Final Report

Development of Harmonized Outcome Measures for Use in Patient Registries and Clinical Practice: Methods and Lessons Learned

AHRQ
Agency for Healthcare Research and Quality

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Development of Harmonized Outcome Measures for Use in Patient Registries and Clinical Practice: Methods and Lessons Learned

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None of the investigators have any affiliations or financial involvement that conflicts with the material presented in this report.

The information in this report is intended to help EPCs and AHRQ understand health-systems need and use of evidence to inform their decision making. This report is not intended to be a substitute for the application of clinical judgment. Anyone who makes decisions concerning the provision of clinical care should consider this report in the same way as any medical reference and in conjunction with all other pertinent information, i.e., in the context of available resources and circumstances presented by individual patients.

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Preface

The Agency for Healthcare Research and Quality (AHRQ), through its Evidence-based Practice Centers (EPCs), sponsors the development of evidence reports and technology assessments to assist public- and private-sector organizations in their efforts to improve the quality of healthcare in the United States.

The reports and assessments provide organizations with comprehensive, science-based information on common, costly medical conditions and new healthcare technologies and strategies. The EPCs systematically review the relevant scientific literature on topics assigned to them by AHRQ and conduct additional analyses when appropriate prior to developing their reports and assessments.

To improve the scientific rigor of these evidence reports, AHRQ supports empiric research by the EPCs to help understand or improve complex methodologic issues in systematic reviews. These methods research projects are intended to contribute to the research base in and be used to improve the science of systematic reviews. They are not intended to be guidance to the EPC program, although may be considered by EPCs along with other scientific research when determining EPC program methods guidance.

AHRQ expects that the EPC evidence reports and technology assessments will inform individual health plans, providers, and purchasers as well as the healthcare system as a whole by providing important information to help improve healthcare quality. The reports undergo peer review prior to their release as a final report.

If you have comments on this Methods Research Project they may be sent by mail to the Task Order Officer named below at: Agency for Healthcare Research and Quality, 5600 Fishers Lane, Rockville, MD 20857, or by email to epc@ahrq.hhs.gov.

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Executive Summary

Significant variation exists in both the types and definitions of outcome measures used in patient registries, even within the same clinical area. This variation, makes it difficult to compare, link, and aggregate data across a range of registries reflective of the spectrum of clinical care and reporting, thus reducing the potential utility of registry data. To address these limitations, the Agency for Healthcare Research and Quality (AHRQ) developed the Outcome Measures Framework (OMF), a conceptual model for classifying outcomes that are relevant to patients and providers across most conditions; it is intended to serve as a content model for developing harmonized outcome measures for specific clinical areas.[1]

AHRQ contracted L&M Policy Research, and its partners OM1 and AcademyHealth, to assess the feasibility of using the OMF to develop standardized libraries of outcome measures in five clinical areas: (1) Atrial fibrillation, (2) Asthma, (3) Depression, (4) Non-small cell lung cancer, and (5) Lumbar spondylolisthesis. These clinical areas were selected during the course of the project to represent a range of populations and care settings, different treatment modalities, and varying levels of existing measure harmonization. For each clinical area, the relevant registries and observational studies meeting project criteria were identified, and registry sponsors, informaticists, and clinical subject matter experts were invited to participate in a registry workgroup that focused on harmonizing outcome measures through a series of in-person and web-based meetings. A stakeholder group, primarily composed of patient and provider representatives and Federal partners, was also assembled for each clinical area to discuss challenges and provide feedback on the harmonization effort.

Key goals of this effort were to identify a minimum set of priority measurement concepts for each condition, standardize the definitions of the outcome measures within those concepts, and, where differences remain in the definitions, identify the specific elements or components that are dissimilar. As a final step in the harmonization process, clinical informaticists mapped the narrative definitions generated by the workgroups to standardized terminologies to produce a library of common data definitions that can eventually be implemented within electronic health records to facilitate standardized outcome data collection.

Challenges and Lessons Learned

This feasibility effort confirmed that the OMF is a robust model that supports classification and harmonization of outcome measures across an intentionally diverse group of clinical areas. While at least some level of harmonization was feasible in each of the five clinical areas, several factors affected the degree to which harmonization was reached in each of the workgroups, ranging from the implementation of the workgroups to outcome measure-related issues, such as gaps in existing evidence, lack of validated measurement tools, and variations in clinical practice. Broadly speaking, the challenges and lessons learned fall into four categories: differences across clinical areas, registry participation and variation among participating registries, recruiting and integrating stakeholders into the harmonization process, and translating narrative definitions into standardized terminologies.

Next Steps

Although each workgroup was focused on a specific clinical area, some common themes emerged around the implementation, dissemination, and ongoing governance of the harmonization process. Barriers to implementation exist, as registries often have limited funding and resources that prevent retroactively adopting harmonized measure sets. However, the

development of the value proposition of adopting such a measure set would be beneficial to nascent registries. Additionally, publicizing the harmonized measures aggressively and as widely as possible would give the measures the greatest chance of being adopted by new registries. Strategies such as publishing articles and editorials in journals, blog posts, and presenting at society and association meetings were identified as priority methods. Coordination with other efforts, such as OMERACT and ICHOM, was also identified and prioritized, not only for dissemination purposes, but also so that all parties can leverage each other's work and limit duplication of efforts.

While beyond the scope of this project, a long-term plan for the ongoing curation and updating of outcome measures would appear vital to the ultimate success of any harmonization and standardization of outcome measures effort. A clear ongoing coordinating and governance process is necessary to oversee the harmonized measures, determine when updates and revisions are needed, and determine if new measures should be adopted and harmonized. Regular review and updates are also necessary to reflect changing treatment paradigms and to address challenges encountered by registries that implemented the measure set.

Finally, convening workgroups to harmonize additional clinical areas will allow AHRQ to build upon the experiences and lessons learned from this effort, as well as continually improve the overall harmonization process. Lessons learned during this project reflect the experiences of the five harmonized clinical areas. It is likely that other clinical areas will experience varying challenges for pursuing harmonization and generate additional learnings not yet observed by the project team.

Introduction

Project Overview

Significant variation exists in both the types and definitions of outcome measures used in patient registries, even within the same clinical area. This variation, makes it difficult to compare, link, and aggregate data across a range of registries reflective of the spectrum of clinical care and reporting, thus reducing the potential utility of registry data. To address these limitations, the Agency for Healthcare Research and Quality (AHRQ) developed the Outcome Measures Framework (OMF), a conceptual model for classifying outcomes that are relevant to patients and providers across most conditions; it is intended to serve as a content model for developing harmonized outcome measures for specific clinical areas.[1]

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Key goals of this effort were to identify a minimum set of priority measurement concepts for each condition, standardize the definitions of the outcome measures within those concepts, and, where differences remain in the definitions, identify the specific elements or components that are dissimilar. As a final step in the harmonization process, clinical informaticists mapped the narrative definitions generated by the workgroups to standardized terminologies to produce a library of common data definitions that can eventually be implemented within electronic health records to facilitate standardized outcome data collection.

This report describes the process developed and used by the project team to assess the overall feasibility of using the OMF to develop standardized libraries of outcome measures, including the selection of clinical areas, recruitment of the registry and stakeholder workgroups, methodology for harmonizing outcome measures, and approach to creating standardized data definitions. The report also discusses the results from each clinical workgroup, as well as the lessons learned from each phase of the project. The final section of the report includes recommendations for future work to expand beyond the feasibility-testing stage.

Background and Rationale

Patient registries can provide valuable, real-world evidence on the effectiveness, safety, and value of products and interventions to inform decision-making. A particular strength of registries is their ability to enroll large numbers of patients and follow them over multiple years to assess long-term outcomes that are important to patients, providers, and other decision-makers. A patient registry is defined as “an organized system that uses observational study methods to collect uniform data (clinical and other) to evaluate specified outcomes for a population defined

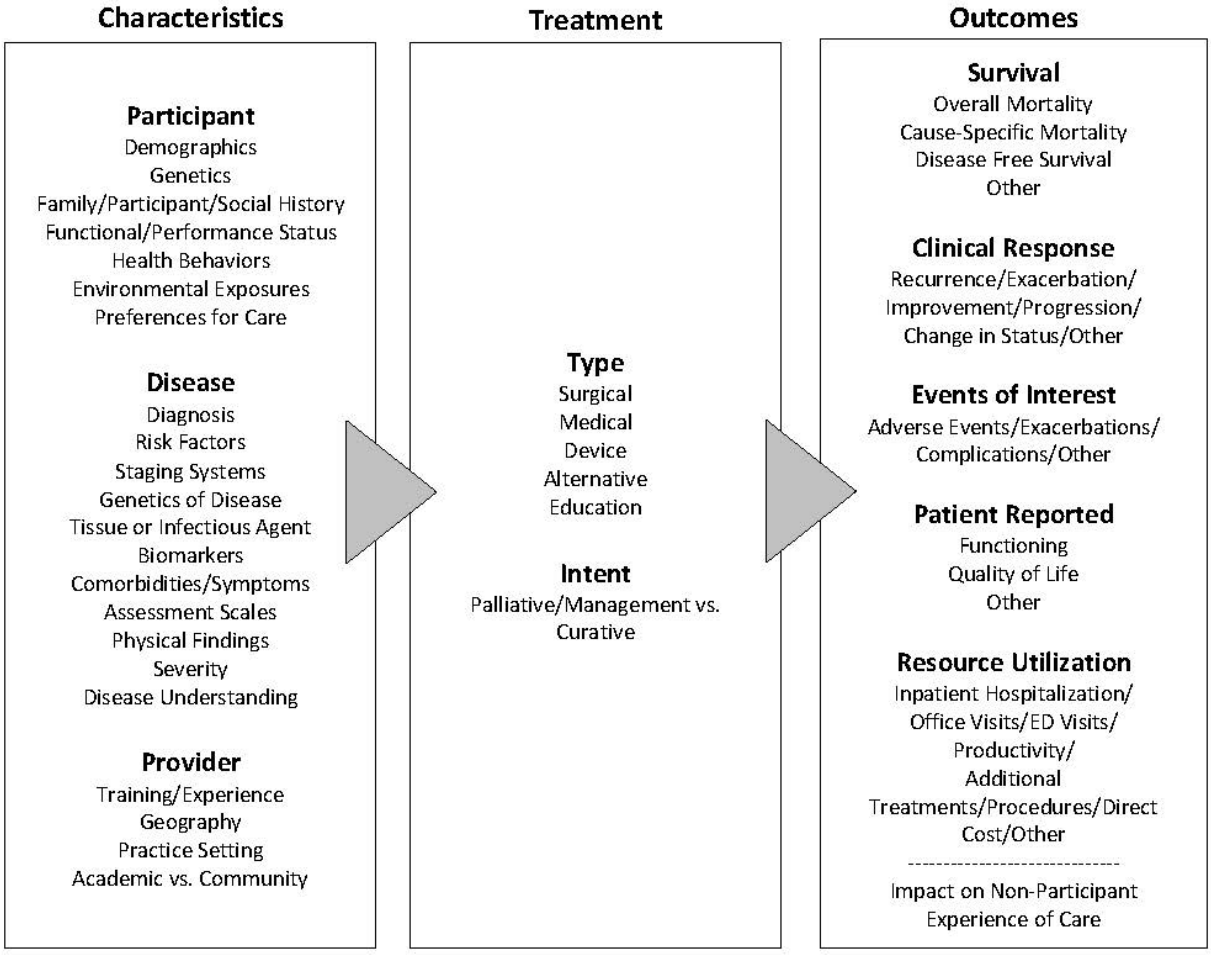
by a particular disease, condition, or exposure and that serves one or more pre-determined scientific, clinical, or policy purposes."[2]

Patient registries have existed for many years and have fulfilled myriad purposes, as documented in the publication, Registries for Evaluating Patient Outcomes: A User's Guide.[2] In recent years, with the rapid increase in availability of electronic health data, national attention has focused on a learning health system and national health data infrastructure. A 2013 Institute of Medicine report defined a learning health system as a system that is "designed to generate and apply the best evidence for the collaborative healthcare choices of each patient and provider; to drive the process of discovery as a natural outgrowth of patient care; and to ensure innovation, quality, safety, and value in health care."[3] Registries can be a central component of this system by providing data and tools to support population health management, clinical decision-making, quality improvement, and clinical research.[4,5] In particular, registries frequently serve as a connection between the research conducted in clinical trials and clinical practice by monitoring the safety and effectiveness of new products in a real-world setting. Registries are also an important source of data on patient-reported outcomes.[2,6,7,8,9]

To fully realize the potential of patient registries within the learning health system, registries must be connected to other registries, EHRs, and other data sources. Use of common measure concepts and definitions consistently derived from available data is a fundamental requirement for building these connections. As a first step, harmonizing the outcome measures captured within patient registries and other health information technology (IT) systems would enable comparisons, aggregations, and meta-analyses across data sources. Currently, significant variation exists in both the concepts and definitions of outcome measures used in registries within the same clinical area. Even when registries agree on an outcome measure concept, standardized definitions for the measure frequently do not exist. This lack of standardization introduces the potential for different providers to use different definitions and different value sets to calculate the measure, raising questions about the validity of comparisons of results across providers and across registries. Variation limits the role of registries in the learning health system and reduces the utility of registry data. To address these issues, harmonization efforts must focus on harmonizing both the outcome measure concepts captured by patient registries, as well as standardizing the underlying data definitions.

As part of a broader effort to improve the quality and efficiency of patient registries and the transparency of registry-based research, AHRQ has supported the development of the OMF. The OMF is a conceptual model for classifying outcomes that are relevant to patients and providers across most conditions (see Figure 1).

Figure 1. Outcome Measures Framework[1]



The OMF was developed through an iterative process that incorporated feedback from over 400 stakeholders, representing researchers, clinicians, government agencies, industry, patient/consumer organizations, payers, and journal editors, over a 2-year period (January 2011 – December 2012). The development and structure of the OMF has been described elsewhere.[1] Subsequently, outcome measures captured in registries in four conditions areas were abstracted from ClinicalTrials.gov and other sources and mapped to the OMF to test the robustness of the framework. While most outcome measures mapped to the OMF, review of the measures that did not map to the framework led to minor modifications to the framework, as documented in a recent AHRQ report.[1]

Work completed to date has shown that the OMF is a robust tool for classifying a diverse group of outcome measures across clinical areas. Beyond classification of outcomes, the OMF is intended to serve as a content model for developing harmonized outcome measures in specific disease areas. This project tested the feasibility of using the OMF for this purpose.

Key Project Activities

Activities for each of the clinical areas were phased in over the project period. While the process followed was essentially the same for each of the clinical areas, some refinements were made over the course of implementation to address the specific needs and preferences of each workgroup and to reflect the project team's improved understanding of the most effective approaches.

Selection of Clinical Areas

The first step in the process was to select the five clinical areas that would serve as the focus of the workgroups and for which standardized data libraries would be developed. In order to start the harmonization process quickly, AHRQ and the project team selected atrial fibrillation (AFib) as the initial clinical area at the project outset. AFib affects between 2.7 and 6.1 million people nationwide, resulting in more than 750,000 hospitalizations, contributing to 130,000 deaths and costing the U.S. more than $6 billion each year.[10] Several registries focused on cardiovascular disease exist at the local, regional, and national level and are well-established as resources for quality improvement and research, although they collect different data. Additionally, several consensus-based efforts aimed at harmonization and standardization exist, providing a foundation for the work of this project. Furthermore, effective February 8, 2016, CMS issued a Coverage with Evidence Decision, which stated that percutaneous left atrial appendage (LAA) closure therapy would be covered for patients with non-valvular atrial fibrillation under specific conditions. Among these is the noteworthy requirement that the "patient is enrolled in, and the treating physician team is participating in a prospective national registry,"[11] thus offering a timely opportunity to test the ability of the OMF to support harmonization of outcome measures within the context of a patient registry.

The selection process for the remaining four clinical areas was iterative, with the project team conducting background research on specific conditions, discussing potential areas with knowledgeable stakeholders, and presenting the results of these efforts to AHRQ staff leads and representatives from the National Library of Medicine (NLM) and the U.S. Food and Drug Administration (FDA) collaborating with AHRQ on this project. This process, described below, took place over the first eight months of the project, in a phased approach, and resulted in the selection of asthma, depression, non-small cell lung cancer (NSCLC), and lumbar spondylolisthesis (see Appendix 1 for more information about each clinical area).

Considerations for Selection

In selecting the remaining four clinical areas, the project team sought to identify a varied set of conditions in terms of the following dimensions:

- Patient populations affected, including prevalence in a range of high priority populations, e.g., women, children, and minorities as well as persons living in rural and urban areas, and persons with both public and private health coverage;
- Significant disease burden with respect to prevalence and spending; and
- Multiple treatment modalities and care provided by multiple specialties.

Other criteria used to assess the suitability of clinical areas for selection included:

- Number and maturity of existing registries collecting patient outcomes along with the extent of overlapping outcome measures within identified registries; and

- Prior attempts at registry and/or outcome harmonization, as identified in the literature review completed in the base year of the contract and through discussions with stakeholders.

Compiling Information on Potential Clinical Areas

In order to inform the selection process, the project team compiled information on each of the clinical areas under consideration. While a more thorough search was undertaken once clinical areas were selected (as described in the next section of this report), initial work in identifying registries was conducted to inform the selection process. At this stage, the project team focused on the first two steps in the process described below, obtaining a preliminary count of the number of registries and examining their distribution in terms of number of enrolled patients, purpose, and source of funding.

Information on the factors of interest was assembled in a series of tables for presentation to AHRQ, with the goal of choosing clinical areas representing a broad group of populations and practice modalities to fully test the applicability and flexibility of the OMF. Overall, we identified and presented information on 21 clinical areas prior to final selections being made. (See Appendix 1 for a listing of the clinical areas considered and the relevant information compiled.)

For specific clinical areas, we engaged with experts in the field to learn about ongoing harmonization and standardization efforts and to gather perspectives on the utility of undertaking a new harmonization effort in specific areas. For example, based on work completed by OMERACT (Outcome Measures in Rheumatology) related to rheumatoid arthritis, we contacted the American College of Rheumatology; in consultation with members of their quality measures subcommittee, it was decided that the already extensive work in the area obviated the need for another effort.

During this period, the team also conducted two Open Door Forum (ODF) webinars presenting an overview of the project, identifying the first few clinical areas selected, and soliciting input on the overall process as well as on additional conditions to target. There were approximately 50 attendees across the two webinars; several organizations provided recommendations and were instrumental in final selections.

Identifying Registries Within Clinical Areas

Once the clinical areas were selected, the project team focused on identifying and reviewing existing and newly launched patient registries. The objective was to identify all registries in a specific clinical area collecting information on patient outcomes. The project team established the following inclusion and exclusion criteria to evaluate registries:

- Currently collects data or is planning to begin collecting data within one year
- Enrolls patients in the United States
- Meets the following definition of a patient registry:
  - An organized system that uses observational study methods to collect uniform data (clinical and other) to evaluate specified outcomes for a population defined by a particular disease, condition, or exposure and that serves one or more pre-determined scientific, clinical, or policy purposes.[2]

Registries were excluded if they did not collect patient outcomes (e.g., registries designed solely to track vaccination status). This process is summarized in Table 1.

Table 1. Steps in registry identification process

Source	Purpose and approach
Registry of Patient Registries (RoPR) **https://patientregistry.ahrq.gov**	Used to identify any registries that self-identified as a registry using the 'patient registry' subtype selection for observational studies when registering in ClinicalTrials.gov Specific search terms identified for each clinical area Applied inclusion/ exclusion criteria
National Institutes of Health (NIH) U.S. National Library of Medicine **ClinicalTrials.gov** **https://ClinicalTrials.gov**	Used to identify registries that use the term 'registry' but did not select the 'patient registry' subtype (possibly because they were entered prior to the introduction of that subtype in 2012) Specific search terms identified for each clinical area Applied inclusion/ exclusion criteria Restricted to 'observational study' entries that use the term 'registry' in their title or description
Physician Quality Reporting System **Qualified Registries (PQRS)** **https://www.cms.gov/Medicare/Quality-Initiatives-Patient-Assessment-Instruments/PQRS/Downloads/2016QualifiedRegistries.pdf**	Used 2016 list to identify registries that are qualified under Centers for Medicare & Medicaid Services (CMS) rules for measure submission. Applied inclusion/ exclusion criteria
FDA **Center for Drug Evaluation and Research (CDER)** ***https://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/default.htm*** **Center for Biologics Evaluation and Research (CBER)** **https://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CBER/** **Center for Devices and Radiologic Health (CDRH)** **https://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/**	CDER monitors drugs and over-the- counter products, CBER evaluates biological products, and CDRH monitors medical devices and provides accessible information for consumers and providers. Reviewed: Post-Marketing Requirements and Commitments database Post-Approval Studies (PASs)
Patient-Centered Outcomes Research Institute (PCORI) **https://www.pcori.org**	Reviewed-- Clinical Data Research Networks (CDRNs) Patient-Powered Research Networks (PPRNs) PCORI uses high-quality, evidence-based information to help make informed healthcare decisions
NIH Reports and Health Services Research Projects in Progress (HSRProj) **https://wwwcf.nlm.nih.gov/hsr_project/home_proj.cfm**	Used to identify additional government-funded projects

Source	Purpose and approach
Other Organizations	Websites of organizations that compile or list registries, such as the American Medical Association (AMA)'s National Quality Registry Network (NQRN).
Literature and website scans	Used PubMed, Google Scholar, and Google to: Identify registries not listed in other sources Identify publications or conference proceedings
Stakeholder and workgroup feedback	*Ad hoc* conversations to obtain feedback and recommendations with experts Reviewed registry list with workgroup participants to solicit additional registries

The finalized list of registries for each clinical area was used for the next step in the process, recruiting participants for the registry workgroup.

Engaging Registries and Other Stakeholders

The workgroups for each of the five clinical areas were developed with several goals related to size, composition of registry and stakeholder representatives, and diversity in expertise and perspectives. In particular, the project team aimed to have each workgroup total 20 to 25 members, with 10 to 15 members representing registries and five to 10 individuals from various Federal agencies, payers, EHR vendors, health system representatives, patient representatives, healthcare accreditation associations, provider associations and clinical societies, and pharmaceutical and device manufacturers. In addition to registry and stakeholder participants, the team recruited chairs or co-chairs and clinical consultants for each clinical area to help guide the workgroups.

The project team recruited registry workgroup members using the list of eligible registries described above to identify the principal investigators (PIs) or directors of the registries and contacted them using a standard email invitation and follow-up phone calls as needed. In each of the clinical areas, the list of registries was first prioritized internally, and the subset of registries deemed most relevant were targeted for outreach and recruitment. In general, the PI or a designee participated as the registry representative. Registry members contributed critical information including the definitions of outcome measures used in their registries, the data elements that comprise the outcome measures, and the data definitions for the various data elements used to calculate their outcome measures.

Stakeholder organizations were identified based on a combination of recommendations from AHRQ and independent searches of organizations working to improve, advocate for, or support research and practice of the clinical areas; patient representatives, in particular, were targeted for recruitment due to their being at the nexus of patient-centered care. The executive staff of these organizations were invited to join the workgroup or specify a designee. The project team focused on diversity of organization types and perspectives when recruiting stakeholder members. Stakeholders who agreed to participate attended the first and last workgroup meetings to provide their perspectives to ensure the harmonized measures were useful and applicable across the learning health system. Table 2 below lists the sample rationale for various stakeholder types participating in the harmonization efforts and how they use registry data within the learning health system.

Table 2. Stakeholder participation rationale

Stakeholder	Sample Rationale
Payers	Coverage determinations, Value-based care
Federal Agencies	Regulatory decisions, Public health policy, Research funding, Population surveillance
Professional Societies and Associations	Clinical research, Clinical guidelines, Accreditation, Clinical decision support
Patient Representatives	Patient-centered care, Shared decision-making
Healthcare Quality	Quality measures, Measure development
Electronic Health Record Developers	EHR development, Data integration

The workgroup chairs helped shape session agendas, reviewed meeting materials, and helped moderate discussions during the workgroup meetings. Clinical consultants were selected based on their areas of expertise. For example, in NSCLC, both a thoracic surgeon and a medical oncologist were engaged as clinical consultants to ensure that different clinical perspectives were represented during the harmonization work. The clinical consultants helped review the outcome measures submitted by the participating registries and map them to the OMF. The consultants also provided input on outcome measures used in the minimum measure set and guided development and refinement of definitions and other materials to support the workgroups.

The numbers of registry and stakeholder participants for the five workgroups are shown in Table 3 below. There were between 12 and 15 registries represented in each workgroup, while the number of stakeholder organizations participating varied from 8 to 16. A listing of specific registries and organizations is provided in Appendix 2. In some cases, more than one representative from a registry or stakeholder organization participated in the workgroup meetings.

Table 3. Registry and stakeholder organization participation, by clinical area

	Atrial Fibrillation	Asthma	Depression	Lung Cancer	Lumbar Spondylo-listhesis
Registries Contacted	19	21	26	34	26
Registries Participating	14	14	15	14	12
Stakeholder Organizations Contacted	23	26	26	13	25
Stakeholder Organizations Participating	8	11	16	8	12

The registries participating in each clinical area workgroup represented a wide range of interests, including academic, industry (both pharmaceutical and device), Federal, and societies and associations, with purposes ranging from clinical to quality to patient experience to surveillance. Overall, most of the registries represented were focused in the United States, with a

few international participants. Recruitment of international registries, while not a specific priority, was a challenge due to travel logistics and/or time zone differences for remote participation, particularly with NSCLC, which had many internationally-based registries. Appendix 2 lists all participating registries and stakeholders, including their representatives.

Convening Registry and Stakeholder Workgroups

The workgroups were convened for a series of five meetings to develop and refine a Minimum Measure Set (MMS), a set of measures intended to serve as the core set of recommended measures for registry data collection, and to discuss and harmonize outcome measure definitions. As shown in Table 4, the series of meetings generally followed the pattern of three virtual meetings (Meetings 1, 3, and 4) as well as two in-person meetings (Meetings 2 and 5) held in Washington, D.C.[*] Additionally, preparation and debrief conference calls were conducted for each of the five meetings with the chairs/co-chairs, clinical consultants, moderators, and project team to facilitate an efficient work process. Some of the activities for these conference calls included preparing relevant meeting materials, developing question prompts and reviewing key discussion topics, identifying potential informational gaps, and resolving any potential points of contention.

Table 4. Overview of workgroup meeting sequence

Meeting 1: Virtual Kick-Off (Registries & Stakeholders)	Meeting 2: In-Person (Registries)	Meeting 3: Virtual (Registries)	Meeting 4: Virtual (Registries)	Meeting 5: In-Person (Registries & Stakeholders)
Conducted team and workgroup introductions	Reviewed proposed minimum measure set (MMS) developed based on the first virtual activity.	Using results of virtual activities, continued refining the MMS.	Using results of virtual activities, continued refining the MMS.	Reviewed and finalized the standardized measure definitions
Reviewed project background and objectives	Discussed the appropriateness of the measures to be included and the categorization of measures in the OMF	Continued harmonization exercises.	Continued harmonization exercises.	Reviewed and finalized risk adjustment characteristics
Reviewed the harmonization process and workgroup goals	Began harmonization exercises by reviewing alternative definitions and discussing the clinical significance of differences.	Began discussing key participant, provider, and disease characteristics that should be collected to support risk adjustment.	Continued discussion of participant, provider, and disease characteristics.	Discussed lesson learned and implementation and use cases.
Reviewed preliminary set of outcome measures and discussed plans for the first virtual activity	Discussed plans for additional virtual activities.	Discussed plans for additional virtual activities.	Began discussions of dissemination and implementation opportunities.	Discussed dissemination opportunities.

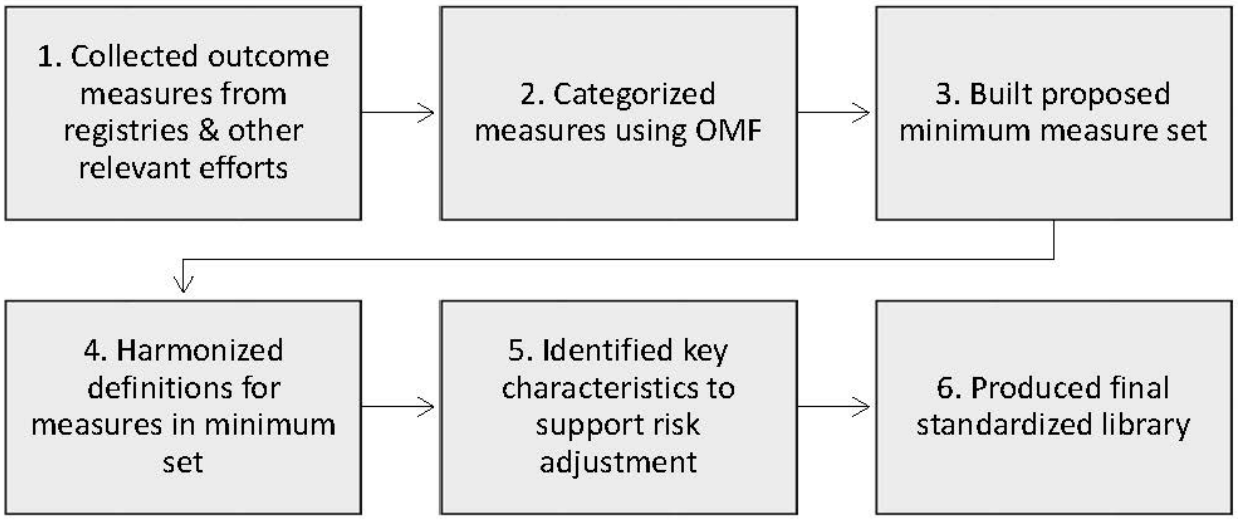
[*] In two of the clinical areas, AFib and NSCLC, the second and third meetings had to be reversed due to logistical challenges so that Meeting 3 was in-person and Meeting 2 was virtual.

Between meetings, virtual activities were conducted using a combination of web-based surveys and a cloud-based collaboration tool (Codigital). The web-based survey tool was consistently used in all five clinical areas to prioritize measures for inclusion in the MMS and for collecting other types of feedback. In addition to these surveys, Codigital was used to refine measure definitions in all workgroups, except for depression where the workgroup conducted all of its harmonization activities during the course of their meetings. Codigital is a real time, cloud-based tool for groups to generate and refine ideas, where specific questions or topics are posted and individual, anonymous responses are submitted for the group to view, edit, and rank. Because meeting time is limited and definition reconciliation requires substantial thought, the Codigital tool provided an additional opportunity for individuals to deliberate on definitions and interact with each other in a continuous, iterative manner.

Identification and Categorization of Outcome Measures

Following the organization of the workgroups, the project team identified and collected outcome measures for categorization in the OMF and potential harmonization as part of the MMS. The first step in the harmonization process summarized (see Figure 2), was to review the outcome measures submitted by the registries participating in the workgroups.

Figure 2. Harmonization methodology overview



Collection of Outcome Measures

One stipulation for registries participating in the workgroups was the requirement to share their outcome measures. Specifically, for each outcome measure, registry representatives were asked to provide: (1) the outcome measure definition, (2) the data elements that comprise the outcome measure, and (3) the data definitions for each of the data elements used to calculate the outcome measure. For example, some registry representatives provided the outcome measures as defined by a study protocol, along with the study case report form, and the accompanying data dictionary. In some cases, multiple discussions were necessary to obtain the necessary details.

For example, in atrial fibrillation, one registry provided 'major bleeding' as an outcome measure. Upon follow-up, the registry provided a reference to the published consensus definition of 'major bleeding' used in the registry. However, during further discussion, the registry clarified that they modified the definition for feasibility purposes. Across the clinical areas, the project team found that different stakeholders had different levels of understanding of the purpose and requirements of the project, and individual conversations were most effective for obtaining the necessary documents.

While the member registries' outcome measures served as a starting point to build the MMS, the project team conducted additional research to identify other relevant outcome measures and measure definitions that may not have been submitted by workgroup members. In some cases, measures were not used by any of the participating registries; in other cases, the project team identified a measure produced by another harmonization effort. This additional research allowed the project team to ensure as complete a set of outcome measures as possible for each workgroup, as well as to build upon other harmonization efforts.

Additional sources of measures were identified through discussions with registry representatives, clinical consultants, workgroup chairs, and through environmental scans of ClinicalTrials.gov, Google Scholar, peer-reviewed journals, the Core Outcome Measures in Effectiveness Trials (COMET) Initiative database,[12] and other relevant organizations/associations. The additional sources ranged from consensus documents for broadly accepted definitions, findings from outcome measure focused workgroups (e.g., the Asthma Outcome Workgroup sponsored by the NIH[13]), established value-based care models (e.g., CMS oncology care model[14]), measures produced by the International Consortium for Health Outcomes Management (ICHOM)[15], and endorsed quality measures (e.g., those listed in the National Quality Forum (NQF) database[16]).

Comparison of Outcome Measures Across Sources

The project team organized the outcome measures submitted by participating registries and those from other sources into a spreadsheet in order to (1) more easily compare measures across sources to identify similar or overlapping measures, and (2) sort the measures into the OMF categories. For each measure, the measure title, method of measurement (e.g., use of a validated instrument), timeframe, measure definition, reference and/or registry, and the numerator and denominator (when relevant) were compared. Additionally, the project team, sometimes with the help of the clinical consultant, sorted and placed the measures into the appropriate OMF categories (survival, clinical response, events of interest, patient reported, resource utilization, and experience of care). When measures could be classified into multiple categories, which most commonly occurred with patient-reported and clinical response outcomes, they were brought to the workgroups for resolution.

Within each clinical area, some registries collected similar or overlapping measures, for which harmonization was needed. However, many of the outcome measures collected through this effort were only captured in one or a small number of registries (as discussed further in the chapter below on Challenges and Lessons Learned). As a result, prioritization was necessary to focus the workgroup activities on the most clinically relevant and broadly applicable measures.

Prior to each workgroup's second meeting, registry participants rated the patient and/or clinical relevance of each outcome measure concept and suggested any missing measure concepts that should be included in the MMS (this feedback was provided through a web-based survey designed by the project team). For the first clinical area (AFib), we used a 5-point Likert

scale, and then transitioned to a 7-point Likert for the remaining workgroups, which helped provide more granularity to the results. This virtual activity yielded valuable information on which measures to include in the MMS; however, because of the subjectivity of the ratings, we did not rely solely on the results of the virtual activity. Instead, we used the ratings to frame the discussions of the MMS during subsequent workgroup meetings, so measures may have been included or dropped based on these discussions. Additionally, rather than asking about specific tools or scales, we asked workgroup members about measure concepts, which made it easier to focus discussions on the utility of a measure and avoid debate (at least initially) about specific measurement tools.

The project team, in collaboration with the clinical consultant and workgroup chairs, used the ratings to develop a proposed MMS that served as a starting point for discussion during each workgroup's second meeting. During these discussions, we found that there were often measures that participants wanted to include but may not have been widely applicable. Therefore, the team began grouping the measures by "minimum measures" and "supplemental measures"; this was meant to lessen the burden on registries by reducing the over number of measures in the MMS and presenting the supplemental measures as "nice to haves" or optional.

Refining Minimum Measure Sets and Harmonization

Identifying the MMS and harmonizing the measures in the MMS was an iterative process that occurred over approximately five months and involved multiple workgroup meetings and virtual activities, using web-based surveys and a cloud-based collaboration tool (Codigital). The web-based survey tool was consistently used in all five clinical areas to prioritize measures for inclusion in the MMS, as discussed above, and for collecting other types of feedback. These topic-specific surveys between meetings were used to incorporate flexibility in the overall process, address problem areas as they arose during discussions, and capture workgroups input on issues requiring additional thought. For example, in the depression workgroup, a survey was used to solicit recommendations of depression-specific characteristics to be included in the OMF. In NSCLC, a survey was used to prioritize patient-reported domains and instruments. In addition to these surveys, Codigital was used by each workgroup to refine measure definitions, except for the depression workgroup as previously noted. For example, the asthma workgroup modified the exacerbation definition during the second meeting, but some questions remained following the meeting. A Codigital activity showing the proposed definition was sent to the workgroup after the second meeting and workgroup members edited the definition and added comments with new ideas; the revised definition and comments were discussed at the following meeting until the group reached consensus.

Defining Participant, Provider, and Disease Characteristics

The first OMF domain describes characteristics of the participant, disease, and provider that are important for fully defining an outcome measure. These characteristics may be used to define the relevant patient population or to support appropriate risk adjustment. For each of the five clinical areas, the project team developed an initial list of participant, disease, and provider characteristics, which were then reviewed and refined through workgroup meetings and/or virtual activities. For asthma and depression, a web-based survey was used to refine the proposed characteristics. The results of these virtual activities were discussed by the group during subsequent meetings. In lumbar spondylolisthesis, characteristics were discussed during the second meeting and no additional virtual activity was required. The use of meeting time *versus* a

virtual activity to define characteristics depended on the time allocation of meetings and the degree to which there was a pre-existing consensus surrounding characteristics in each clinical area. Although the project team encouraged workgroup members to limit inclusion of characteristics to those for which there is evidence in the peer-reviewed literature documenting their correlation with outcomes, there was some variation across the groups in the level of evidence justifying inclusion.

Defining Treatments

The second domain of the OMF describes treatment types and treatment intent. In general, it is critical to consider treatment options for two main reasons. First, understanding what types of treatments are included informs the outcome measures included in the MMS, as the measures need to be relevant and related to those treatment options. Second, the intent of each individual treatment may vary. Understanding the rationale and intent of a selected treatment is critical for choosing the appropriate outcomes for assessment. Additionally, introducing new treatment modalities could necessitate revisions to the outcomes of interest in a given clinical area.

Data Element Development: Measure Definitions and Data Element Descriptions

As a final step in the harmonization process, clinical informaticists mapped the narrative definitions (generated by the workgroups) to standardized terminologies to produce a Library of Common Data Definitions. Standardizing the definitions of the components that make up the harmonized outcome measures is important so that users can understand the level of comparability between measures across different systems and studies.

Development of Standardized Terminologies

The registry and stakeholder workgroups focused on harmonizing the narrative definitions of outcome measures. While use of a harmonized narrative definition has the potential to improve the comparability of information collected in different registries, narrative definitions still allow for inconsistency in data collection, particularly when data are abstracted from existing systems, such as EHRs. To improve consistency and reduce the burden of implementation, narrative definitions produced by the workgroups were translated into standardized terminologies to facilitate capture within an EHR. The project team's clinical informaticists worked with clinical experts to map the narrative definitions to standardized terminologies, such as ICD-10, SNOMED, and LOINC.

For each measure, the recommended reporting period, initial population for measurement, outcome-focused population, and data criteria and value sets were defined. EHR data often will not contain all the requisite components of an outcome definition that would allow for the computational confirmation of that outcome. The approach used for this project was to gather the clinician's assertion of an outcome condition and as much supporting evidence as possible, so that even where the expression logic cannot computationally confirm an outcome, some structured evidence might still be available.

Relationships between events raise a challenge because relationships are often not directly asserted in an EHR. Thus, where possible, relationships have been inferred based on time stamps and intervals. Where this is not possible (e.g., cause of death), the logic requires an asserted relationship.

For each outcome, the following were defined:

- *An object representing the outcome condition itself:* In many cases, the only structured data will be an assertion of an outcome, with all the supporting evidence being present in the narrative.
- *Fast Healthcare Interoperability Resources (FHIR) resources for evidence for the outcome:* These include labs, diagnostic imaging, etc.
- *FHIR resources for additional relevant events:* These might include procedures, encounters, etc.
- *Temporal aspects for all events:* These allow for inferred relationships.

Leveraging Existing Resources

A key goal of this project was to leverage existing resources and build connections across initiatives, where possible. To support that goal, the existing common data elements and value sets were used whenever possible. Existing common data elements and value sets were identified through review of four sources, as shown in Table 5.

Table 5. Sources of existing common data elements and value sets

Name	Description and URL	Relevance
eCQI Resource Center	Centralized location for news, information, tools, and standards related to electronic clinical quality improvement (eCQI) and electronic clinical quality measures (eCQMs), coordinated by the CMS and the Office of the National Coordinator for Health Information Technology (ONC). https://ecqi.healthit.gov/	Overlapping criteria for defining patient populations
Value Set Authority Center (VSAC)	Repository for public value sets created by external programs. Value sets are lists of codes and corresponding terms that define clinical concepts to support effective and interoperable health information exchange. https://vsac.nlm.nih.gov/	Overlapping value sets
Consolidated-Clinical Document Architecture (C-CDA)	The C-CDA implementation guide contains a library of CDA templates, incorporating and harmonizing previous efforts from Health Level Seven (HL7), Integrating the Healthcare Enterprise (IHE), and Health Information Technology Standards Panel (HITSP). It represents harmonization of the HL7 Health Story guides, HITSP C32, related components of IHE Patient Care Coordination (IHE PCC), and Continuity of Care (CCD). http://www.hl7.org/implement/standards/product_brief.cfm?product_id=408	Overlapping data representations
NIH Common Data Elements Repository	Repository of structured human and machine-readable definitions of data elements that have been recommended or required by NIH Institutes and Centers and other organizations for use in research and for other purposes. https://www.nlm.nih.gov/cde/	Overlapping data element definitions

Each website has a specific, unique purpose, and data representations vary, so while there are some direct comparisons with similar use cases, there are also important differences both in terms of data structures and use cases. For example, eCQMs are based on the NQF's Quality Data Model, as expressed as HL7 Quality Reporting Document Architecture (QRDA) templates, whereas this project is based on FHIR version 1.8.0 objects. In addition, VSAC does not currently provide intentionally-defined value sets, making comparison more difficult. For this project, comparisons were done based on enumerated lists. Results of the comparisons were documented in the narrative document for each Library of Common Data Definitions, and existing common data elements and value sets were used where appropriate.

Public Comment

As a final step in the overall harmonization process, the Libraries of Common Data Definitions for each clinical area were posted to the AHRQ website for four-week public comment periods. Public comments submitted through the AHRQ website were reviewed and the respective libraries revised as appropriate.

Challenges and Lessons Learned

This feasibility effort confirmed that the OMF is a robust model that supports classification and harmonization of outcome measures across an intentionally diverse group of clinical areas. While at least some level of harmonization was feasible in each of the five clinical areas, several factors affected the degree to which harmonization was reached in each of the workgroups, including:

1. Differences across clinical areas. The clinical areas selected for this feasibility assessment were diverse and presented different challenges for the harmonization process.
2. Registry participation and variation among participating registries. Registries are heterogeneous, with a wide range of purposes, study designs, and sponsors. This project aimed to recruit a representative group of registries for each clinical area so that the feasibility of harmonization across different types of registries could be assessed, but identification and recruitment of registries was challenging.
3. Recruiting and integrating stakeholders into the harmonization process. This project attempted to recruit a broad group of stakeholders for each clinical area to incorporate patient, registry data user, and other broader health system perspectives. Recruitment of EHR developers was particularly challenging, and earlier inclusion of patient perspectives would have been beneficial,
4. Translating narrative definitions into standardized terminologies. Narrative definitions must be specified fully in order to support translation into standardized terminologies

Next Steps

During each workgroup's final meeting, registry and stakeholder members discussed the next steps for this harmonization effort, including the implementation, dissemination, and ongoing governance of the MMS and harmonization process developed during the course of this project. Although each workgroup was focused on a specific clinical area, some common themes emerged across these three areas. Finally, the project team notes that convening additional workgroups to harmonize other clinical areas will allow AHRQ to build upon the experiences and lessons learned from this feasibility effort, as well as continually improve the overall harmonization process.

Implementation

Workgroup members were enthusiastic about the prospect of new registries implementing the MMS and the long-term implications for data aggregation, comparison, and future research. However, a number of barriers were identified that could impede implementation. Existing registries noted that changing their current data collection to conform to the MMS would require adding substantial resources and have staffing, cost, and workflow implications.

Getting registries engaged with the idea of implementing a MMS by presenting the value proposition of the MMS to new registries was discussed at length. Workgroup members noted that adoption of the MMS by new registries could significantly reduce their development costs by providing a set of measures already in use and potentially reduce their ongoing collection burden (particularly after EHRs have implemented the MMS). Reducing the cost of collecting data may be the most compelling value proposition across different types of registries if these definitions can be embedded into EHRs. As such, promotion and coordination with payers, EHR

developers, and technical groups such as International Health Terminology Standards Development Organization (SNOMED), LOINC, and HL7, was identified as a key priority going forward. If standardized definitions and their terminologies are adopted widely, the cost of data collection at individual sites could be reduced dramatically.

Additionally, patient advocacy could be important in encouraging the adoption of the MMS. Patients could push for collection of the MMS, because the adoption of consistent reporting standards that allow for comparison across multiple data sets can be used to support their shared decision-making processes.

Dissemination

Workgroup members agreed that publicizing the harmonized measures aggressively and as widely as possible would give the measures the greatest chance of being adopted by new registries. Strategies such as publishing articles and editorials in journals, blog posts (such as AHRQ blog, New England Journal of Medicine's Catalyst, etc.), and presenting at society and association meetings were identified as priority methods. Coordination with other efforts, such as OMERACT and ICHOM, was also identified and prioritized, not only for dissemination purposes, but also so that all parties can leverage each other's work and limit duplication of efforts.

It was also suggested that continued outreach to and leveraging of stakeholder relationships with other measure development and oversight organizations (e.g., NQF) could be beneficial, as well as the exploration of promotion by Federal agencies and organizations, such as CMS, FDA, and NIH. For example, adoption of harmonized measures would benefit by CMS requirements, the FDA promoting their use in trials and post-approval studies, and their use in NIH-funded research.

Ongoing Governance

Workgroup members noted that a long-term plan for the ongoing curation and updating of outcome measures is vital to the ultimate success of any harmonization and standardization of outcome measures effort. A clear process is necessary to oversee the harmonized measures, determine when updates and revisions are needed, and determine if new measures should be adopted and harmonized. Regular review and updates are necessary to reflect changing treatment paradigms and to address challenges encountered by registries that implemented the measure set.

Additionally, this process would need to coordinate with other harmonization efforts, societies and associations, relevant government agencies, and other relevant organizations to continually promote the adoption of and encourage the use of the harmonized measures. Tracking the implementation and use of the MMS over time would also inform the long-term curation and revision of the measure set, as well as inform the value proposition for using the MMS.

Additional Clinical Areas

During the course of this project, the team developed a harmonization process that maintained a degree of flexibility but was also continually refined with each clinical area. However, limitations experienced in both the process and degree to which outcome measures could be harmonized are restricted to the project team's experience with these five clinical areas; additional clinical areas could present different challenges and insights. The harmonization process will need to be further refined in order to become a fully generalizable process that can be used for all clinical areas, regardless of their idiosyncrasies. It is recommended that a

continued phased roll out of clinical areas continue, and that a more formal process of continued refinement be developed and implemented to better adapt the harmonization process for the long-term.

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Abbreviations

AHRQ	Agency for Healthcare Research and Quality
AMA	American Medical Association
C-CDA	Consolidated Clinical Document Architecture
CBER	Center for Biologics Evaluation and Research
CCD	Continuity of Care
CDER	Center for Drug Evaluation and Research
CDRH	Center for Devices and Radiologic Health
CDRN	Clinical Data Research Network
CMS	Centers for Medicare and Medicaid Services
COMET	Care Outcome Measures in Effectiveness Trials
CTCAE	Common Terminology Criteria for Adverse Events
eCQI	Electronic Clinical Quality Improvement
eCQM	Electronic Clinical Quality Measure
EHR	Electronic Health Record
FDA	U.S. Food and Drug Administration
FHIR	Fast Healthcare Interoperability Resources
HAM-D	Hamilton Depression Rating Scale
HITSP	Health Information Technology Standards Panel
HL7	Health Level Seven
HSRProj	Health Services Research Projects in Progress
ICHOM	International Consortium for Health Outcomes Management
IHE	Integrating the Healthcare Enterprise
IHE PCC	Integrating the Healthcare Enterprise Patient Care Coordination
IT	Information Technology

LAA	Left Atrial Appendage
MADRS	Montgomery-Åsberg Depression Rating Scale
MMS	Minimum Measure Set
NSCLC	Non-Small Cell Lung Cancer
NIH	National Institutes of Health
NLM	National Library of Medicine
NQF	National Quality Forum
NQRN	National Quality Registry Network
ODF	Open Door Forum
ODI	Oswestry Disability Index
OMERACT	Outcome Measures in Rheumatology
OMF	Outcome Measures Framework
ONC	Office of the National Coordinator for Health Information Technology
PAS	Post-Approval Study
PCORI	Patient-Centered Outcomes Research Institute
PHQ-9	Patient Health Questionnaire-9
PI	Principal Investigator
PPRN	Patient-Powered Research Networks
PQRS	Physician Quality Reporting System
PRO	Patient-Reported Outcome
PROMIS	Patient-Reported Outcomes Measurement Information System
QRDA	Quality Reporting Document Architecture
RECIST	Response Evaluation Criteria in Solid Tumors
RoPR	Registry of Patient Registries
VSAC	Value Set Authority Center

Appendix A. Proposed Clinical Areas

(1) Proposed Clinical Areas	(2) General Information	(3) Existing Evidence and Treatment Modalities	(4) Registries†	(5) Other Related Work
Anxiety disorders	Most common mental health illness in the U.S.; impacts 40 million adults or 18 % of the population (NIMH) Costly – represents about 1/3 of the mental health costs in the U.S. (study commissioned by ADAA) Impact women more often than men (ADAA)	Psychotherapy Self-help / support groups Stress management techniques Drug therapies	32 studies identified in ClinicalTrials.gov (currently enrolling); difficult to assess if all the studies are current as many of the NIH studies do not include an expected completion date 20 of the 32 studies have enrollment targets of 500 or less; 10 have enrollment targets between 501 – 5,000; the remaining 2, have targets over 5,001 1 registry is funded by the Naval Health Research Center, 1 is funded by Industry, 1 is funded by NIH, the remaining registries are funded through a combination of NIH and University or hospital system funding Other registries found: Assessing Stress, Health, Emotion and Response (ASHER) at Northwestern University; American Psychiatric Association is working on creating a registry for mental health disease (PsychPRO);	ICOHM has a measure set for depression and anxiety (http://www.ichom.org/medical-conditions/depression-anxiety/) ACORN – a collaborative research network – has put together patient questionnaires and clinical decision support tools for mental health and substance abuse. In addition, they have a data repository that track patient outcomes, which is meant to be one of the largest for mental health conditions in the world. (https://psychoutcomes.org/COMMONS/ACORNHistory)

† For all clinical areas except for asthma, depression, and low back pain, the number of ClinicalTrials.gov registries listed in the table represents the *total number of registries* returned from our initial searches – this is meant to provide a sense of the prominence of work being done in the clinical area. As we honed in on clinical areas, the team reviewed the listings for trials that meet our criteria. For asthma, depression, and low back pain, the registries were reviewed more thoroughly and registry counts include other sources.

(1) Proposed Clinical Areas	(2) General Information	(3) Existing Evidence and Treatment Modalities	(4) Registries†	(5) Other Related Work
Asthma	Asthma impacts 8.6% of children (Age<18) and 7.4% of adults (Ages 18+) The incidence is higher in women than men (9.0% vs. 6.3%) The incidence is higher in African Americans than persons who are white or Hispanic – 9.9%, 7.6%, and 6.7% respectively The proportion of Americans diagnosed with asthma has grown about 15% in the past decade (CDC)	Treatment modalities: medication only Long-term control medications, e.g., inhaled corticosteroids, Cromolyn, Omalizumab, inhaled long-acting beta2-agonists, Leukotriene modifiers, Theophylline Quick-relief or 'rescue' medications, e.g., inhaled short-acting beta2-agonists, anticholinergics Current therapies, particularly combination therapies, are highly effective for asthma control, but adherence is poor. There is a need for new treatments for severe asthma There is less evidence supporting treatment approaches in subgroups, such as children and pregnant women Some new research focuses on developing treatments for different phenotypes or endotypes of asthma, and new drugs may affect different aspects of the inflammatory process, leading to the need for new outcome measures	There are 40 open and active registries listed in ClinicalTrials.gov (asthma, open and observational studies recruiting in the US) 19 of the studies may be of interest, although 7 have measures that may not be appropriate for harmonization 2 have more than 5,000 enrollees, 2 have between 1,000-5,000; the remaining 15 studies have fewer than 1,000 enrollees The majority of the 19 studies are funded by some combination of Federal agencies (13 of the 19) – and in a few cases with additional funding from the American Lung Association. Other funding was either private or could not be found through Internet searches Of the 12 registries that seem most appropriate for harmonization, 7 are general in nature and focus on characterizing asthmatic patients, tracking patient outcomes, and improving researchers' understanding of disease progression. The other 5 are narrower in nature and focus on topics ranging from how microbiota (gut or airway) influence adult asthma, to environmental impacts on asthma (e.g. exposure to diesel fumes)	National Quality Forum National Voluntary Consensus Standards for Patient Outcomes (Phase I) http://www.qualityforum.org/Publications/2011/07/National_Voluntary_Consensus_Standards_for_Patient_Outcomes_2009.aspx Asthma Outcomes workgroup hosted by NIH agencies and AHRQ in 2010. Published recommendations - http://www.jacionline.org/issue/S0091-6749(12)X0003-4

(1) Proposed Clinical Areas	(2) General Information	(3) Existing Evidence and Treatment Modalities	(4) Registries†	(5) Other Related Work
Chronic venous insufficiency (advanced stage venous disease, most common cause of CVI is superficial venous disease)	Fairly common chronic disease – impacts approximately 40% of the American population Impacts both men and women, although it is more common in women Most commonly seen in persons over the age of 50	Medical, behavioral, surgical interventions Behavioral includes: exercise, weight loss, compression stockings Medications include: coumarins (α-benzopyrenes), flavonoids (γ-benzopyrenes), saponosides (horse chestnut extracts) Non-surgical treatments include: sclerotherapy, endovenous thermal ablation Surgical treatments include: ligation and stripping, microincision / ambulatory phlebectomy, vein bypass Moderate evidence of effectiveness for medications, but little long-term evidence Further study of newer ablation techniques and surgical techniques is needed	Initial search of Clinical Trials.gov (venous insufficiency, open and observational studies recruiting in the US) suggests few registries - 8 returned, however, not all of them meet criteria (it is likely that only 3 – 4 would be included) The enrollment varies widely for these registries – one estimates 86 enrollees, another estimates 1,800, while another estimates 175,000 (CVI is one of 15 chronic conditions included in the registry) 4 of the 8 registries are funded by private organizations; one is funded by a vascular research institute, two are funded by federal agencies, and another by a hospital and academic institution 3 of the 8 are more general in their objectives (collecting outcomes on standard procedures); 1 is looking at using a varicose vein device on CVI, and the other 4 are focused more on wound care resulting from CVI	Other work includes the American College of Phlebology PRO Venous Registry – way to collect both physician and patient report outcomes through EMRs (also collects some PQRS measures) A related venous registry is sponsored by the American Venous Forum (VQI – Varicose Vein Registry)

(1) Proposed Clinical Areas	(2) General Information	(3) Existing Evidence and Treatment Modalities	(4) Registries†	(5) Other Related Work
Colorectal Cancer (ODF participants suggested cancer and the research team narrowed to colorectal cancer)	Among cancers, affects large number of people (3rd most common type for men and women in US, per the ACS, excluding skin cancers) Higher incidence among African Americans and persons with Type 2 diabetes	Medical, surgical options, depending on cancer stage Surgery Chemotherapy Evidence is lacking in some areas – e.g., use of adjuvant chemotherapy for stage II cancer, use of targeted therapies	Initial search of ClinicalTrials.gov (colorectal cancer, open and observational studies in US) (60+ returned) but many are broad (include many cancer types); few registries likely fit our criteria and goals Outcome measures such as genetic markers, tissue samples, and so on seem to predominate, though there are some more traditional health outcome measures MD Anderson Cancer Center is a major player, multiple studies (probably the majority) Other registries (not found in ClinicalTrials.gov) seem broader in focus but information on size and other details harder to find	• At least one PCORI-funded study focused on patient preferences; appears to be and a lot of other work on patient-reported outcomes for CRC • There is an ICHOM Standard Set for colorectal cancer • Also, published consensus study on core outcomes for colorectal cancer surgery CONSENSUS-CRC (Core Outcomes and iNformation SEts iN SUrgical Studies – ColoRectal Cancer) Working Group ‡

‡ http://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1002071

(1) Proposed Clinical Areas	(2) General Information	(3) Existing Evidence and Treatment Modalities	(4) Registries†	(5) Other Related Work
Dementia§ - focused on Alzheimer's disease	Estimated 5.1 million people in the US have Alzheimer's disease – by 2050, this number is expected to be 14 million It is the most common form of dementia 6th leading cause of death among adults; 5th leading cause of death among elderly adults (65 – 85 years old) CDC.gov	There is no cure for Alzheimer's disease Treatment focuses on improving quality of life and is done mostly through medications and through: Managing behavioral symptoms Delaying onset of symptoms Improving mental focus	28 studies identified in ClinicalTrials.gov Most of the studies are fairly small, however 2 are really large: 17 studies estimate that they will have between 24 – 1,000 enrollees; 6 estimate between 1,000 – 12,000; 3 estimate between 12,001 – 50,000; 2 estimate having 500,000 enrollees 4 of the studies are funded by industry, 3 are funded by the Federal government (NIH or other), 10 are funded by an associations, universities or health systems; the remaining 11 are funded by a combination of NIH, universities and health systems Approximately half of the clinicalTrials.gov studies seem broader in nature Other registries include: Mayo clinic is sponsoring Rochester (Minnesota) Epidemiologic Program Project (REPP) – it is a population-based data resource which can provide rates and clarify risk factors and outcome for Alzheimer's disease, and St. Louis Alzheimer's Association Research Registry	• American Academy of Neurology, American Geriatrics Society, American Medical Directors Association American Psychiatric Association and Physician Consortium for Performance Improvement established a workgroup to define quality measures to improve outcomes for dementia patients (DWG – Dementia Measures Workgroup) • ICOHM (dementia measure set)

§ Dementia is a general term for memory loss and memory loss conditions. Alzheimer's disease makes up approximately 60-80% of the dementia cases. Vascular dementia, which commonly follows a stroke, is the second most common form of dementia (https://www.alz.org/what-is-dementia.asp). The research team focused our exploratory research on Alzheimer's disease.

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Depression	One of the most common mental disorders in the US Major depression is twice as common in women than men Can affect all ages but median onset of first episode is 32 years Risk increases with neurological conditions, after childbirth, major environmental stresses	Medications, psychotherapy most common treatment modalities (used individually or in combination). Medications include multiple drug classes: TCAs, MAOIs, SSRIs, atypical antidepressants (these are more recent to market and varied) Psychotherapy includes: cognitive behavioral therapy (CBT), interpersonal therapy, and problem-solving therapy. Brain stimulation therapies, e.g., electroconvulsive therapy (ECT) can be effective for severe cases Strong evidence for general approach (medication + therapy), weak evidence, little comparative evidence for selecting specific medication Many new drugs, but generally similar to existing treatments. Also, efforts to combine drugs (e.g., adding antipsychotic to antidepressant). Several novel drugs are being studied in trials currently. Other new research focuses on brain stimulation therapies (e.g., repetitive transcranial magnetic stimulation (rTMS), vagus nerve stimulation (VNS))	34 open observational studies in the USA for Depression/Major Depressive Disorder found on ClinicalTrials.gov 13 of the studies may be of interest, although 7 have measures that may not be appropriate for harmonization Registry sizes: 100,000, 50,000, 500, 330, 100-200 (5), <100 (4) Majority of Sponsors/Collaborators are Universities and Hospitals/Health Systems, one NIMH, one commercial For the 13 studies, funders breakdown: 1 NIH, 1 Industry, 12 Other (including individuals, universities, and community-based organizations) 9 of the studies appear to be more general in nature with general outcomes such as patient scores, biorhythms, fMRI; 4 appear to be very specific e.g. microbiome, brain inflammation, genetic markers.	Depression measure scales include: PARS, MADRS, HAM-D, CGI-S, CDRS-R, PHQ-9 Other outcomes measures can be general ranging to very specific to the study, e.g. “depressive symptoms” to “Levels of Glutamate in Basal Ganglia Anxiety and Depression Association of America (ADAA); Depression and Bipolar Support Alliance HEDIS Depression Quality Measures: Utilization of the PHQ-9 to Monitor Depression Symptoms for Adolescents and Adults, Depression Remission or Response for Adolescents and Adults, and (planned for 2018) Depression Screening and Follow-up for Adolescents and Adults

(1) Proposed Clinical Areas	(2) General Information	(3) Existing Evidence and Treatment Modalities	(4) Registries†	(5) Other Related Work
Diabetes (Type 1)	Chronic autoimmune disease in which the pancreas produces little to no insulin. Usually develops in children or teenagers. 40,000 new cases each year. Affects both men and women.	No cure. but treatment focuses on maintaining normal blood sugar levels. Insulin therapy through injections, an insulin pump, or closed loop insulin delivery (artificial pancreas.) Frequent blood sugar needle checks, and potentially continuous glucose monitoring (CGM.) Diets rich in fruits, vegetables, and whole grains. Exercise Pancreas transplant Islet cell transplant Stem cell transplant	Initial search of CT.gov and Google yielded 26 initial registries with 13 meeting criteria for potential inclusion 8 additional registries were found through internet searches At least 6 registries are very broad in scope, with the goal of serving as a broad recruiting or research database Others focus on validating QoLmeasures; expanding knowledge of immune tolerance, learning behavior, device use, etc. Most registries are based at universities, with several receiving funding from NIDDK, NIAID, JDRF, ADA, and T1D Exchange	

(1) Proposed Clinical Areas	(2) General Information	(3) Existing Evidence and Treatment Modalities	(4) Registries†	(5) Other Related Work
Diabetes (Type 2)	As of 2014, 29.1 million people in the United States, or 9.3% of the population, have diabetes. One in four people with diabetes don't know they have the disease. An estimated 86 million Americans aged 20 years or older have prediabetes. (NIDDK) Deaths: Diabetes remains the 7th leading cause of death in the United States in 2010, with 69,071 death certificates listing it as the underlying cause of death, and a total of 234,051 death certificates listing diabetes as an underlying or contributing cause of death Common chronic disease with particularly high rates among African Americans, Hispanics, and American Indians/Alaska Natives	Medications, surgery, lifestyle modifications Medications include: metformin, sulfonylureas, meglitinides, thiazolidinediones, DPP-4 inhibitors, GLP-1 receptor agonists, SGLT2 inhibitors, insulin therapy Bariatric surgery may be an option for some patients Lifestyle modifications include: diet, exercise, blood sugar monitoring Many new medications introduced in recent years, with little comparative evidence to support treatment decisions	Initial search of ClinicalTrials.gov (Type 2 diabetes, open and observational studies in US) suggests adequate registries (44 returned) At least half are very small, narrow in scope, or have ended but 14+ eligible studies Many studies funded by NIDDK, NHLBI, NICHD; 2 by the American Heart Association, 6 by AstraZeneca focused on 1 drug, and 1 PCORI-funded Merck launched global patient registry in 2014 of about 20,000 patients to evaluate their real-world experience with medication, blood sugar levels, diet, exercise, use of healthcare, and quality of life The Diabetes Collaborative Registry® led by the American College of Cardiology, also American Diabetes Association, American College of Physicians, American Association of Clinical Endocrinologists, and Joslin Diabetes Center. Also, AstraZeneca and Boehringer Ingelheim are involved American College of Cardiology and National Heart Centre Singapore creating global diabetes registry	ICHOM measure set "ramping up" (not sure of timeline) NQF Diabetes measure set: value-based episodes of care

(1) Proposed Clinical Areas	(2) General Information	(3) Existing Evidence and Treatment Modalities	(4) Registries†	(5) Other Related Work
Hypertension	About 75 million American adults (32%) have high blood pressure, 1 in every 3 adults High blood pressure was a primary or contributing cause of death for more than 410,000 Americans in 2014, more than 1,100 deaths each day High blood pressure costs the nation $48.6 billion each year, including cost of healthcare services, medications and missed work days (CDC fact sheet)	Lifestyle changes including healthy eating, being physically active, maintaining a healthy weight, limiting alcohol intake, and managing and coping with stress Medications include: Diuretics Beta blockers Angiotensin-Converting Enzyme (ACE) Inhibitors Calcium Channel Blockers Alpha Blockers Alpha-Beta Blockers Central Acting Agents Vasodilators	Initial search of ClinicalTrials.gov (hypertension, open and observational studies in US) suggests adequate registries (58 returned) Approximately 35 relevant Half have enrollments of <150; small number with >500 Mostly university based with a small number funded by NIH and several collaborating with device manufacturers Objectives of these studies are relatively narrow, e.g., identification of genetic markers; use of lung Doppler signals to diagnose pulmonary hypertension; how Noncirrhotic Portal Hypertension (NCPH) develops; clinical course and treatment of chronic thromboembolic pulmonary hypertension (CTEPH); impact of hypertension on cognitive performance; etc American Society of Hypertension (ASH) Hypertension Registry Initiative (information on enrollment and measures not readily available) Intracranial Hypertension Research Foundation IH Registry (information on enrollment and measures not readily available)	The Million Hearts® Clinical Quality Measures (CQM) is a set of evidence-based clinical quality measures focused on the Million Hearts®ABCS (Aspirin when appropriate, Blood pressure control, Cholesterol management, and Smoking cessation)

(1) Proposed Clinical Areas	(2) General Information	(3) Existing Evidence and Treatment Modalities	(4) Registries[†]	(5) Other Related Work
Low Back Pain	In a 3-month period, more than one-fourth of U.S. adults experience at least 1 day of back pain. Race, heredity, age, and lifestyle can contribute to different forms of low back pain (NIAMS) Direct costs for LBP are estimated between $20 billion and $98 billion in the US. With indirect annual costs included, estimates are as high as $200 billion. Lifetime prevalence is reportedly 75-84% of the general population studied in developed countries; 1-month period prevalence has ranged from 35% to 52.2% [**]	Multiple surgical and non-surgical interventions. Also, medications and alternative approaches. Surgical interventions include: discectomy, laminectomy, kyphoplasty, vertebroplasty, spinal fusion Glucocorticoid and other injections include: epidural injections, intradiscal injections, local or trigger point injection, facet joint injection and medial branch block, sacroiliac joint injection, piriformis syndrome injection Botox injection Electrothermal and radiofrequency therapies Medications include: NSAIDs, muscle relaxants, narcotics, antidepressants Alternative approaches include: massage, acupuncture, yoga Limited evidence of effectiveness for some approaches. Good or fair evidence for others. Little comparative evidence. Ongoing development of new surgical approaches and new devices, e.g., nerve ablation device approved in 2016	Up to 12 registries identified from all sources, several large registries (10k+) and several small; at least one has primarily genetic outcome measures and 2 are surgeon-reported data for FDA PM surveillance of devices QOD/Lumbar Spine Registry has 23,000 patients enrolled across 80 centers; purpose to be continuous national clinical registry for neurosurgical procedures and practice patterns; only surgically-treated patients AAPM&R/AANS[††] working with technology vendor to create spine registry, launching 1/1/2017 Kaiser Permanente Spinal Implant Registry (1 pub had 15k patients); there are publications available online but not a lot of publicly available information Funded mix includes associations, systems, large physician practice, at least 1 device manufacturer, 1 public (US Army) Larger registries have very broad objectives (beyond LBP, often to include broad range of spine-related conditions)	ICHOM measure set for low back pain

[**] http://bmcmusculoskeletdisord.biomedcentral.com/articles/10.1186/1471-2474-15-283
[††] American Academy of Physical Medicine and Rehabilitation and the American Association of Neurological Surgeons

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Non-Small Cell Lung Cancer (ODF participants suggested cancer and the research team narrowed to non-small cell lung cancer)	High burden - for 2016, 2nd highest estimated new cancer cases; leading cause of cancer deaths in the US Impacts both men and women (it is the 2nd most common cancer diagnosis for both men and women) Lung cancer is a higher risk in at least one of AHRQ's priority areas (black men are 20% more likely than white men to develop lung cancer) Chronic condition Impacts primarily elderly populations (2 of 3 persons diagnosed are 65 years or older)	Multiple treatment methods Surgical approaches include: wedge resection, segmental resection, lobectomy, pneumonectomy Chemotherapy – multiple combinations used Radiation therapy Targeted drug therapies (e.g., afatinib, bevacizumab, etc.) Rapid evolution of treatment approaches with introduction of new drugs, new radiation therapy approaches, as well as recognition of histologic subsets of NSCLC – all requiring further study	Initial search of ClinicalTrials.gov (non-small cell lung cancer, open and observational studies in the US) suggests adequate registries (123 returned) In reviewing 13 of the studies (those labeled specifically patient registries), 3 have between 1,000-5,000 enrollees, 3 have more than 5,000 enrollees. The remaining 7 studies have fewer than 1,000 enrollees 5 of the 13 studies are funded by private industry, 3 are funded by different cancer institutes, and 4 seem to be funded by different academic university/medical centers. It is difficult to ascertain how 1 of the registries is funded. 6 of the 13 studies seem to be more general in nature, covering issues such as characterizing patterns of care, observations of patient characteristics for those receiving a treatment, and gathering self-reported outcomes of cancer survivors. Of these 5, 2 include other forms of cancer. The other 7 registries are fairly narrow and focus on tracking gene expressions, use of a specific diagnostic test, and use of specific treatments.	ICHOM measure set of non-small cell lung cancer

(1) Proposed Clinical Areas	(2) General Information	(3) Existing Evidence and Treatment Modalities	(4) Registries[†]	(5) Other Related Work
Management of anterior cruciate ligament injuries	Recommendation from AAOS Impacts a large proportion of the active population	Medical or surgical approaches Medical includes: self-care followed by physical therapy Surgery includes: ACL reconstruction followed by physical therapy Limited evidence in pediatric, young adult populations, also in patients with ACL and meniscal tears, limited evidence on return to sports timing Moderate comparative evidence for medical vs. surgical for less active patients	1 pediatric study identified, not yet recruiting - estimated enrollment is 405; no other US studies identified in ClinicalTrials.gov (7 identified but all of them are outside US--Sweden, Finland, UK, France) Studies in ClinicalTrials.gov are generally randomized, interventional studies Other US-based registries found in Google search (Hospital for Special Surgery, NY; Interventional Orthopedics Foundation) [‡‡]	AAOS has evidence base clinical practice guidelines

[‡‡] https://www.hss.edu/research-acl-registry.asp; https://interventionalorthopedics.org/interventional-orthopedics-patient-registry-database/; https://consultqd.clevelandclinic.org/2015/07/the-moon-group-and-acl-surgery-a-decade-of-research-redefines-what-a-cohort-can-achieve/

(1) Proposed Clinical Areas	(2) General Information	(3) Existing Evidence and Treatment Modalities	(4) Registries†	(5) Other Related Work
Management of fragility fractures (searched fragility fractures, vertebrae fractures, neck of the femur fractures, and wrist fractures)	From https://medicine.umich.edu/dept/orthopaedic-surgery/patient-care-services/trauma/fragility-fracture-clinic 1/2 of all women and up to 1/4 of all men will suffer a fragility fracture in their lifetime 80% of individuals who have already had at least one osteoporotic fracture are neither identified nor treated. Among older Americans, there are over 2 million fractures occurring each year - more than heart attacks, stokes, and breast cancer combined From AOT: Most patients that have fragility fractures are not diagnoses or treated	Drug therapies Nutrition – supplements Surgery	Through clinicaltrials.gov, found 5 possible registries, all of which seem fairly narrow in nature Estimated enrollment for studies varies widely, from 100 to 100,000 (difficult to know of the 100,000 how many have fragility fractures versus other conditions) Searched more broadly and identified 3 more registries, including Own the Bone, the NOF and NBHA Quality Improvement registry, and a Trauma Registry	

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Management of hip fractures	Recommendation from American Academy of Orthopedic Surgeons (AAOS) Affects significant proportion of orthopedic patients Approximately 254,000 hip replacement surgeries in 2000, half to patients over 75 years of age (NIAMS) Some overlap with osteoarthritis (depending on how defined)	Surgery, rehab, medication Surgery may include: internal repair, partial hip replacement, total hip replacement Physical therapy and occupational therapy Medication may include bisphosphonates to reduce risk of second hip fracture Strong to moderate evidence for most guidelines related to hip fracture management However, most guidelines note the need for further research	Search of ClinicalTrials.gov found 3 studies using 'hip fracture,' 6 studies using 'hip replacement,' 8 studies using 'hip arthroplasty' (overlapping) 2 very large: one with over 30,000 joints (HealthEast Community Hip and Knee Replacement Registry), estimated enrollment of 200,000 through 2091; and another (ICORE) with estimated enrollment of 10,000; 3 others have 200-300 enrollees The 2 large registries are very broad in focus; the other few registries are narrower with a focus on specific devices (2) or identification of biomarkers (1) Several device manufacturers as funders A substantial proportion of registries are based outside US	AAOS has evidence based clinical practice guidelines on this topic There has been a lot of work done, with FDA backing and ICOR (International Consortium of Orthopedic Registries) group; ICOR specifically says that they are " …harmonizing and linking clinical registry information from diverse registries"

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Migraine/headache	Migraine is a neurological disease characterized by recurrent episodes of severe headache, often accompanied by a variety of symptoms, including nausea, vomiting, sensitivity to light and sound and changes in vision. Estimated 36 million Americans, about 12% of population, suffer from migraines at least periodically (American Migraine Foundation) Migraine can be extremely disabling and costly, accounting for more than $20 billion in direct and indirect expenses each year in the US[§§]	Treated with pharmaceuticals for both pain relief and prevention Pain relief: Nonprescription pain relievers for less severe migraines Triptans Ergots Anti-nausea medications Opioids Glutocorticoids Prevention: Cardiovascular drugs Antidepressants Anti-seizure drugs Botox Alternative medicine, including acupuncture, biofeedback, massage therapy, cognitive behavioral therapy, herbs, vitamins and minerals	Only one relevant registry on ClinicalTrials.gov American Registry for Migraine Research (American Migraine Foundation): unable to determine size; supported by multiple pharmaceutical companies INVIDA Outcomes Network, National Migraine Association Translational Genomics Research Institute (TGen) Migraine Research Registry: unable to determine size	National Migraine Association has resources for treatment and management

[§§] Steiner TJ, Stovner LJ, Birbeck GL. Migraine: the seventh disabler. *The Journal of Headache and Pain*. 2013;14(1):1.

Headache disorders. World Health Organization website. http://www.who.int/mediacentre/factsheets/fs277/en/. Accessed June 8, 2016. Types of Headache/Migraine. American Migraine Foundation website. https://americanmigrainefoundation.org/living-with-migraines/types-of-headachemigraine/ Accessed June 8, 2016.

(1) Proposed Clinical Areas	(2) General Information	(3) Existing Evidence and Treatment Modalities	(4) Registries[†]	(5) Other Related Work
Osteoarthritis (of the extremities)	Recommendation from American Academy of Orthopedic Surgeons (AAOS) Common chronic disease that affects significant proportion of orthopedic patients (with an estimated overall prevalence in the general adult population of 11% for hip OA and 24% for knee OA) Osteoarthritis is the most common form of arthritis and affects approximately 27 million Americans (NIAMS) By 2030, an estimated 20% of Americans (70m people) will be 65+ and at increased risk for osteoarthritis (NIAMS)	Medications, physical or occupational therapy, surgery, alternative approaches Medications to reduce pain include: NSAIDs, acetaminophen, duloxetine Injections include: cortisone, hyaluronic acid Surgery may include: osteotomy, arthroplasty Alternative approaches may include: yoga, acupuncture, glucosamine and chondroitin New devices, but questions about effectiveness, long-term outcomes from various procedures	Use of 'osteoarthritis' results in 36 studies in clinicaltrials.gov (only 1 using 'osteoarthritis of the extremities') 10+ studies eligible: 1 with estimated enrollment of 100,000; 1 with estimated enrollment of 30,000; others 100-500; several studies (not counted as eligible) also have fewer than 100 enrollees The majority of studies involve knees, though there are some that cover knees and hips, or knees, hips, or shoulders ~half funded by device manufacturers; 1 AHRQ; others based at universities but unable to determine funding objectives and outcome measures generally broad: standard knee and hip scores as well as adverse events	ICHOM measure set for hip and knee osteoarthritis AAOS has evidence based clinical practice guidelines on this topic and there are outcome measures for pain/disability and radiologic indexes[***] Several European registries

[***] https://www.oarsi.org/research/outcome-measures

(1) Proposed Clinical Areas	(2) General Information	(3) Existing Evidence and Treatment Modalities	(4) Registries†	(5) Other Related Work
Rheumatoid Arthritis (RA)	Chronic autoimmune disorder causing joint inflammation, pain, and deformity High burden – 200,000 new cases in US each year Impacts both men and women, but it afflicts three times more women than men Women tend to have earlier onset, between ages 30 and 60, while men experience it later in life Potential genetic component Specialties involved include rheumatologists, geriatricians, orthopedists, and PCPs	No cure, but various treatment modalities aim to minimize disease activity (inflammation) and achieve remission Early diagnosis and aggressive treatment are crucial, given the irreversibility of joint damage Stretching and physical therapy Current research focuses on new drugs Medications can slow disease activity and/or alleviate symptoms Medications include NSAIDs, antirheumatic drugs (DMARDS), corticosteroids, biologics (to block Tumor Necrosis Factor), and JAK inhibitors Surgical options include arthrocentesis to drain fluid from a joint and arthroplasty to repair or replace a joint	Initial search of ClinicalTrials.gov, HSRProj, RoPR, and Google for open and observational rheumatoid arthritis studies/registries yielded 20 registries suitable for inclusion. 5 of the 20 have more than 10,000 enrollees, 5 have between 1,000 and 3,000 enrollees, 1 has between 500 and 1,000 enrollees, 8 have between 100 and 500 enrollees, and 1 has fewer than 100 enrollees. 8 are primarily funded by universities or their medical centers, 3 are funded by private hospitals, 6 are funded by private industry, and 3 are funded by non-profit rheumatology or arthritis associations. The majority of these registries are general in nature, collecting data on patterns of care, patient-reported outcomes, and clinical observations. 11 registries are devoted exclusively to RA, while others tested a device applicable to RA patients and/or included other rheumatic conditions or types of arthritis. Of 6 registries that look at items related to biomarkers, only two of them do not look at clinical and patient-reported outcomes.	Outcome Measures in Rheumatology (OMERACT)

(1) Proposed Clinical Areas	(2) General Information	(3) Existing Evidence and Treatment Modalities	(4) Registries†	(5) Other Related Work
Robotic surgery	In 2012, approximately 400,000 robotic surgeries were performed across all types of surgery in the U.S. The rate of robotic surgeries is increasing 25% annually. The market is expected to grow due to technological innovations such as the capsule robot system, software/applications and imaging system, increasing geriatric population base and increasing per capita healthcare expenditures. Major players in the market include Intuitive Surgical, MAKO Surgical (now owned by Stryker), Accuray, Mazor Robotics and Titan Medical.††† A study of costs associated with robotic surgery found that, on average across 20 types of robotic surgery, the additional variable cost of using a robot-assisted procedure was about $1,600, or about 6% of the cost of the procedure.	The FDA has cleared robotically-assisted surgery (RAS) devices for use by trained physicians in an operating room environment for laparoscopic surgical procedures in general surgery cardiac, colorectal, gynecologic, head and neck, thoracic and urologic surgical procedures. Some common procedures that may involve RAS devices are gall-bladder removal, hysterectomy and prostatectomy. A consistent theme in the literature covering robotic-assisted surgical devices (RASD) technology is its association with both reduced blood loss and decreased postoperative recovery time. Other potential benefits include increased precision and accuracy of motion and access to confined surgical sites. Many researchers cite higher monetary costs and increased operating times associated with RASD technology as potential disadvantages. Complication rates vary by procedure, but, with exceptions, overall appear to be acceptably low as compared to conventional methods.‡‡‡	5 relevant studies identified through ClinicalTrials.gov. 1 for robotic assisted hernia repair, 1 treatment of low-risk pharyngeal cancer, 1 pediatric scoliosis, 2 spinal surgeries more broadly 3 with enrollment of 2,000, 1 with expected enrollment of 900, and 1 with 44 3 sponsored by Mazor Robotics, 1 MD Anderson w funding unclear, 1 another device manufacturer	Center of Excellence in Robot-Assisted Laparoscopic Surgery (COERALS) program, including comprehensive surgical outcomes database and patient registry that will provide clinical data and support research efforts to improve patient safety, care and surgical outcomes (sponsored by Clinical Robotic Surgery Association) Institute for Surgical Excellence and FDA joint sponsorship of Conference on Furthering National Standards for Robotic Registry FDA created discussion paper and held workshop to outline topics related to the design, development, and evaluation and regulation of robotic-assisted surgical devices (RASD) The Medical Device Epidemiology Network Initiative (MDEpiNet) can potentially be leveraged to include RASD evidence evaluation

††† http://www.beckersasc.com/asc-turnarounds-ideas-to-improve-performance/11-things-to-know-about-robotic-surgery.html
‡‡‡ https://www.fda.gov/downloads/MedicalDevices/NewsEvents/WorkshopsConferences/UCM454811.pdf

(1) Proposed Clinical Areas	(2) General Information	(3) Existing Evidence and Treatment Modalities	(4) Registries†	(5) Other Related Work
Scoliosis	Affects 2-3 percent of the population, or an estimated 6 to 9 million people in the U.S. Every year, an estimated 30,000 people are fitted with a brace and 38,000 undergo surgery for spinal fusion Scoliosis can be classified by etiology: idiopathic accounts for about 80%, adolescent idiopathic scoliosis is usually diagnosed during puberty Congenital results from embryologic malformation of 1 or more vertebrae Neuromuscular is secondary to neurological or muscular diseases (National Scoliosis Foundation)	Treatment includes Observation (for those who are still growing and have a mild curve); Bracing (to stop a curve from getting worse when a person is still growing and has a moderate curve), and Surgery (which can involve fusing 2 or more bones in the spine, or implanting a metal rod or other device) (NIAMS) posterior spinal fusion with instrumentation and bone graft anterior approach with visually assisted thorascopic (VAT) surgery decompressive laminectomy minimally invasive surgery	13 studies from clinicaltrials.gov are suitable (7 apply to children only, 4 adults only, and 6 both children and adults) 5 studies with 200 enrollees or fewer, 3 from 300-600, 4 from 1,000-4,000, 1 with 10,000 Several had relatively broad objectives (e.g., examine treatment of patients with early onset scoliosis) but at least 5 were focused on specific device or procedure (e.g., robotic surgery, bone graft, spinal fusion) Approximately half funded by device manufacturers, others based at university medical centers and other funding unclear, 2 funded by NIH Scoliosis Outcomes Database Registry (NYU) Scoliosis Outcomes Database Registry (Nemours)	

(1) Proposed Clinical Areas	(2) General Information	(3) Existing Evidence and Treatment Modalities	(4) Registries†	(5) Other Related Work
Stroke	High burden – leading cause of adult disability in the US; fifth leading cause of death in America Strokes are higher risk in a few AHRQ priority populations (women, racial/ethnic minorities) Impacts all age groups, although most common in persons over 55 years old AFib and stroke connection (AFib is a confirmed clinical area so there may be some overlap)	Multiple treatment methods, use depends on type of stroke Ischemic stroke: tPA, mechanical thrombectomy Hemorrhagic stroke: endovascular procedures, surgical treatment to stop bleeding Also, rehab following stroke Multiple new devices have been introduced in the past decade, also devices aimed at improving diagnosis and preventing recurrent strokes Strong evidence for some treatment areas (e.g., tPA for ischemic stroke), weak or limited evidence in other areas (e.g., non-invasive vascular imaging)	Initial search of ClinicalTrials.gov (stroke, open and observation studies recruiting in the US) suggests adequate registries (56 returned) In reviewing 7 of the studies (those labeled specifically as patient registries), 2 have between 1,000-5,000 enrollees, 3 have between 10,000-50,000 enrollees. 1 registry has 900 estimated enrollees and another has over 3 million enrollees. The funding for the 7 registries is primarily private. Some funding comes from associations; one is funded by a hospital foundation and health system. 2 of the registries are funded by industry. Of the 7 registries, 5 are more general in nature and focus on adhering to general practice, developing a repository of samples for future analysis, collecting general patient outcomes post-stroke, and collecting patient outcomes post-surgery (a few of these registries cover more than stroke with overall large enrollments). 2 of the registries are narrower in their focus, e.g., the outcomes relate to results for using a specific device.	The National Institute of Neurological Disorders and Stroke (NINDS) Common Data Elements project published recommended data for collection ICHOM measure set for stroke

(1) Proposed Clinical Areas	(2) General Information	(3) Existing Evidence and Treatment Modalities	(4) Registries†	(5) Other Related Work
Thyroid cancer	64,000 estimated new cases and 1,980 estimated deaths in 2016. In 2013, estimated 637,000 people living with thyroid cancer in US Accounts for 0.3% of all cancer deaths and 3.8% of all new cancer cases 98% survival over 5 years Rates have been rising on average 4.5% per year over the last 10 years§§§	Surgery is the main treatment for most cases, including removal of tumor and all or part of remaining thyroid gland (lobectomy, thyroidectomy, lymph node removal) Radioactive iodine treatment-used to ablate (destroy) any thyroid tissue not removed by surgery or to treat some types of thyroid cancer that have spread to lymph nodes and other parts of the body. Thyroid hormone therapy-may prevent some thyroid cancers from returning External beam radiation therapy-used as part of the treatment for medullary thyroid cancer and anaplastic thyroid cancer Chemotherapy-seldom helpful for most thyroid cancers Targeted therapy-several drugs to treat medullary thyroid cancer, including Vandetanib and Cabozantenib; for papillary or follicular thyroid cancer-Sorafenib, Lenvatinib (evidence still unclear)****	8 studies in clinicaltrials.gov eligible: 3 with enrollment of 300 or less, 3 from 700 to 1,350, and 2 with no stated number of limit. 4 studies based at NIH (3 NCI, 1 NIDDK), 3 at university-based cancer centers (funding unclear), one pharma company Broad research goals, studying natural history, with 2 focused on familial non-medullary thyroid cancer and 1 focused on papillary thyroid cancer Outcome measures include growth rate of tumors/lesions, time to symptomatic progression, overall survival and collection of family history, imaging rests, genetic testing and other biomarkers Thyroid Cancer Care Collaborative (TCCC) maintains collaborative database with detailed record of individual thyroid cancer patients' disease and treatment; established in 2010 and funded by Thyroid, Head, and Neck Cancer (THNC) Foundation (unable to find enrollment #s)	

§§§ https://seer.cancer.gov/statfacts/html/thyro.html
**** https://www.cancer.org/cancer/thyroid-cancer/treating.html

Appendix B. Registry and Stakeholder Participants

Atrial Fibrillation

Registry	Representative(s)
A Novel Healthcare Information Technology Tool to Improve Care in Patients with Atrial Fibrillation (AFCare)	Jonathan Hsu
American Medical Association-Physician Consortium for Performance Improvement (AMA-PCPI)	Jamie Jouza
American Heart Association Get with The Guidelines - Afib	William Lewis
Bristol-Myers Squib	Lisa Rosenblatt
Does Atrial Fibrillation (AF) Termination Without Additional Ablation Influence Outcome? (TARGET)	Mitra Mohanty
GARFIELD AF	Gloria Kayani
Heart Rhythm Society	Laura Blum
Left Atrial Appendage Occlusion Registry (LAAO)	Lara Slattery
Medtronic	Robert Kowal
Outcomes Registry for Better Informed Treatment of Atrial Fibrillation II (ORBIT-AF II)	Jonathan Piccini
PCORI PATH Atrial Fibrillation Cohort	Saman Nazarian
PINNACLE (ACC)	Lara Slattery
Registry on WATCHMAN Outcomes in Real-Life Utilization (EWOLUTION)	Elisa Vireca
Stanford / Retrospective Evaluation and Assessment of Therapies in AF (TREAT-AF)	Mintu Turakhia

Stakeholder Organization	Representative(s)
Centers for Medicare & Medicaid Services	Kevin Larson and Reena Duseja
U.S. Food and Drug Administration	Danica Marinac-Dabic
Geisinger	Brent Williams
Lahey Clinic	Matthew Reynolds
National Library of Medicine	Lisa Lang
National Quality Forum	Kyle Cobb
StopAfib.org	Mellanie True Hills
U.S. Department of Veterans Affairs	David Atkins

Asthma

Registry	Representative(s)
AAAAI Allergy, Asthma and Immunology Quality Clinical Data Registry	Sheila Heitzig
Capricorn Asthma Working Group	Sharmile Nyenhuis
Children's Health Foundation Pediatric Asthma Registry	Julie Harris
Colorado Pediatric Collaborative Asthma Patient Registry	Maggie Reyes Leczinski
Duke Asthma Center	Loretta Que
Immune Interactions in Severe Asthma	Sally Wenzel
Kaiser Permanente	William Crawford
Longitudinal Observational Study of Severe Asthma	Amisha Barochia
Mechanisms of Response to Diesel Exhaust in Subjects with Asthma	Reynold Panettieri
MN Community Measurement	Collette Pitzen
Pulmonary Health and Deployment to Southwest Asia and Afghanistan	Eric Garshick
Severe Asthma Research Program III (WU SARPIII)	Mario Castro
The Genetics of Severe Asthma in Children	Christopher Carroll
Vitamin D, Steroids, and Asthma in African American Youth (AsthMaP2)	Robert Freishtat

Stakeholder Organization	Representative(s)
Allergy Asthma Network Mothers of Asthmatics	Tonya Winders
American Thoracic Society	Patricia Finn
Asthma and Allergy Foundation of America	Deidre Washington
COPD Foundation	Elisha Malanga
Kaiser Permanente - Medical Groups in Northern California	Imran Junaid
Montefiore Asthma Center	Deepa Rastogi
National Quality Forum	Kyle Cobb
OCHIN	Erik Geissal and Anisha Abdul-Ali
Propeller Health	Leanne Kaye
The National Institute of Allergy and Infectious Diseases	Lisa Wheatley
The National Library of Medicine	Lisa Lang

Depression

Registry	Representative(s)
American Psychiatry Association Registry	Phillip Wang
Dallas 2K: A Natural History Study of Depression	Madhukar Trivedi
HealthQuality.va.gov	Crowe Chris
Mental Health Research Network	Greg Simon
Minnesota Community Measurement	Collette Pitzen
Mood Patient Powered Research Network (MoodNetwork)	Andrew Alan Nierenberg
National Network of Depression Centers (NNDC) Mood Outcome Program	J. Raymond DePaulo, Jr.
NCQA - HEDIS	Mary Barton
PRIME Registry/American Board of Family Medicine	Lars Peterson
Treatment-Resistant Depression: A Narrative and Systematic Review of Definitions and Methods in Clinical Research Studies	Bradley Gaynes
Treatment-Resistant Depression Registry	Bryan Olin
University of Texas-Southwestern Depression Cohort: A Longitudinal Study of Depression	Madhukar Trivedi
Quantified Mobile Sensing for Improving Diagnosis and Measuring Disease Progression	Thilo Deckersbach

Stakeholder Organization	Representative(s)
American Psychological Association	C. Vaile Wright
Blue Cross Blue Shield of Massachusetts	Rosemary Brown
Centers for Medicare & Medicaid Services	Kevin Larsen
Depression and Bipolar Support Alliance	Allen Doederlein
U.S. Food and Drug Administration	Danica Marinac-Dabic and Wen-Hung Chen
International Foundation for Research and Education on Depression (iFRED)	Kathryn Goetzke
Menninger Clinic	M. Justin Coffey
National Alliance on Mental Illness	Paul Surgenor
National Cancer Institute	Ashley Wilder Smith
National Institute of Mental Health	Michael Freed
SAMSHA	Lisa Patton
National Library of Medicine	Lisa Lang
National Quality Forum	Kyle Cobb
OCHIN	Erik Geissal and Anisha Abdul-Ali
Providence St. Joseph Health/Swedish	Phil Capp
University of Michigan	Sagar Parikh

Lung Cancer

Registry	Representative(s)
AACR Project GENIE	Seth Sheffler-Collins
Cancer Experience Registry (CER)	Joanne Buzaglo and Alexandra Zaleta
Cancer Research and Biostatistics	Kari Chansky
Genentech	Laura Chu and Sarika Ogale
National Comprehensive Cancer Network	Gregory Riely
National Institutes of Health	Lynne Penberthy
National Program of Cancer Registries	Loria Pollack
PANORAMA - Real World Molecular Testing, Treatment Patterns, and Clinical Outcomes EGFR Mutation-Positive NSCLC, AstraZeneca	Brian Seal
Prospective Study to Determine Impact of Early Palliative Care Consult on Quality of Life (QOL), Cancer Related Symptoms in Advanced Lung Cancer Patients: Thoracic Pilot Project	Sriram Yennu
RSSearch® Patient Registry	Joanne Davis
SBRT (Stereotactic Body Radiation Therapy) vs. Surgery in High Risk Patients with Early Stage Lung Cancer	Clifford Robinson
Society of Thoracic Surgeons	Felix Fernandez
Targeted Agent and Profiling Utilization Registry (TAPUR)	Tithi Biswas and Ramya Thota
Thoracic Oncology Outcomes Database at Ohio State University	Carolyn Presley

Stakeholder Organization	Representative(s)
American Lung Association	Albert Rizzo
Flatiron Health	Nate Nausbaum
U.S. Food and Drug Administration	Paul Kluetz
Free to Breathe	Mary Henningfield
Lung Cancer Alliance	Jennifer King
Lung Cancer Foundation of America	Apar Ganti
LUNGevity	Andrea Ferris
National Cancer Institute	George Chang, Ashley Wilder Smith, and Denise Warzal

Lumbar Spondylolisthesis

Registry	Representative(s)
American Academy of Physical Medicine and Rehabilitation Registry	Kavitha Neerukonda
American Academy of Orthopaedic Surgeons, American Association of Orthopaedic Surgeons	Will Shaffer
Comparative Study of Anterior vs. Posterior Surgical Treatment for Lumbar Isthmic Spondylolisthesis (I-Spondy)	Paul Arnold
InterFuseÂ® S and T for the Treatment of Scoliosis, Spondylolisthesis and Degenerative Disc Disease (DDD)	William Lavelle
Medtronic, Inc.	Jason Kemner
Michigan Spine Surgery Improvement Collaborative	David Nerenz
MIS ReFRESH: Robotic vs. Freehand Minimally Invasive Spinal Surgeries	Doron Dinstein
NASS Spine Registry	Pam Hayden
Nuvasive Spinetrack Registry	Kyle Malone
Quality Outcomes Database (QOD)	Mo Bydon
Spine Institute for Quality Conservative Spine Care (QCDR)	Christine Goertz
Vanderbilt University	Kristin Archer

Stakeholder Organization	Representative(s)
Aetna	J. Dawn Waters
Arthritis Foundation	Guy Eakin
Centers for Medicare & Medicaid Services	Jyme Schafer
Electronic Health Record Association	Ida Mantashi
U.S. Food and Drug Administration	Wen-Hung Chen and Hong Cheng
National Institutes of Health	Chuck Washabaugh
National Institute on Drug Abuse	Kristen Huntley
National Library of Medicine	Lisa Lang
National Osteoporosis Foundation	Catrell Harris
National Quality Forum	Jeff Dunkel
Scoliosis Research Society	Frank Schwab
Spinal Research Foundation	Christopher Gorini and Sabrina Woodlief