sync for Science (S4S) data donation workflow.

The *All of Us* Research Program (formerly known as the Precision Medicine Initiative Cohort Program) is a national, large-scale research enterprise designed to support discoveries that increase our ability to better treat and prevent disease by enrolling one million or more volunteers. S4S is beginning a provider pilot, using HL7's FHIR standards and CMS' Blue Button 2.0 API to significantly improve the ease of data donation from Medicare beneficiaries to *All of Us*. The FHIR framework translates data into a standardized, structured format that can be accepted by a wide range of applications and the Blue Button 2.0 API simplifies the data transfer.

In practice, the implementation of S4S FHIR and the Blue Button 2.0 API will enable beneficiaries to directly donate their Medicare claims data to research studies in which they choose to participate. This data would be highly valuable to the *All of Us* Research Program, and the lessons learned through this pilot phase could be applied to future efforts that enable individuals to donate their Medicare claims data to the larger medical research community to support a wide range of healthcare studies.

Project Purpose and Goals: This project aims to provide a safe and secure mechanism for Medicare beneficiaries to donate least three years of their individual Medicare claims data to scientific research studies. NIH will be the lead agency, developing the technical guidelines and CMS will leverage its previous work (i.e., a FHIR-based API, launched as Blue Button 2.0, to enable beneficiaries to connect their Medicare claims to third-party applications and services they trust) to allow data donation to S4S/*All of Us*.

The two teams would work in concert to achieve the following specific goals:

- Finalize a CMS-defined profile for the FHIR financial resources including (at least) Explanation Of Benefit (EOB) in FHIR System for Trial Use version 3 (Stu3) format
- Expand S4S resource definitions to include this CMS profile on the FHIR EOB resource
- Ensure that CMS's Blue Button API supports the S4S permissions and API calls to retrieve EOB and patient resources
- Ensure that CMS's Blue Button API is compatible with the S4S authorization specifications (SMART on FHIR)
- Deploy S4S support into the CMS Blue Button 2.0 API for a pilot patient population
- Conduct an S4S pilot in which CMS Medicare beneficiaries donate their claims data to *All of Us* via the CMS Blue Button 2.0 API

Accomplishments and Deliverables: Since work on the project began in September 2017, the project team has made progress on several activities, which will eventually result in the team publishing their documented source code to an open platform for sharing; and creating and publishing documentation for all APIs, user experience guides, and reference tools online in a format available to the public.

CMS launched the Blue Button 2.0 production API on March 6, 2018. This means that app developers can now request production access to the API, which will then allow Medicare beneficiaries to share their

claims data with third-party applications they choose to trust. S4S/*All of Us* will be able to connect to this production API in this manner.

Coordination with Other Federal Agencies: This project is a collaboration between NIH and CMS, with support from ASPE, which will involve ongoing joint and independent activities working toward project goals.

Contributions to PCOR Data Infrastructure Functionalities: This project addresses the services and standards components and two of the five functionalities of the HHS Strategic Framework:

- *Linking of Clinical and Other Data for Research.* This project will allow researchers to collect longitudinal patient information from Medicare and to link data sets with other relevant information for NIH-led research.
- *Use of Enhanced Publically-Funded Data Systems for Research.* This project leverage current investments in federal data infrastructure to inform future infrastructure development—combining advances in Blue Button on FHIR (Blue Button 2.0) and S4S to enhance data collection by the *All of Us* initiative.

Both functionalities were identified as a potential gap area in the RTI evaluation.

Leveraging Project Products for HHS Initiatives: The API has immediate potential to facilitate data donation to NIH's landmark *All of Us* initiative, increasing the ease and volume of longitudinal data that can be collected from Medicare patients. Lessons learned through this pilot phase could be applied to future efforts that enable individuals to donate their Medicare claims data to the larger medical research community to support a wide range of healthcare studies. In addition, the API-related documentation, source code, user experience guides, etc., will be open source so that other federal agencies and the public can make use of them. This has the potential to be useful for many HHS priority areas and research domains. For example, this project will support efforts in alignment with the 21st Century Cures Act to help researchers harness data from diverse "real world sources," allowing direct data donation from patients, as well as from diverse health systems. Similarly, these tools could facilitate data gathering for opioid-related research.

NIH Period of Performance:
9/7/17 – 4/29/19

NIH Federal Point of Contact:
Ed Ramos

CMS Period of Performance:
9/7/17 – 4/30/18

CMS Federal Point of Contact:
Carly Medosch

Developing a Strategically Coordinated Registry Network to Support Research on Women's Health Technologies

The Developing a Strategically Coordinated Registry Network (CRN) to Support Research on Women's Health Technologies is a joint project between the FDA, NIH/NLM, and ONC, to facilitate PCOR focused on women's health by connecting three existing registries and several other federal data sources (e.g., Sentinel, claims data, PCORnet). The Women's Health Technologies CRN (WHT-CRN) was initiated to improve clinical evidence generation and to better answer clinical questions on medical device technologies in clincal areas unique to women. Initially, the WHT-CRN focuses on three clinical areas: sterilization and long-acting contraception, uterine fibroid treatment, pelvic floor disorders and stress urinary incontinence.

Registries provide critical infrastructure that can be used for a variety of analyses related to patient care and outcomes. While single-purpose registries can meet the demand for data on real-world patient care, they can be expensive to maintain, use proprietary data formats, and often focus on a single therapy, when routine care can involve combinations of devices or therapies in multiple care settings. A network of registries, or CRN approach, presents an opportunity to address these challenges. The project will leverage structured data capture standards to extract relevent clinical information from EHRs to populate the registry. WHT-CRN registries will also use standard data elements and measure definitions to harmonize the data available for research. Finally, this data will be shared across registries using standard API interfaces, which can support more complex study designs evaluating the effect of combinations of devices or therapies.

WHT-CRN Registries

- ***COMPARE UF Registry.*** *A nationwide patient-centered outcomes registry of women with uterine fibroids funded by AHRQ and PCORI.*
- ***National Pelvic Floor Disorder Registry.*** *A private-public partnership for FDA mandated post-market surveillance of uro-gynecological mesh devices.*
- ***Collaborative Registry of Sterilization Therapies.*** *Registry infrastructure development supported through the CRN project. The registry will capture elective female sterilization therapies.*

Project Purpose and Goals: The project's primary goals are to establish a CRN for research on women's health technologies; and to develop and test tools for the collection of standardized data and evaluate the completeness and flexibility of the HL7 FHIR exchange messaging standard to support the evaluation of medical devices in clinical areas unique to women.

While working collaboratively to accomplish these goals, lead agency FDA, NIH/NLM, and ONC have a number of additional objectives:

- Convene a community of stakeholders (e.g., patients, providers, manufacturers, EHR vendors, SDOs, researchers, etc.) interested in improving data infrastructure in the area of women's health device safety (FDA lead)
- Establish a multi-stakeholder data governance model (FDA/NIH collaboration)
- Define clinically-meaningful patient-centered outcome measures for each device area using CDEs and value sets specified using standard vocabularies and codes sets (i.e. NLM CDE Repository, the NLM Value Set Authority Center, ONC EHR certification criteria, etc.) (FDA lead)
- Pilot and test FHIR profiles developed by other OS-PCORTF projects (SMART on FHIR platform and the ONC SDC initiative to extract clinical data from EHRs into the CRN (FDA/ONC collaboration)
- Create a harmonized, interoperable platform and reusable tools (i.e., a data sharing framework) that will link the WHT-CRN registries to each other (ONC lead)
- Develop and ballot the HL7 FHIR profiles incorporating the WHT-CRN data elements; conduct a pilot to demonstrate the capture and exchange of data within the CRN (ONC/FDA collaboration)
- Evaluate the completeness of the piloted HL7 FHIR resources for meeting the project's research goals (FDA/NIH/ONC collaboration)

Contributions to PCOR Data Infrastructure Functionalities: This project addresses standards and services across a number of the functionalities needed to build research data capacity.

- *Standardized Collection of Standardized Data.* The use of a data exchange standard like HL7 FHIR provides an opportunity to collect structured, standardized, analysis-ready patient data at

the point of care. Capturing standardized data will streamline data collection and support exchange of data across networks. The resulting data will be not only more consistent across organizations, but also more reflective of real-world evidence, such as supporting the inclusion of both the medication (using the clinical research standards and controlled terminologies) and the implantable device data (available through links to unique device identifier (UDI) data and meta-data available in the Global UDI Database). This standardization supports the increased use of clinical data captured and will allow researchers to collect longitudinal patient information and to link data sets with other relevant information for research (e.g., other research networks such as Sentinel, PCORnet, and available state data infrastructure).

Accomplishments and Deliverables: Significant progress has been made towards defining the CDEs and creating minimum data sets for all three device areas using these CDEs.

- Three clinical working groups were established to address each of the three device areas. The working groups are using a formal consensus to create the core data sets from list of CDEs identified earlier in the project. A working group of informatics leaders representing the FDA, NIH, and ONC was formed to begin the process of translating the clinical data sets, definitions, and value sets into standard vocabularies used in data capture and exchange. While the minimum data sets are will be defined at the device level, the final deliverable will include an overarching data set for all three registries.
- A critical component of this project is the collaborative governance structure established between the clinical and informatics teams, designed to ensure the final deliverables retain their clinical relevance and utility for clinical care, quality improvement, and device surveillance, as well as for research.

Disseminated Products:

- In collaboration with the Medical Device Epidemiology Network (MDEpiNet)[xli], a public-private partnership to improve the infrastructure for medical device evaluation, the WHT-CRN project team developed a website (hosted by MDEpiNet) to raise awareness of the WHT-CRN project. The website is accessible at: http://mdepinet.org/womens-health-crn/ and links to relevant working group activities. Additionally, the FDA project lead presented at the 2017 MDEpiNet Annual Meeting.

Coordination with Other Federal Agencies: This multi-agency initiative has direct representation from other HHS agencies including AHRQ, CDC, and the Office of Women's Health, on its working groups. Notably, there is cross-agency collaboration with AHRQ's Outcome Measures Framework—a conceptual model for developing standard outcome measures. The WHT-CRN team has begun discussions on how to potentially leverage the findings and best practices from this project to inform ARHQ's Outcome Measure Framework. Upon the project's conclusion, NIH/NLM aims to include the data element resources within the NLM CDE Library, promoting the uptake of the standardize CDEs in future research projects.

Leveraging Project Products: The WHT-CRN directly aligns with the objectives of the 21st Century Cures Act by helping researchers utilize data from diverse "real world sources" to efficiently conduct outcomes research and support regulatory decisions. This CRN will serve as infrastructure for the evaluation of medical devices in clinical areas of significance to women's health and will enable data networks to conduct studies reflective of real world combinations of multiple therapies. Furthermore, the development of device-specific FHIR profiles furthers a key goal of interoperability emphasized in the 21st Century Cures Act.

It is expected that the outputs of this project (both the new HL7 FHIR resources and profiles and conceptual lessons learned) can help other registries and OS-PCORTF projects, which are searching for more efficient and sustainable methods of data collection.

FDA Period of Performance:
2/15/17 – 5/15/19

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NIH/NLM Period of Performance:
2/15/17 – 5/15/19

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ONC Period of Performance:
2/15/17 – 5/15/19

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Harmonization of Various Common Data Models and Open Standards for Evidence Generation

In order to achieve a sustainable data network infrastructure, promote interoperability and foster the creation of a Learning Health System as laid out in the Connecting Health and Care for the Nation a Shared Nationwide Interoperability Roadmap,[xliii] there is a need to map and transform data across various CDMs and leverage open-source standards. The Harmonization of Various CDMs and Open Standards for Evidence Generation project is a collaborative project among the FDA, NIH/NCI, NIH/NCATS, NIH/NLM, and ONC. This project aims to leverage existing OS-PCORTF investments, including DAF and the NIH CDE Repository, as well as existing infrastructure (e.g., the NCI cancer Data Standards Registry and Repository (caDSR) and the NLM Value Set Authority), which can help with building reusable data mapping and transformation services. By mapping various CDM data elements and leveraging existing OS-PCORTF investments, it is feasible to reuse the data, methods, and other resources from existing networks (i.e., PCORnet, Sentinel, the Observational Health Data Sciences and Informatics (OHDSI), i2b2).

After mapping the CDMs, the identified observational data will be utilized to evaluate factors associated with the safety and effectiveness of newly approved oncology drugs (immune checkpoint inhibitors, PD1 and PDL1) in combination with other immunotherapy agents. Oncology as a field has recently been transformed by the emergence of immunotherapy in cancer care. As immunotherapy represents an entirely new modality of therapy which has not been commonly used until now, our information about the experience of treating cancer patients with these drugs is largely limited to the clinical trials setting. Observational data is lacking, and in the real world, patients have a wide array of comorbid conditions that may affect the safety and efficacy of these drugs and may not be identified in clinical trials.

By harmonizing various CDMs, the research community will have an opportunity to aggregate more data, resulting in access to a larger sample size and additional demographics (e.g. elderly, pediatrics, non-US population, etc.). For example, PCORnet has a network of approximately 70 million patients from mainly EHR sources. Sentinel has access to 350 million patients from mainly administrative claims plans. By harmonizing the CDMs in these two networks, the researchers will have access to not only EHR data, but to administrative claims data. Researchers will have a unified access tool to multiple networks of observational data. The data itself is a much more robust sample, including patients (i2b2-ACT); national and international networks of EHR and administrative claims (OHDSI); U.S. population in administrative claims (Sentinel); EHRs and registries; and PCORI community-based patients in EHRs. The much larger

and representative patient cohorts also have a greater breadth of information useful particularly for rare events or where a broad international scope will support analysis from a global perspective.

In addition, tools and programs developed by one network of observational data can be re-used by other networks. This solution has the potential to support a diverse range of exploration from basic PCOR queries, to data mining to generate hypotheses for future research, to large-scale sophisticated analysis, including randomized clinical trials.

Project Purpose and Goals: This project will harmonize CDMs developed by four different networks (Sentinel, PCORnet, OHDSI and i2b2-ACT). It will enable researchers in federal agencies or academia to have access to data from a larger network of patients.

Although FDA serves as the lead for the project, the overall scope of the project is shared by a number of agencies working with FDA. The FDA will initially focus on the data elements required to assess the safety of newly approved oncology drugs in combination with other immunotherapy agents. The team at NIH/NCATS will serve as co-leads on this project and will provide informatics and implementation strategy. The SMEs at NIH/NCI will serve as oncology researchers, who will evaluate the proposed solution, identify the data elements needed to assess drug safety, and test it against the oncology use case. NIH/NLM, as the designated central coordinating body for clinical terminology standards within HHS, will provide its expertise, tools and assistance to assure the general applicability and utility of the project products for the PCOR community. ONC will serve as advisors in data standards and proposed approach. Once initial data model mapping are complete from the chosen data models to FHIR/DAF, ONC will convene discussions among data model owners to ensure that these mappings are reflected accurately.

Project deliverables include a mapping tool to serve as the common data architecture; a web-based portal accessible to researchers to map their source data into the target data; and analytics and visualization tools for researchers will be developed as part of this project.

The overall project objectives are to:

- Develop common data architecture as the intermediary between the four research network CDMs.
- Develop a flexible data model that can be used to create outbound data in multiple formats for multiple purposes.
- Test the common data architecture by using it to study factors associated with the safety and effectiveness of newly approved oncology drugs that boost patients' immune response to cancer.
- Establish methods and develop processes, policies and governance for ongoing curation, maintenance and sustainability of the common data architecture, building upon existing resources, standards and tools.

Contributions to the PCOR Data Infrastructure Functionalities:

- *Use of Clinical Data for Research*. This project will ultimately provide PCOR researchers with access to larger and more diverse types of observational data, or data derived from the delivery of health care in routine clinical settings (with appropriate data partner permissions). The enhanced data infrastructure created through this project will have the capacity to support evidence generation on patient-centered outcomes that can inform regulatory and clinical decision making within federal programs.

- *Standardized Collection of Standardized Clinical Data*. A key dimension of this project is to develop standards that support secure, electronic query of structured data across clinical research and delivery systems, including standards for open-source access.
- *Linking Clinical and Other Data for Research.* This project will enable the harmonization of several existing CDMs in order to support research and analyses across multiple data networks. The aim is to advance the utility of data and its interoperability across networks to facilitate PCOR.

Accomplishments and Deliverables: The project team has made good progress on the aims and associated tasks.

FDA

- As an initial step to developing the CDM Mapping Tool, the FDA, in collaboration with source CDMs, NIH/NCATS, and other experts, documented existing CDM artifacts (environmental scan) and their mappings into an aggregate resource. ONC completed an evaluation report that addressed: 1) the feasibility of using an intermediary data model for data extraction (the Federal health Architecture's Federal Health Information Model); and 2) the feasibility of using Model Driven Health Tools in Model-Driven Message Interoperability as tooling capabilities for model mapping and transformations.
- FDA and NHI/NCI oncologists finalized the protocol-based assessment for the safety of immune-oncology products evaluation use case. The health care organization partners that will test the use case have been selected.
- In the fall of 2017, the project team held its first workshop of CDM SMEs to evaluate the overall project architecture.

NIH/NCATS

- The project team, led by NIH/NCATS, surveyed the market for an existing open source ETL software tool to automate the data mapping process and documented their efforts via an environmental scan. After completing an evaluation of existing ETL tools, the team opted to partner with a software and data integration company, to advance this work. This partner will also provide the analytic and visualization package.

NIH/NCI

- The CDMs were mapped to the selected transition model, the Biomedical Research Integrated Domain Group (BRIDG) model. NCI will use this mapping to load the model data elements into caDSR. Information from that test will help customize the ETL tool.

NIH/NLM

- NIH/NLM initiated assessment and exploration of adjustments needed to the NIH CDE Repository to support use of the standards as envisioned by the CDM harmonization.
- NIH/NLM continued the work towards development of an initial strategic plan for needed educational resources to support the CDM tool in the context of other data and terminology resources needed by the NIH clinical research community

Disseminated Products:

- The Harmonization of Various CDMs project was presented at the Drug Information Association (DIA) 2017 Annual Conference (June 2017).

Cross-Agency Collaboration: The project team has engaged with the FDA Cross-Network Directory Service project to explore the re-use of that investment to further this CDM project and better understand

the complexities of mapping query requests across research networks. The project team has also presented within their respective agencies to raise awareness of the work (e.g., FDA CDER Real Work Evidence Workgroup and NCI Genomic Data Commons).

Leveraging Project Products: The products delivered under the auspices of this project will provide the data access, tools and infrastructure needed for researchers to address critical questions that have direct relevance to the HHS priority areas. Specifically, the CDM Mapping Tool will help build reusable data mapping and transformation services. A web-based portal will be built that will allow researchers to map their source data into target data. This infrastructure may be leveraged to increase access to diverse data sources by researchers exploring complex topics including the opioid crisis, for example. It will also support data access from a cloud-based environment, a stated need of the *All of Us* Research Program. Lastly, this project will yield analytics and visualization tools that may be leveraged across HHS initiatives.

FDA Period of Performance:
2/8/17 – 5/7/19

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2/8/17 – 5/7/19

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Enhancing Data Resources for Researching Patterns of Mortality in Patient Centered Outcomes Research: Projects 1 - 4

An important objective of the OS-PCORTF is to build data capacity for PCOR in order to collect, link, and analyze data on outcomes and effectiveness from multiple sources. This group of projects consists of four independently-led but supportive components designed to enhance data resources for researching patterns of mortality in PCOR. They are being undertaken by the CDC, FDA, and CMS, in consultation with each other and ASPE. Mortality is an important outcomes in PCOR and efforts to better harmonize, connect, and enrich the federal mortality data through the four projects described below will accelerate its availability and utility for PCOR.

Project 1 (CDC) – Adding Cause-Specific Mortality to National Center for Health Statistics' National Hospital Care Survey by Linking to the National Death Index. This project will leverage data from CDC's NCHS and CMS to create new data infrastructures for PCOR to advance studies on mortality following hospital care by making "cause of death" available. Together these linkages will enable the development of national estimates of cause-specific death rates following emergency department (ED) visits and/or hospital inpatient stays for specific conditions. In addition, this project will provide the first-ever data linkage of EHR data from a nationally representative U.S. sample to the NDI, enable evaluations of

This project will provide the first-ever data linkage of EHR data from a nationally representative U.S. sample to the NDI.

EHR and claims data on their quality and complementarity, and create new approaches to optimize linkage by using the personally identifiable information available in claims and EHR data.

Project 2 (FDA) – Pilot Linkage of NDI+ to Commercially and Publicly Insured Populations. Information on death and cause of death is often needed in PCOR, but administrative claims and EHR databases generally do not have complete capture of information on fact, cause, and manner of death. This project will develop a standard, repeatable, and efficient process for linking a distributed data network of commercial and public health plans with the NDI+. The capability to link distributed data networks like Sentinel or PCORnet to the NDI+ will enable many types of PCOR, including adverse event surveillance, predictive risk modeling, and comparative effectiveness research.

Project 3 - (CMS) – Enhancing Data Resources for Researching Patterns of Mortality in Patient Centered Outcomes Research. Currently, Medicare and Medicaid research data contain information on fact of death, but only certain years of Medicare data (1999-2008) and Medicaid data (1999-2007) contain information on the cause and manner of death. CMS will link the NDI data on cause and manner of death with claims data to produce updated research files with Medicare descendants data from 2008-2016 and Medicaid decedents data from 2007-2015. Linking health care claims data, including diagnoses with cause and manner of death enables many types of PCOR research, including descriptive epidemiology, predictive modeling to identify high value intervention targets, and comparative effectiveness. The benefit of linkage is particularly high for recent years of data given changes to the programs, e.g. Medicare prescription drug benefits starting in 2006, and Medicaid expansion in many states starting in 2012.

Project 4 (CDC) – NDI Workshop and Strategy Paper. NCHS will work together with FDA, ASPE, CMS, NIH, CDC Centers, states, and others to develop a long-term national strategy on access and use of NDI data particularly to support PCOR. NCHS will hire a Service Fellow expert in vital statistics and contract with the National Association for Public Health Statistics and Information Systems (NAPHSIS) to review/evaluate the outcomes of the MITRE work (Project 2) and to expand on that work in assessing the non-economic barriers limiting access to and use of the NDI data for PCOR. The NAPHSIS will also conduct a state-level assessment of the laws/policies/preferences and perceptions of its members in restricting the use of the death data by the Federal Government and, given those restrictions, explore opportunities for minimizing the barriers to the use of NDI data.

The NDI is the only central data source containing information on both fact and cause of death for all deaths occurring within the U.S. It is heavily used by researchers in medical and health studies, for mortality ascertainment to assess the causes and risk factors of diseases and conditions and for the effectiveness of a wide range of interventions and drug therapies. Together, these projects attempt to build capabilities for systematic and more complete ascertainment of death information that is linkable, shareable across health systems, and more useful to PCOR researchers.

Project Purpose and Goals:

Project 1 (CDC) – This project will link health care claims and EHR data from the NHCS to death record information from the NCHS NDI; and separately to administrative data from the CMS Master Beneficiary Summary File (MBSF) and Chronic Conditions Warehouse (CCW). A data set that includes the 2014 NHCS claims and 2014/2015 NDI linked data will be available to the NCHS Research Data Center (RDC).

Specifically, the objectives of this project are to:

- Link the 2014 NHCS inpatient and emergency department (ED) claims data to the 2014 and 2015 NDI (to ensure at least 12 months of post-discharge follow up for each hospital event),

- Link the 2014 CMS MBSF and CCW to 2014 and 2015 NDI,
- Link the 2016 NHCS inpatient and ED claims and EHR data to the 2016 and 2017 NDI.

Project 2 (FDA) – The project will create the capability to link distributed data networks to NDI+ with the goal of enabling many types of PCOR, and will address the logistical challenges of data linkage across multiple health plans through its primary objectives:

- To develop standard, repeatable, and efficient technical solutions for linking the NDI's death and cause of death data to large, publicly insured populations; and
- To demonstrate the feasibility of linkage by using use cases to assess associations between select medications and death or cause of death as an outcome.

Project 3 (CMS) – The primary objectives are:

- To develop standard, repeatable, and efficient technical solutions for linking the NDI's death and cause of death data to Medicare and Medicaid claims data; and
- To produce an up to date research file of linked data from the NDI on cause and manner of death for decedents in Medicare from 2008 to 2016 and in Medicaid for 2007-2015.

Project 4 (CDC) – The primary objective of Project 4 is to examine the barriers to the access and use of NDI for PCOR (economics, legal, statutory, technical, operational, policy, etc.) and then, using a national workshop approach, attempt to develop a long-term strategy for NDI acceptable to the federal researchers and the states. At a minimum, these meetings and workshop will examine and make recommendations for

1. Altering the economic model used to support NDI;
2. Identifying and minimizing the non-economic barriers to accessing and using NDI;
3. Re-using cause of death data (e.g., sharing the data with other research proposals; multiple use of approved data for other research studies);
4. Improving the efficiency of the administrative aspects of linkages;
5. Improving the timeliness and quality of the NDI data; and
6. Improving the timeliness of the NDI approval process.

The outcome of this project will be a report on the long-term strategy for NDI.

Contributions to PCOR Data Infrastructure Functionalities:

Project 1 (CDC):

- *Use of Clinical Data for Research/Linking of Clinical and Other Data for Research.* This project aims to link multiple types of data including EHR data, claims data and NDI data which will support research related to the inpatient setting as well as post-discharge care and outcomes.
- *Use of Enhanced Publically-Funded Data Systems for Research.* The linkages described in Project 1 will enhance the value of NDI data as well as administrative data sets including the CMS MBSF and CCW.

Project 2 (FDA):

- *Linking of Clinical and Other Data for Research.* In the immediate future, the data created by the linkages from this project will be available to researchers in participating health plans under contract to FDA according to the data use agreements required by the NDI Program. This

addresses a gap identified in the portfolio-wide evaluation of "Developing technical services and standards for services that allow patient data to be securely linked to other data sources."

- *Use of Enhanced Publically-Funded Data Systems for Research.* The project plans to establish services and tools to support data access, querying, and use, including privacy-preserving analytics and queries. These services and tools would be leveraged nationally and are not likely to be developed by the private sector.

Project 3 (CMS):

- *Linking of Clinical and Other Data for Research*. Project 3 will support the further development of key federally-initiated data systems for research. It will also support the enhancement of strategic publicly-funded data systems (including CMS data) to facilitate their access and use, and ease retrieval of data for research purposes.

Project 4 (CDC):

- *Use of Enhanced Publically-Funded Data Systems for Research*. This project will support the enhancement of strategic publicly-funded data systems (including CMS data) to facilitate their access and use, and ease retrieval of data for research purposes, and in particular a coordinated, multi-agency long term strategy for this pursuit.

Accomplishments and Deliverables: Since work on the projects began in February 2017, the project teams have made progress on several early deliverables.

The CDC Project 1 team has made significant progress in linking NHCS data to NDI data. The team has used multiple linkage methodologies to link the 2014 NHCS data collected from inpatient and emergency department settings to the 2014 and 2015 NDI data. The team is currently evaluating the different matching methodologies and has proposed changes to both streamline and increase the match rate. They are also developing an alternative methodological approach for partial agreement weight scenarios.

Project 1 (CDC) reports partial completion of:

- Linked 2014 NHCS claims – 2014/2015 NDI data that will be available to the RDC
- Report on 2014 NHCS claims – 2014/2015 NDI data linkage
- Report on EHR – NDI data linkage

Disseminated Products:

- CDC posted a methodological report describing the linkage of the 2014 NHCS to the 2014/2015 NDI. The report includes a brief overview of the data sources, a description of the methods used for linkage, and analytic guidance to assist researchers while using the files. This report is available here: https://www.cdc.gov/nchs/data/datalinkage/NHCS14_NDI14_15_Methodology_Analytic_Consider.pdf.
- A codebook for the 2014 NHCS claims data linked to the 2014 and 2015 NDI file is available on the NCHS Research Data Center (RDC).

Project 2 (FDA) reports:

- Administrative progress: It has made a contract award to Harvard Pilgrim Health Care who has begun the process to initiate subcontracts with health plans and scientific collaborators and the

process to initiate conversations with NDI to ensure that the single IRB process is accepted by NDI as part of the application development.

- Scientific progress: Protocol development is underway for the proposed technical approach (methods and processes) for linkage and the study team has discussed the selection of use cases from regulatory and scientific perspectives.

Project 3 (CMS) has paid for NDI data and sent a finder file to NDI for matching. Now that CMS has started receiving NDI data, they are in the process of validating and quality checking the data.

Project 4 (CDC) reports progress on several important contracting, planning, and information gathering activities:

- Secured a CMS representative to work with the CDC Division of Vital Statistics Director on the project.
- NCHS awarded a contract to the NAPHSIS to conduct an assessment of the barriers to NDI and the rationale for those barriers from the perspective of the states. The survey instrument was developed and approved by the NCHS Project Officer.
- NAPHSIS has fielded the survey of the perception of state vital registration officials of the laws and statutes governing access and use of the mortality data from the state perspective. The survey had an 88 percent (50 out of 57 jurisdictions) response rate.
- The dates for the national NDI Workshop has been finalized as March 14 – March 15, 2018 and the meeting space secured.
- NCHS conducted a series of interviews with federal researchers and the NDI Advisory Committee about their experiences with NDI and the issues from their perspectives.
- CDC convened the national NDI Workshop from March 14 – March 15, 2018.
- Findings from the assessment, interviews, and Workshop are being used to develop a draft strategic plan to outline the issues identified by all the stakeholders and the strategies to resolve these issues.

Leveraging Project Products: Implementing the Project 1 will further demonstrate the feasibility of linking population-based claims and EHR data to cause and manner of death to support PCOR and public health surveillance. Analyses of data linking NHCS to NDI and to CMS data will help inform consumers, providers and payers (chief among them CMS, which tracks readmissions and mortality for three conditions - acute myocardial infarction, heart failure, and pneumonia), serving both research and quality improvement purposes. This project advances national PCOR data infrastructure by leveraging information on factors such as comorbidities (e.g., CMS' CCW) and coverage (e.g., Medicare Fee-for Service versus Medicare Advantage) that may be associated with hospital-related service utilization and health outcomes. It also has direct applications to value-based purchasing in better linking outcomes (i.e., mortality) to patient health and the care received.

While Project 2 is for a one-time linkage, the resulting standard, repeatable, and efficient technical solution for linking the NDI+ to large commercial health plans data network would make any similar future linkages much simpler. This addresses a priority identified in the 2017 Planning Guide to facilitate linkages among data sources and, specifically, to provide death data to support research on issues like opioids and initiatives like *All of Us*. It will also provide valuable information on how mortality data can inform the evaluation of the safety of FDA regulated products for use in quality improvement and safety monitoring.

Project 3 fills current gaps in the mortality data available in CMS research files, meaning researchers will have improved ability to investigate questions within the Medicare and Medicaid populations. As above, although this is a one-time linkage, the resulting standard, repeatable, and efficient technical solution for linking the NDI+ to CMS data enriches the current research files and would make any similar future linkages much simpler. Linkages between CMS and NDI are frequently called for in the Planning Guide because of their broad applicability for PCOR, as well as for opioid and quality-related research. In addition, lessons in linking to the NDI could be applied to other agencies who currently lack reliable death information for research and/or administrative purposes.

Project 4 addresses the barriers to the access and use of NDI for PCOR (economics, legal, statutory, technical, operational, policy, etc.) and then, using a national workshop approach, attempt to develop a long-term strategy for NDI acceptable to the federal researchers and the states. This will have wide ranging significance across HHS, since the NDI is the primary source of mortality data for federal and non-federal researchers. This project will take the overarching goals of the others: 1) to develop standard, repeatable, and efficient technical solutions for linking the NDI's death and cause of death data to large, commercially and publicly insured populations; and 2) to demonstrate the feasibility of linkage by using use cases to assess associations between select medications and death or cause of death as an outcome and apply a long term strategy to improve NDI access and utility across the board.

CDC Project 1 Period of Performance:
2/1/17 - 1/31/21

CDC Project 1 Federal Point of Contact:
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FDA Project 2 Period of Performance:
2/1/17 - 7/31/19

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CMS Project 3 Period of Performance:
3/1/17 - 4/29/18

CMS Project 3 Federal Point of Contact:
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CDC Project 4 Period of Performance:
2/1/17 - 1/31/21

CDC Project 4 Federal Point of Contact:
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X. Patient-Centered Outcomes Research Resource Center for Data Infrastructure

In 2016, ASPE established and funded the PCOR Resource Center for Data Infrastructure (Resource Center). The Resource Center is charged with facilitating the building of data infrastructure for PCOR by providing ASPE and the OS-PCORTF awardees with technical assistance, vehicles for communication and collaboration across the portfolio, mechanisms for dissemination activities, and overall operational support. NORC at the University of Chicago, in partnership with AcademyHealth, conducts this work on behalf of ASPE, in order to support and maximize the impact of its OS-PCORTF programs and projects.

Project Purpose and Goals: The Resource Center is an important mechanism for ASPE and HHS to continue building data infrastructure capacity and to ensure awardee efforts are properly coordinated, rigorously monitored, and supported to optimize their success and to inform each other and the community of progress in the field.

In this role, the Resource Center supports the following activities:

- *Technical Assistance White Papers & Manuscripts.* White papers and manuscript publications serve as a critical resource to disseminate findings from OS-PCORTF project activities, and to inform audiences about the topics of interest to ASPE and their HHS partners.
- *Communication and Dissemination Assistance.* The Resource Center will use a variety of communication tools and dissemination vehicles that will maximize ASPE's investment in OS-PCORTF-funded projects by facilitating uptake of the resulting project products. These vehicles range from supporting an online OS-PCORTF portal for bi-directional communication and exchange with the PCOR community, to a PCOR-focused educational webinar series, to conference and industry meeting participation.
- *OS-PCORTF Portfolio Operational Support.* The Resource Center, working closely with ASPE, provides administrative support for the monitoring of all active OS-PCORTF projects.

Strategic areas of focus for the Resource Center include:

- *Use and reuse of tools and products developed by OS-PCORTF projects*
- *Collaboration across HHS agencies and with non-federal stakeholders to ensure broad awareness of OS-PCORTF projects*
- *Engagement with potential end-users of Federal PCOR data infrastructure*

Accomplishments and Deliverables: Below, we highlight key program resources and activities undertaken specifically by the PCOR Resource Center, working in collaboration with ASPE staff and OS-PCORTF awardees, to support continued development of data infrastructure to facilitate patient-centered research in calendar year 2017.

- Resource Center paper topics focused on understanding the challenges related to clinical data heterogeneity to (e.g., mortality and PRO data) and exploring potential solutions and mitigation strategies. Work is underway on the next series of papers, which examine the use of existing data (e.g., T-MSIS data) to support research on opioid addiction and the use of EHRs to facilitate the collection and exchange of social determinants of health data.
- In collaboration with ASPE, the Resource Center convened the PCOR Data Workshop: Toward a Collective Vision for Data Infrastructure Investment & Support. The workshop, attended by 97 participants, focused on generating and sharing best practices and soliciting OS-PCORTF awardee perspectives on future work in the field.
- The Resource Center prepared a strategic planning guide to inform ASPE and the Resource Center's short- and long-term activities for the OS-PCORTF portfolio in 2018 and 2019.
- In collaboration with ASPE, the Resource Center conducted nine webinars. The webinars included presentations from OS-PCORTF awardees highlighting major accomplishments and lessons learned, and featured presentations from guest speakers on non-federal PCOR-related initiatives (e.g., Leveraging PCORnet for Knowledge Sharing and Capacity Building for PCOR and Health eHeart and the Eureka Research Platform).
- The Resource Center prepared the annual Portfolio Report of the OS-PCORTF projects (this report) describing each funded project and highlighting key accomplishments.

- To support awardees and project officers, the Resource Center launched the Research Data Infrastructure Learning Community online portal.
- To facilitate efficient and accessible project monitoring, the Resource Center developed and launched an online data collection system for OS-PCORTF projects. The Resource Centers uses the data reported by OS-PCORTF awardees to develop project and portfolio dashboards for ASPE.

Period of Performance:
9/26/16 – 9/26/19

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XI. Conclusion

As a whole, the OS-PCORTF portfolio aims to improve research infrastructure. Specifically, these projects are building enhanced data capacity to enable interoperable data flows; this will allow the collection, linkage, and analysis of health and outcomes data from multiple sources for PCOR. The projects funded through the OS-PCORTF represent a broad range of topics that address the core research functionalities necessary for PCOR and the development of a robust data infrastructure.

The next to step to fully realizing the OS-PCORTF projects' goals is optimizing the utility of their products. This requires understanding the use cases for the products and their applications to real world problems in research, both within and outside HHS. In 2018 and 2019, ASPE will continue identifying opportunities to apply the OS-PCORTF products to known gaps in knowledge and technical solutions in the context of the complex legal and regulatory environment in which PCOR research is conducted. ASPE looks forward to continuing to support their HHS partners in disseminating the findings and lessons to support continued development of data infrastructure to facilitate patient-centered research.

There are many opportunities available for disseminating the OS-PCORTF products, both to broaden their use and enhance their intrinsic value. The gaps that the OS-PCORTF addresses, from products that ease data exchange from both a technical and a contracting perspective, to standards and services that improve data quality and integration of data from multiple sources, among many other functionalities, are sorely needed in PCOR. Their broad dissemination at conferences and via white papers, their demonstration via webinars and other learning opportunities, and the creation of a platform or website through which the products can be made publicly available would be a boon to the research community at large. In addition, the 2018 OS-PCORTF Workshop, led by ASPE and the Resource Center, represents one such opportunity to capture the attention of potential end users and to ensure these products are made available to them for PCOR. Moreover, involving strategic partners like PCORI in the upcoming workshop could be a productive strategy to bring the right audience to the table and coordinate messaging on these important products.

ASPE is committed to optimizing the success of these projects and accelerating uptake of the important knowledge and products that result from their work. In support of this goal, future portfolio reports will provide updates to current projects and newly funded projects, highlighting key achievements, products, collaborations, applications to HHS initiatives, in an effort to support dissemination and the long-term impact of the portfolio.

Appendix A. OS-PCORTF Project Portfolio

Table A1. Active OS-PCORTF Projects

Funded Agency	Project Title
Agency for Healthcare Research and Quality	Advancing the Collection and Use of Patient-Reported Outcomes through Health Information Technology (IT)*
	Harmonization of Clinical Data Element Definitions for Outcome Measures in Registries
Centers for Disease Control and Prevention	Development of a Natural Language Processing Web Service for Public Health Use*
	Enhancing Data Resources for Researching Patterns of Mortality in Patient Centered Outcomes Research* Project 1 – Adding Cause -Specific Mortality to NCHS's National Hospital Care Survey by Linking to the National Death Index
	Enhancing Data Resources for Researching Patterns of Mortality in Patient Centered Outcomes Research* Project 4 – NDI Workshop and Strategy Paper
	Improving the Mortality Data Infrastructure for Patient-Centered Outcomes Research
	Privacy and Security Blueprint, Legal Analysis and Ethics Framework for Data Use, and Use of Technology for Privacy*
Centers for Medicare and Medicaid Services	Enhancing Data Resources for Researching Patterns of Mortality in Patient Centered Outcomes Research* Project 3
	Improving Beneficiary Access to their Health Information through an Enhanced Blue Button Service
	Technologies for Donating Medicare Beneficiary Claims Data to Research Studies*
Food and Drug Administration	Collection of Patient-Provided Information through a Mobile Device Application for Use in Comparative Effectiveness and Drug Safety Research
	Cross-Network Directory Service
	Development of a Natural Language Processing Web Service for Public Health Use*
	Developing a Strategically Coordinated Registry Network to Support Research on Women's Health Technologies*
	Enhancing Data Resources for Researching Patterns of Mortality in Patient Centered Outcomes Research* Project 2 – Pilot Linkage of NDI+ to Commercially and Publicly Insured Populations
	Harmonization of Various Common Data Models and Open Standards for Evidence Generation*
	Source Data Capture from Electronic Health Records: Using Standardized Clinical Research Data
	Standardization and Querying of Data Quality Metrics and Characteristics for Electronic Health Data
	Utilizing Data from Various Data Partners in a Distributed Manner

Funded Agency	Project Title
National Institutes of Health	Creation of LOINC Equivalence Classes
	Developing a Strategically Coordinated Registry Network to Support Research on Women's Health Technologies*†
	Harmonization of Various Common Data Models and Open Standards for Evidence Generation*†
	Technologies for Donating Medicare Beneficiary Claims Data to Research Studies*
	Use of the ADAPTABLE Trial to Strengthen Methods to Collect and Integrate Patient-Reported Information with Other Data Sets and Assess Its Validity
Office of the National Coordinator for Health Information Technology	Advancing the Collection and Use of Patient-Reported Outcomes through Health Information Technology (IT)*
	Conceptualizing a Data Infrastructure for the Capture and Use of Patient-Generated Health Data
	Creating the Foundational Blocks for the Learning Health Care System: Data Access Framework
	Creating the Foundational Blocks for the Learning Health Care System: Structured Data Capture
	Developing a Strategically Coordinated Registry Network to Support Research on Women's Health Technologies*
	Harmonization of Various Common Data Models and Open Standards for Evidence Generation*
	Privacy and Security Blueprint, Legal Analysis and Ethics Framework for Data Use, and Use of Technology for Privacy*
	Security and Privacy Standards for Patient Matching, Linking and Aggregation

* OS-PCORTF project funding awarded to multiple agencies.

† OS-PCORTF project funding awarded within NIH

Table A2. Completed OS-PCORTF Projects

Funded Agency	Project Title
Assistant Secretary for Planning and Evaluation	Beta Testing of the Multi-Payer Claims Data^
	Comparative Effectiveness Research Inventory
Centers for Disease Control and Prevention	Expanding Data Collection Infrastructure of the National Program of Cancer Registries for Comparative Effectiveness Research
Centers for Medicare and Medicaid Services	Maintenance and Support of the Chronic Conditions Warehouse for Comparative Effectiveness Research
Health Resources and Services Administration	Strengthening and Expanding the Community Health Applied Research Network (CHARN) Registry to Conduct Patient-Centered Outcomes Research
National Libraries of Medicine	Development of Data Infrastructure for Use of EHRs in Comparative Effectiveness Research*
Office of the National Coordinator for Health Information Technology	Strategic Opportunities for Building Data Infrastructure for Patient-Centered Outcomes Research
	Development of Data Infrastructure for Use of EHRs in Comparative Effectiveness Research*

^ The Multi-Payer Claims Data (MPCD) project was a $16 million CMS project with a contract period of performance of 09/14/2010 to 09/15/2013. On 09/24/2012, the contract was modified with ASPE-provided OS PCORTF funding to conduct a Beta Test. ASPE was responsible for leadership oversight of the Beta Testing of MPCD.

* OS-PCORTF project funding awarded to multiple agencies.

Appendix B. Abbreviations

Acronym	
AHRQ	Agency for Healthcare Research and Quality
API	Application Programming Interface
ASPE	Office of the Assistant Secretary for Planning and Evaluation
ASPR	Office of the Assistant Secretary for Preparedness and Response
CDC	Centers for Disease Control and Prevention
CDE	Clinical Data Element
CDM	Common Data Model
CMS	Centers for Medicare and Medicaid Services
CNDS	Cross-Network Directory Service
CRN	Coordinated Registry Network
CTO	Chief Technology Officer
DAF	Data Access Framework
DQ	Data Quality
eCRF	Electronic case report form
EDC	Electronic Data Capture
EDRS	Electronic Death Registration Systems
EHR	Electronic Health Record
ETL	Extract-Translate and Load
FAERS	Food and Drug Administration Adverse Event Report System
FDA	U.S. Food and Drug Administration
FHIR	Fast Healthcare Interoperability Resources
HEART	Health Relationship Trust Profile
HHS	U.S. Department of Health and Human Services
HITECH	Health Information Technology for Economic and Clinical Health Act
HL7	Health Level Seven International
HP	Office of Health Policy
ICD-10	International Classification of Diseases 10th Edition
IG	Implementation Guide
IHE	Integrating the Healthcare Enterprise
IRB	Institutional Review Board
IT	Information Technology
LOINC	Logical Observation Identifiers Names and Codes
MACRA	Medicare Access and CHIP Reauthorization Act
NCHS	National Center for Health Statistics
NCATS	National Center for Advancing Translational Science

Acronym	
NCI	National Cancer Institute
NDI	National Death Index
NIH	National Institutes of Health
NLM	National Library of Medicine
NLP	Natural Language Processing
NORC	NORC at the University of Chicago
ONC	Office of the National Coordinator for Health Information Technology
OS	Office of the Secretary
PCOR	Patient-Centered Outcomes Research
PCORI	Patient-Centered Outcomes Research Institute
PCORnet	PCORI's National Patient-Centered Clinical Research Network
PCORTF	Patient-Centered Outcomes Research Trust Fund
PGHD	Patient-generated health data
PHCP	Public Health Community Platform
PMN	PopMedNet™
PMAL	Patient Matching, Linking, and Aggregation
PPI	Patient-Provided Information
PRO	Patient-Reported Outcome
S4S	Sync for Science™
SDC	Structured Data Capture
SNOMED	Systematized Nomenclature of Medicine
VAERS	Vaccine Adverse Event Reporting Systems
VBP	Value-Based Payment
WHT-CRN	Women's Health Technologies Coordinated Registry Network

Appendix C. Glossary

Key Terms	
Blue Button	A standard that makes patients the custodians of their data by allowing them to share and access it.
Clinical Element Models (CEM)	An approach to representing detailed clinical data models and the instances of data which conform to these models.
Clinical Data Research Networks (CDRN)	System-based networks (such as hospital systems) that have the potential to become an ideal electronic network, without structural impediments.
Common Data Elements (CDE)	Data elements shared between multiple data sets.[xliii]
Common Data Models (CDM)	An aggregated or centralized data model copies data from original sources and brings and standardizes these data in a centralized place. The copied data can then be queried and analyzed.
Data Governance	The process by which stewardship responsibilities are conceptualized and carried out, that is, the policies and approaches that enable stewardship.
Distributed Research Network (DRN)	A DRN is an approach in which data holders maintain control over their protected data and its uses. A DRN features a central portal that performs network functions, such as operations (e.g., workflow, policy rules, auditing, query formation, distribution) and security (e.g., authentication, authorization) and distributed data marts that remain under the control of the data holders.
Electronic Clinical Data (ECD)	Data in electronic form that may include clinical data from sources such as long term care facilities, pharmacies, laboratories, genetic tests, emergency medical services, and other clinical settings.
Electronic Health Record (EHR)	An electronic record of health-related information for a patient that contains information captured in clinical visits, lab and imaging studies, and other information important to the patient's medical past.
Fast Healthcare Interoperability Resources (FHIR)	A standard for translating health information data into a structured that can be accepted by a wide range of applications.
Health Information Technology for Economic and Clinical Health (HITECH) Act	A law passed by Congress in 2009 that authorizes expenditures of approximately $20 billion over five years to promote the adoption and use of electronic health record technologies that will be connected through a national health information network.
Interoperability	The ability of health information technology (health IT) systems from different vendors to communicate and share information.
Institutional Review Board (IRB)	A group that follows federal regulations, state laws, and institutional policy to review, monitor, and approve research in order to protect the ethical rights and privacy of the subjects involved.
Learning Health Care System	A health care system in which knowledge generation for research, science, quality assessment, outcomes, and safety standards are aligned for improvement and innovation.
Logical Observation Identifiers Names and Codes (LOINC)	A universal coding system for laboratory tests and other clinical observations. It is a national and international standard with widespread adoption and recognition of recognition of its utility.
Meaningful Use	Objectives regarding electronic health record use that eligible professionals and hospitals must achieve to qualify for Centers for Medicare and Medicaid Services (CMS) Incentive Programs.[xliv]

Key Terms	
Medicare Access and CHIP Reauthorization Act (MACRA)	The Medicare Access and CHIP Reauthorization Act of 2015 ended the Sustainable Growth Rate formula and consolidated three existing quality programs into two new tracks under the Quality Payment Program.
Metadata	The term metadata refers to "data about data". The term is ambiguous, as it is used to describe two fundamentally different concepts. Structural metadata concerns the design and specification of data structures and is more properly called "data about the containers of data"; descriptive metadata, on the other hand, concerns individual instances of application data, that is, the data content.
Natural Language Processing (NLP)	A computational model that analyzes texts using several linguistics approaches, such as syntax, semantics, and pragmatics, for the purpose of achieving human-like language results.
Patient-Centered Outcomes Research (PCOR)	Patient-Centered Outcomes Research helps people make informed health care decisions and allows their voices to be heard in assessing the value of health care options. It answers four patient-focused questions: "Given my personal characteristics, conditions and preferences, what should I expect will happen to me?" "What are my options and what are the benefits and harms of those options?" "What can I do to improve the outcomes that are most important to me?" "How can the health care system improve my chances of achieving the outcomes I prefer?"
Patient-Generated Health Data (PGHD)	Patient-generated health data is health-related data created, recorded, gathered, or inferred by or from patients or their designees to help address a health concerns.
PCORI's National Patient-Centered Clinical Research Network (PCORNet)	A "network of networks" that brings together Clinical Data Research Networks and Patient-Powered Research Networks to support patient-centered outcomes research.[xlv]
PopMedNet™	PopMedNet™ is an open source software application that enables the creation, operation, and governance of distributed health data networks through a no cost license.
Semantic Interoperability	The ability of computer systems to transmit data with unambiguous, shared meaning.
Sentinel	A distributed research network, using existing electronic health care data from multiple sources to support monitoring FDA regulated medical products and devices.
Systematized Nomenclature of Medicine (SNOMED)	A standard for the electronic exchange of clinical health information that has been designated for use by U.S. Federal Government systems.[xlvi]
Value-Based Purchasing (VBP)	VBP programs reward health care providers with incentive payments for quality and safety improvements in patient-centric care.

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