Methods Research Report

Outcome Measures Framework: Information Model Report

Agency for Healthcare Research and Quality

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Registry of Patient Registries

Prepared for:
Agency for Healthcare Research and Quality
U.S. Department of Health and Human Services
5600 Fishers Lane
Rockville, MD 20857
www.ahrq.gov

Contract No. 290-2014-00004-C

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AHRQ Publication No. 17(18)-EHC012-EF
February 2018

This report is based on research conducted by L&M Policy Research, LLC, under contract to the Agency for Healthcare Research and Quality (AHRQ), Rockville, MD (Contract No. 290-2014-00004-C). The findings and conclusions in this document are those of the authors, who are responsible for its contents; the findings and conclusions do not necessarily represent the views of AHRQ. Therefore, no statement in this report should be construed as an official position of AHRQ or of the U.S. Department of Health and Human Services.

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

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Suggested citation: Gliklich RE, Bibeau K, Eisenberg F, Hanna J, Leavy MB, Campion D, Christian JB. Registry of Patient Registries Outcome Measures Framework: Information Model Report. Methods Research Report. (Prepared by L&M Policy Research, LLC, under Contract No. 290-2014-00004-C.) AHRQ Publication No. 17(18)-EHC012-EF. Rockville, MD: Agency for Healthcare Research and Quality; February 2018.
www.effectivehealthcare.ahrq.gov/reports/final/cfm.
DOI: https://doi.org/10.23970/AHRQROPRMETHODS.

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Registry of Patient Registries

Structured Abstract

Objectives. This report details the research undertaken to understand registries listed on clinicaltrials.gov, as well the burden required to record some of the most intricate, necessary data so that it is available to all other registries and viewers. The published Outcome Measures Framework (OMF) was used to evaluate the completeness of entries.[1]

Data Sources. We searched the records for patient registries posted in the ClinicalTrials.gov database. For both the quantitative and qualitative studies, all records on ClinicalTrials.gov on June 23, 2015 that were defined as Patient Registries in the 'Study Type' field were downloaded for inclusion in the analyses.

Review Methods. A literature review, quantitative analysis, and qualitative analysis were undertaken to understand all facets of registration of patient registries. The report provides information on what fields within clinicaltrials.gov are populated most frequently, whether those fields were required or not, and explains how more complete data on the study population could be elicited and validated. It also describes how dominant definitions will be chosen as well as process measures such as treatments or procedures, and the associated outcome of the patients or participants involved.
A qualitative analysis on four condition areas was conducted to measure the degree to which outcome data, as entered in clinicaltrials.gov, mapped to the framework developed in the OMF. The conditions examined were depression, asthma, rheumatoid arthritis, and cardiac surgery. Two of these conditions, cardiac surgery and rheumatoid arthritis, were considered "deeper dives" and examined more in-depth detail on the level of data available in clinicaltrials.gov or other registry-run Web sites, as applicable.

Results. These research approaches were conducted with the intent to inform researchers on the development of an Internet-based database intended to house a fully functional system to clearly define, and eventually harmonize, outcome measures. This system has been termed the Outcome Measures Repository (OMR). The information model and governance structure is described in this report.

Conclusions. The intent of this report and the resulting OMR is to capture that data elements and sub-elements with the utmost attention to detail to ensure the optimal amount of information is captured while also avoiding undue burden on behalf of the registry steward responsible for entering the data into the OMR.

[1] Gliklich RE, Leavy MB, Karl J, et al. A framework for creating standardized outcome measures for patient registries. J Comp Eff Res. 2014 Sep;3(5):473-80. doi: 10.2217/cer.14.38.

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Introduction

Background

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 predetermined scientific, clinical, or policy purposes."[1] Common purposes for patient registries include evaluating the safety, effectiveness, or quality of medical treatments, products, and services, and studying the natural history of diseases. Some registries are developed and maintained solely to assist in care delivery, coordination, and quality improvement, but many serve broader research purposes. When properly designed and conducted, patient registries can provide unique insights into real world clinical practice, effectiveness, safety, and quality.

Interest in and use of patient registries has increased in recent years. Patient registries collect a broad range of data elements, which are frequently analyzed to calculate and assess outcome measures, ideally those outcomes that are important to patients and providers. Survival, disease progression or improvement, complications, and functional status are examples of outcome measures that are used to understand the natural history of disease, the impact of treatments or other initiatives, and provider performance.

The purpose of this project was to understand the strengths and identify potential improvements in the existing Outcome Measures Framework (OMF). The OMF, first published in 2014, is a common, conceptual model for classifying the range of outcomes that are relevant to patients and providers across most conditions.[2] The OMF tool is software, based on the OMF, designed for collection and display of information on outcome measures used in patient registries in a standardized way that supports searching for those measures. Ideally, stewards of registry and observational study measures will have a virtual place to house all of these definitions, which will be identified as the Outcome Measure Repository (OMR). Users of the OMR will primarily fall into two types: those stewarding a registry who will provide information on the data they collect in their registry, and those who will search for information about how a particular type of outcome measure is collected within patient registries. For the OMR to succeed, the first group of users – registry stewards – must be able to enter information into the system easily and efficiently. The second group of users – parties interested in seeking information on outcome measures – must be able to find sufficient information efficiently on outcome measures to identify items for use in their own registry or research. Meeting the needs of both sets of users is an important consideration in the design of the OMR.

Purpose of the Outcome Measure Framework and Repository

The initial objective of the OMR is to collect sufficient information to characterize the types of outcome measures that are currently used in patient registries. The long-term objective of the OMR is to support efforts to standardize outcome measures and to facilitate access to standardized outcome measures. The OMR will display information on the outcome measures currently used in registries, with the short-term goal of reducing variation in outcome measures by employing both curation and natural language process techniques to identify commonly used

definitions and support harmonized endpoints. Characterizing the outcome measures currently in use will support long-term efforts to develop standardized outcome measures by identifying areas of common ground where standards may be developed relatively quickly and areas that will require additional work.

The purpose of the OMF is to serve as a content model for developing standardized outcome measures in specific disease areas. While existing outcome measures may fit into the conceptual framework, a long-term goal of building the OMR is to encourage groups that are developing outcome measures to use the conceptual framework to define new measures. The increasing recognition of the value of standardized outcome measures has led to a need for more outcome measures across a broad range of conditions. By promoting the use of the outcome measure conceptual framework, it will be possible to simplify the task of aggregating measures across multiple conditions while encouraging researchers and others to think of outcome measures in a standardized way.

Purpose of This Report

The purpose of this report is to present an information model that can be used to operationalize the OMR. To inform the necessary components of the OMR, an analysis of the outcome measures utilized in different registries was conducted to assess the level of clinical and analytical detail included in these measures and to determine how outcome measures across different registries can be categorized. The findings from this extensive analysis were applied to the framework for outcome measures proposed in the report. The report begins by describing the analysis methods and results. Next, the information model for the OMR is presented, followed by a discussion of the operational policies and procedures and governance plans for the OMR.

This report addresses several key considerations for the OMR information model:

1. It identifies a taxonomy to be used to group the outcome measures into families.
2. It discusses considerations for using existing data dictionaries and partnering with other outcome measure initiatives and copyright holders.
3. It describes the process that will be used to update definitions and archive older definitions.
4. It proposes a governance model and composition of a governance board.
5. It explains how definitions suggested or entered by users will be validated, how equivalent definitions will be assessed, and how dominant definitions will be chosen.

Outcome Measures Framework

Analysis of Outcome Measures

Several analyses of existing outcome measures were undertaken to test and possibly refine the OMF and to inform development of the OMR. First, a quantitative analysis was conducted to assess the degree to which required and optional fields similar to those that would be included in the OMR were populated in records for patient registries posted in the ClinicalTrials.gov database. The results of this analysis provide some information on the feasibility of operating a database such as the OMR in an environment where entry of outcome measure information into the database is voluntary. Second, a qualitative analysis was conducted to evaluate the consistency and levels of data accessibility in the definitions of the outcomes measures and to use this information to assess whether modifications for the OMF are necessary for increased usability.

Quantitative Analysis of ClinicalTrials.gov Patient Registries

On June 23, 2015, all records on ClinicalTrials.gov that were defined as Patient Registries in the 'Study Type' field were downloaded. These files were downloaded in XML format with each XML file representing one ClinicalTrials.gov record. Records in which the 'Recruitment' field equaled Unknown, Terminated, Withdrawn, or Suspended were excluded from the analysis. The remaining 1,545 XML files were combined and analyzed in SAS 9.4 using the Unicode language. Fields most relevant to this analysis were selected. These fields include the ClinicalTrials.gov identifier (commonly referred to as the NCT number) , the brief and official titles, sponsor type, collaborator, intervention type, study design, study status, time perspective, enrollment, age maximum and minimum, duration follow up, condition, primary outcome measures, and secondary outcome measures. A field was considered required if it is required to complete and post a record into the ClinicalTrials.gov database. The fields that were required were: brief title, sponsor type, intervention type, study design, study status, time perspective, enrollment, age, duration follow up, at least one condition, and one outcome measure. These fields were examined to determine whether they had been completed. Completion was defined as having data of any kind entered into the field. Fields with no data were classified as incomplete.

The type of sponsor in ClinicalTrials.gov was defined as either Industry, NIH, Other, or US Fed. Of the 1,545 patient registries found 1,275 (82.5%) were classified as Other, 264 (17.1%), four (0.3%) as US Fed, and only two (0.1%) as NIH. Table 1 shows that all the patient registries examined had at least one condition entered. The majority (n=1,028, 66.5%) of registries only listed a single condition. There were 517 (33.5%) studies with two or more conditions, 266 (17.2%) studies with three or more conditions, and 142 (9.2%) studies with four or more. Two studies listed more than 25 conditions.

Table 1. Frequency of conditions for registries in ClinicalTrials.gov

Number of Conditions	N	%
One or more	1,545	100.0
Only one condition	1,028	66.5
Two or more	517	33.5
Three or more	266	17.2
Four or more	142	9.2

While the type of intervention was a required field, nearly two thirds (n=947, 61.3%) of the studies did not have one listed (Table 2). Of those listing an intervention, 190 (12.3%) studies were categorized as Other, 150 (9.7%) listed Device, 109 (7.1%) listed Procedure, and 94 (6.1%) listed Drug. Other intervention types, such as behavioral, biological, dietary supplement, genetic, and radiation, each represented less than two percent of the records.

Table 2. Frequency of intervention type selection in registries in ClinicalTrials.gov

Intervention	N	%
Behavioral	14	0.9
Biological	11	0.7
Device	150	9.7
Dietary Supplement	4	0.3
Drug	94	6.1
Genetic	8	0.5
Other	190	12.3
Procedure	109	7.1
Radiation	18	1.2
Missing	947	61.3

The distribution of primary and secondary outcomes is shown in Table 3. In ClinicalTrials.gov, one outcome is required. There were 1,305 (84.5%) records with only one outcome, 236 (15.3%) with two or more, 119 (7.7%) with three or more, and 69 (4.5%) with four or more. Fewer records listed secondary outcome measures, likely due to the lack of requirement for their entry. There were 1,032 (66.8%) studies with at least one secondary outcome; of these, 494 (32.0%) listed one secondary outcome, 538 (34.8%) listed two or more, 378 (24.5%) listed three or more, and 271 (17.5%) listed four or more.

Table 3. Distribution of outcome measure for registries in ClinicalTrials.gov

Outcome Measure	N	%
Primary Outcomes		
One or more	1,541	99.7
Only one outcome	1,305	84.5
Two or more	236	15.3
Three or more	119	7.7
Four or more	69	4.5
Secondary Outcomes		
One or more	1,032	66.8

Outcome Measure	N	%
Only one outcome	494	32.0
Two or more	538	34.8
Three or more	378	24.5
Four or more	271	17.5

To analyze the condition specific areas of depression, rheumatoid arthritis (RA), asthma, and cardiac surgery with a focus on valvular conditions, a search was conducted to examine a subset of the patient registries available on ClinicalTrials.gov. Using the Advanced Search feature on ClinicalTrials.gov, the criteria for finding those subsets was conducted by selecting only Study Types of "Patient Registry", excluding the status of those studies using the criteria described earlier. Using the First Received field, the date was set to pull in only registries that were entered before or on June 23rd, 2015. For depression the search term was depression, for RA it was rheumatoid arthritis and juvenile rheumatoid arthritis, and for asthma the term was asthma. For cardiac surgery the search terms were valvular heart disease, aortic valve disease, aortic stenosis, aortic insufficiency/regurgitation, mitral valve disease, mitral stenosis, and mitral insufficiency/regurgitation.

Completion rates in records in the condition-specific areas of rheumatoid arthritis, cardiac surgery, depression, and asthma were also examined (Table 4 and Table 5). There were a total of 21 records for rheumatoid arthritis, 43 for cardiac surgery, 37 for depression, and 19 for asthma. The frequency of completion for individual fields did not vary widely across the condition areas. A slightly higher rate of completion was observed for study design for rheumatoid arthritis (n=19, 90.5%) and depression (n=33, 89.2%) compared with asthma (n=16, 84.2%) and cardiac surgery (n=36, 83.7%). The intervention field was more varied in its completion, with asthma (n=8, 42.1%) being the highest followed by cardiac surgery (n=17, 39.5%), depression (n=12, 32.4%), and rheumatoid arthritis (n=4, 19.1%). All but one of the condition-specific areas had a 100% completion rate for the primary outcome measure field (the exception being rheumatoid arthritis [n=20, 95.2%]).

For optional fields, the primary outcome measure description completion rate was highest for asthma (n=15, 79.0%) and lowest for cardiac surgery (n=23, 53.5%). For secondary outcome measures, the highest completion was asthma (n=14, 73.7%) and the lowest was rheumatoid arthritis (n=12, 27.1%). The description of secondary outcome measures was completed the most by registries for depression (n=20, 54.1%) and the least by registries for rheumatoid arthritis (n=6, 28.6%).

Table 4. Completion of required fields by condition for registries in ClinicalTrials.gov

Field	Rheumatoid Arthritis	Cardiac Surgery	Depression	Asthma
NCT ID	21 (100.0%)	43 (100.0%)	37 (100.0%)	19 (100.0%)
Brief Title	21 (100.0%)	43 (100.0%)	37 (100.0%)	19 (100.0%)
Sponsor	21 (100.0%)	43 (100.0%)	37 (100.0%)	19 (100.0%)
Condition	21 (100.0%)	43 (100.0%)	37 (100.0%)	19 (100.0%)
Study Design	19 (90.5%)	36 (83.7%)	33 (89.2%)	16 (84.2%)
Time Perspective	19 (90.5%)	40 (93.0%)	34 (91.9%)	17 (89.5%)
Enrollment	21 (100.0%)	43 (100.0%)	37 (100.0%)	19 (100.0%)

Field	Rheumatoid Arthritis	Cardiac Surgery	Depression	Asthma
Target Followup Duration	21 (100.0%)	43 (100.0%)	37 (100.0%)	19 (100.0%)
Intervention	4 (19.1%)	17 (39.5%)	12 (32.4%)	8 (42.1%)
Eligibility	21 (100.0%)	43 (100.0%)	37 (100.0%)	19 (100.0%)
Age Minimum	21 (100.0%)	43 (100.0%)	37 (100.0%)	19 (100.0%)
Age Maximum	21 (100.0%)	43 (100.0%)	37 (100.0%)	19 (100.0%)
Primary Outcome Measure	20 (95.2%)	43 (100.0%)	37 (100.0%)	19 (100.0%)

Table 5. Completion of non-required fields by condition for registries in ClinicalTrials.gov

Field	Rheumatoid Arthritis	Cardiac Surgery	Depression	Asthma
Official Title	21 (100.0%)	39 (90.7%)	33 (89.2%)	19 (100.0%)
Primary Outcome Description	13 (61.9%)	23 (53.5%)	25 (67.6%)	15 (79.0%)
Secondary Outcome Measure	12 (57.1%)	30 (69.8%)	27 (73.0%)	14 (73.7%)
Secondary Outcome Description	6 (28.6%)	17 (39.5%)	20 (54.1%)	9 (47.4%)
Collaborator	9 (42.9%)	15 (34.9%)	12 (32.4%)	6 (31.6%)

In summary, examination of the data available in ClinicalTrials.gov shows that many patient registry records have incomplete fields, even among those fields that are required. Fields such as Study Design, Time Perspective, and Intervention type were among those that were incomplete despite being required when entering a new record into ClinicalTrials.gov. The results show that completion rates did not vary by condition area or by sponsor type, and appeared to be uniformly used by the various stewards across the registries examined.

While it is beyond the scope of this analysis to examine each case in which a required field was not completed, the incomplete fields may be due to the requirements for data entry into ClinicalTrials.gov having changed over time. Certain fields, such as Outcome Measures or Intervention, may not have been required in the past. If the data provider has not updated their record since the requirements were changed, the record may not have those required fields completed. Additionally, the analysis found that optional fields – beyond the Official Title – were often incomplete. For example, roughly half of the records provided a description to their Primary Outcome measure in the case of cardiac surgery. A large number of records also lacked information on Secondary Outcome measures and their descriptions. This suggests that asking for information that is not required may result in a large percentage of entries with missing information.

Qualitative Analysis of ClinicalTrials.gov Patient Registries

A qualitative analysis was undertaken to test the strength of the published OMF Information Model and identify any areas of improvement. The result of these analyses help to inform the development of condition-specific implementations and to identify optimal policies and procedures as well as the data model that describes how data are collected and stored.

The primary objectives of this analysis were to:

1. Assess the characteristics of the outcome measures, paying particular attention to the level of clinical and analytical detail included in each measure;
2. Identify the most common types of outcome measures and the variations in terminology, representation, and level of detail used for these measures.

The secondary objectives of the analysis were to:

1. Assess the feasibility of creating a searchable database of outcome measures by examining the level of detail entered for each measure as well as the extent to which users have entered data in optional fields;
2. Identify cross-cutting outcome measures used across clinical domains and the variations in terminology, representation, and level of detail used for these measures.

Registries from ClinicalTrials.gov were identified via the same algorithm used in the quantitative analysis defined earlier.

Because measures are not organized by outcome measure type or other characteristics in ClinicalTrials.gov or the Registry of Patient Registries (RoPR) system, this analysis required a manual review and assessment of each outcome measure. Two reviewers, one trained in epidemiological research methods and one clinician, independently conducted the manual review. The reviewers assessed each measure and compared results. In cases of discrepancy, the reviewers discussed and agreed upon a final assessment; in cases where agreement was not feasible, the Technical Expert Panel (TEP) or other subject matter experts were consulted. The TEP is comprised of key stakeholders experienced in the field of outcome harmonization and value set endorsements.

Upon download of these datasets from ClinicalTrials.gov, four condition areas were selected with input from the TEP. The four condition areas were depression, asthma, rheumatoid arthritis, and cardiac surgery, with a specific focus on valvular heart disease. Depression and asthma were explored to test the strength of the current OMF conceptual model. Rheumatoid arthritis and cardiac surgery were considered for the purposes of this analyses to be the subject of the condition-specific implementations of the OMR information model.

For all four condition areas, the top 10 studies ranked by enrollment as listed on ClinicalTrials.gov were selected for evaluation. In each of these condition areas, outcomes were evaluated for level of data quality provided, the mapping to the existing OMR information model, and output was also used to generate information on the potential alteration to the existing OMR information model.

Condition-Specific Implementations Tested To Evaluate the Strength of the OMF Model

These analyses were conducted with the intention of examining the reproducibility of an outcome measure using the data from within the entry itself. The level of data availability for each of these conditions was evaluated within ClinicalTrials.gov. Within each entry, the level of detail available was defined by the existence of three components: an outcome definition, a measurement used to meet the definition, and a threshold by which this measurement could be

classified. The existence of one of the desired components produced a definition of low availability. If an outcome contained two components but additional information has to be sought elsewhere, the outcome was deemed to have medium data availability. The existence of all three components was identified as a measure with high data availability.

Depression

Eighteen depression registries were evaluated, with 84 outcomes. Of the 84 outcomes, 31 (37%) were ascribed to primary outcomes, and 53 (63%) were secondary outcomes.

The level of data availability within ClinicalTrials.gov was evaluated. Within each entry, the level of detail available was defined by the existence an outcome definition (e.g., Depression severity), a measurement used to meet the definition (e.g., Beck Depression Inventory), and a threshold by which this measurement could be classified (e.g., score >20).

For depression, 39% of outcome measures were defined as having low availability, due to omissions in the definition of the measurement used to define the outcome and the metrics used to define the measurement. As an example, one registry noted only “Altman Self Rated Mania Scale” as the primary outcome, with no information provided on how to evaluate this scale, nor the domain it was intended to measure. In an operational database such as the OMR, these values are critical to the harmonization and standardization of outcomes in the future. Furthermore, 57% of outcomes in the depression registry analysis were found to have medium availability, while only 4% met the criteria for high availability of outcome detail.

Asthma

Seventeen registries were evaluated in the asthma-specific analyses. Within these 17 registries, 57 outcomes were noted within the ClinicalTrials.gov entries. Of the 57 outcomes, 21 were noted as primary outcomes and 36 were secondary outcomes.

The level of data availability within ClinicalTrials.gov was evaluated by the existence of three components: an outcome definition (e.g., asthma severity), a measurement used to meet the definition (e.g., Change in Rhinitis Control Assessment Tests), and a threshold by which this measurement could be classified (e.g., score >22 indicating great control). Forty-seven percent of asthma outcome measures were defined as having low availability due to omissions in the definition of the measurement used to define the outcome and the metrics used to define the measurement. As an example, one registry noted only “wheezing episode” as the primary outcome, with no information provided on how to evaluate this, nor the domain it was intended to measure. Furthermore, 37% of outcomes in the asthma registry analysis were found to have medium availability, while only 16% met the criteria for high availability of outcome detail.

Condition-Specific Implementation of the OMR

For the condition specific implementation examples, Rheumatoid Arthritis and Valvular Heart Disease, additional stakeholder input was sought from members of professional societies, key opinion leaders in the field, and the Centers of Excellence at Quintiles on the identification of relevant registries which may not have been available on ClinicalTrials.gov or have met

inclusion criteria for the qualitative analysis. Additionally, where data on ClinicalTrials.gov was insufficient for the qualitative analysis, supplementary searches were conducted to attempt to identify critical information relevant to the study. As part of this granular examination, each time an outcome measure was mentioned within the ClinicalTrials.gov entry that represented incomplete information, external and internet searches were conducted to identify the source and definition of the outcome measure.

The primary objectives of this analysis were to:

- Assess the characteristics of the outcome measures in valvular heart disease (VHD) or rheumatoid arthritis (RA), paying particular attention to the level of clinical and analytical detail included in each measure;
- Identify the most common types of outcome measures in VHD or RA and the variations in terminology, representation, and level of detail used for these measures.

Valvular Heart Disease (VHD)

Valvular heart disease was chosen as a field where multiple treatment modalities could be examined, such as medical and surgical treatments. These types of treatment modalities provided information on how to make modifications to the OMF conceptual model for the purposes of informing the creation of the OMR Information Model.

VHD is characterized by damage to or a defect in one of the four heart valves: the mitral, aortic, tricuspid or pulmonary. A defective valve can either fail to close completely and leak (regurgitation), or cannot open completely so that blood pumps through a smaller opening (stenosis). The severity of VHD varies. In mild cases there may be no symptoms, while in advanced cases, VHD may lead to congestive heart failure (CHF) and other complications.

The decision to proceed with medical or surgical treatment is currently typically based on clinical symptoms and an echocardiography study. Medical treatment of valve disease has been limited for the most part to palliation of heart failure (HF) immediately preceding surgical intervention. It does not alter its course or delay the need for surgery. The importance of medical treatment lies in stabilizing the patient's condition when the disease is due to abnormal valve structure, and in treating the underlying condition when the condition is due to a functional abnormality.[3]

This information supports an assessment of how outcome measures across different registries could be categorized in the OMR and helps to determine if users can differentiate among registries to select the ones most appropriate to their interests with respect to characteristics of the outcome measures and the level of clinical and analytical detail included in each. In addition, the comparison of the data against the proposed OMR information model was used to assess the added burden that participation in the OMR represents for users already entering outcome measures on ClinicalTrials.gov.

A sample of 35 VHD registries were included in this qualitative analysis. The following algorithm was used to select these registries:

- Registries identified and ranked by enrollment size (a sample of larger registries was selected, rather than seeking to include all registries listed in ClinicalTrials.gov);

- Registries of studies conducted in North America and in the European Union (EU);

- Registries ranked as Top 10 of VHD registries by enrollment and/or external stakeholder;

- Additional registries (n=25) suggested by stakeholders, including registries outside North America and the EU. Review of the results with clinical domain stakeholders highlighted that some registries commonly used in North America and the EU are not included in ClinicalTrials.gov. To assure completeness of the analysis, the team evaluated 25 additional commonly used registries, including some outside North America and the EU to supplement the information from ClinicalTrials.gov

The qualitative analysis included both registries and outcome measures listed in ClincialTrials.gov, as well as other sources of information obtained through consultation with professional/specialty associations and subject matter experts. Additional sources of information included registries not listed on ClinicalTrials.gov but identified by stakeholders as influential in the field, publications in the peer-reviewed literature, registry Web sites or other reports, and direct outreach to registry sponsors.

Within these 35 VHD registries, there were 143 reported outcome measures. In the review process, reviewers mapped these 143 outcomes to 187 various components of the OMF model (some outcomes were mapped to more than one component of the OMF model, resulting in greater than 100% mapping rate). As an example, some outcomes held a mapping to more than one place within the OMF, thus the mapping ratio of outcomes: OMF placement sometimes exceeded and equivalent 1:1 mapping structure (e.g. myocardial infarction may have been classified as disease progression or adverse event). Among the 187 VHD-specific outcome measure mappings, 63% mapped directly to OMF (n=116), and 37% of outcome measures were missing or suggested changes needed to the existing OMF (n=69). Therefore, minor modifications were made to the OMF conceptual model to accommodate outcomes relating to complications to valvular heart surgery.

Data Quality

In the VHD-specific analysis, the level of data availability solely from ClinicalTrials.gov was evaluated. This analysis was conducted with the intention of examining the reproducibility of an outcome measure using the data from within the entry itself. Within each entry, the level of detail available was defined by the existence of three components: an outcome definition (e.g., hypertension), a measurement used to meet the definition (e.g., Systolic Blood Pressure), and a threshold by which this measurement could be classified (e.g., >140mm Hg). The existence of one of these components produced a definition of low availability. If an outcome contained 2 of these components but additional information had to be sought elsewhere, the outcome was deemed to have medium data availability. The existence of all 3 components was identified as a measure with high data availability.

For VHD, 54% of outcome measures were defined as having low availability, due to omissions in the definition of the measurement used to define the outcome and the metrics used to define the measurement. As an example, one registry noted only “Incidence of Complications” as the primary outcome, with no information provided on how to calculate incidence (numerator/denominator), the complications of interest, and the methods used to define the complications. In an operational database such as the OMR, these values are critical to the harmonization and standardization of outcomes in the future. Furthermore, 38% of outcomes in the VHD registry analysis were found to have medium availability, while only 8% met the criteria for high availability of outcome detail.

Rheumatoid Arthritis (RA)

In concert with the TEP in an effort include areas with varying populations, RA was chosen as a way to represent both the pediatric and adult population. During the last two decades, several major epidemiological advances in RA have been achieved, including revised classification criteria for RA,[4] core sets for assessment of disease activity,[5,6] response criteria for the assessment of drug efficacy,[7] and preliminary agreement on a core set of measures for longitudinal observational studies.[8] Rheumatology, and specifically RA and juvenile idiopathic arthritis (JIA), benefit from the existence of a condition specific framework for rheumatology clinical trials defined by the Outcome Measures in Rheumatology group (OMERACT) which may be applied to observational studies.[9]

The Outcome Measures in Rheumatology (OMERACT) initiative has an established process and generalized framework for developing core outcome measure sets for specific condition areas.[10,11] This process, which is described in a detailed handbook,[12] has resulted in numerous published outcome measure sets.[13] The group has also worked to identify conceptual frameworks for outcome measure development.[14,15] Of particular relevance, OMERACT emphasizes the importance of agreeing on the key concepts to measure as a first step before working to harmonize specific data definitions. This approach is important for registries, as registries typically collect less data than clinical trials and must place more emphasis on collecting the minimum necessary data set to achieve their objectives while remaining feasible and sustainable.[16] The group also has published definitions of key terms, noting that researchers have not agreed on common nomenclature for these types of initiatives.[17]

Similar to the VHD analysis, review with clinical domain stakeholders highlighted that ClinicalTrials.gov contained only minimal reference to OMERACT. Therefore, the team evaluated measures in OMERACT in addition to those identified through the study methodology in ClinicalTrials.gov. A total of 23 registries were analyzed for RA and JIA, comprising 79 endpoints addressing 132 specific outcome measures.

Among the 132 specific outcome measures, nine were process measures which are typically not addressed within the OMF, although seven of the nine process measures did map to a potential OMF outcome. Of the remaining 123 specific outcome measures, 10 outcomes were not clearly delineated by the registries and therefore could not be mapped. Of the remaining 113 where outcomes were clear and where mapping could potentially be performed, 17 required additional clarification or had missing corresponding measures in the OMF (13% of the overall 132).

For the total analysis across all four condition areas, 510 specific outcome measures were identified, with 37% of outcomes overall missing corresponding measures or requiring clarification.

Data Quality

In the RA analysis, the level of data availability within ClinicalTrials.gov was evaluated. Similar to the process used for VHD, this analysis was conducted with the intention of examining the reproducibility of an outcome measure using the data from within the entry itself. For each entry, the level of detail available was defined by the existence of three components: an outcome definition (e.g., inflammation), a measurement used to meet the definition (e.g., C-reactive protein), and a threshold by which this measurement could be classified (e.g., >3.0 mg per litre of blood).

Seventy-two percent of outcome measures were defined as having low availability, due to omissions in the definition of the measurement used to define the outcome and the metrics used to define the measurement. As an example, one registry noted only "Evaluate the safety of therapeutic agents in persons with pediatric onset rheumatic diseases" as the primary outcome, with no information provided on how to calculate safety, the therapeutic agents of interest in the study, or the rheumatic diseases in the pediatric population that were of interest. In an operational database such as the OMR, these values are critical to the harmonization and standardization of outcomes in the future. Furthermore, 10% of outcomes in the RA registry analysis were found to have medium availability, while only 18% met the criteria for high availability of outcome detail.

Modification to the OMF Conceptual Model

Based on the results from the analyses in asthma, depression, rheumatoid arthritis, and VHD, the reviewers concluded that the OMF conceptual model performed well when tested in a number of different condition areas. However, some areas of improvement were identified that would enhance the operationalization of the model as it is used to inform the development of the information model for the OMR. These areas of improvement are described below.

First, one of the process items in the OMF is identified via Treatment Type and Intent. The original OMF contained subcategory classification examples of Palliative versus Curative treatment intent. Reviewers suggested that a third subcategory of Management would improve the classification of treatments. Explicitly naming other types of interventions such as patient education was a recurring theme in the analysis of the registries, and thus education was proposed as an added subclassification within the treatment category.

In the Outcome category, a number of examples were suggested to add to the breadth of the category description. Within survival, case-specific mortality was prominent in the review of included registries. It represents a specific type of mortality measure attributable to a specific cause which was recommended to be specifically named in the OMF.

The Disease Response category was renamed to "Clinical Response" to more broadly cover outcomes for non-disease conditions or after trauma. Exacerbation and Improvement were added

to Recurrence as examples that demonstrate the range of outcomes that might be included under "response."

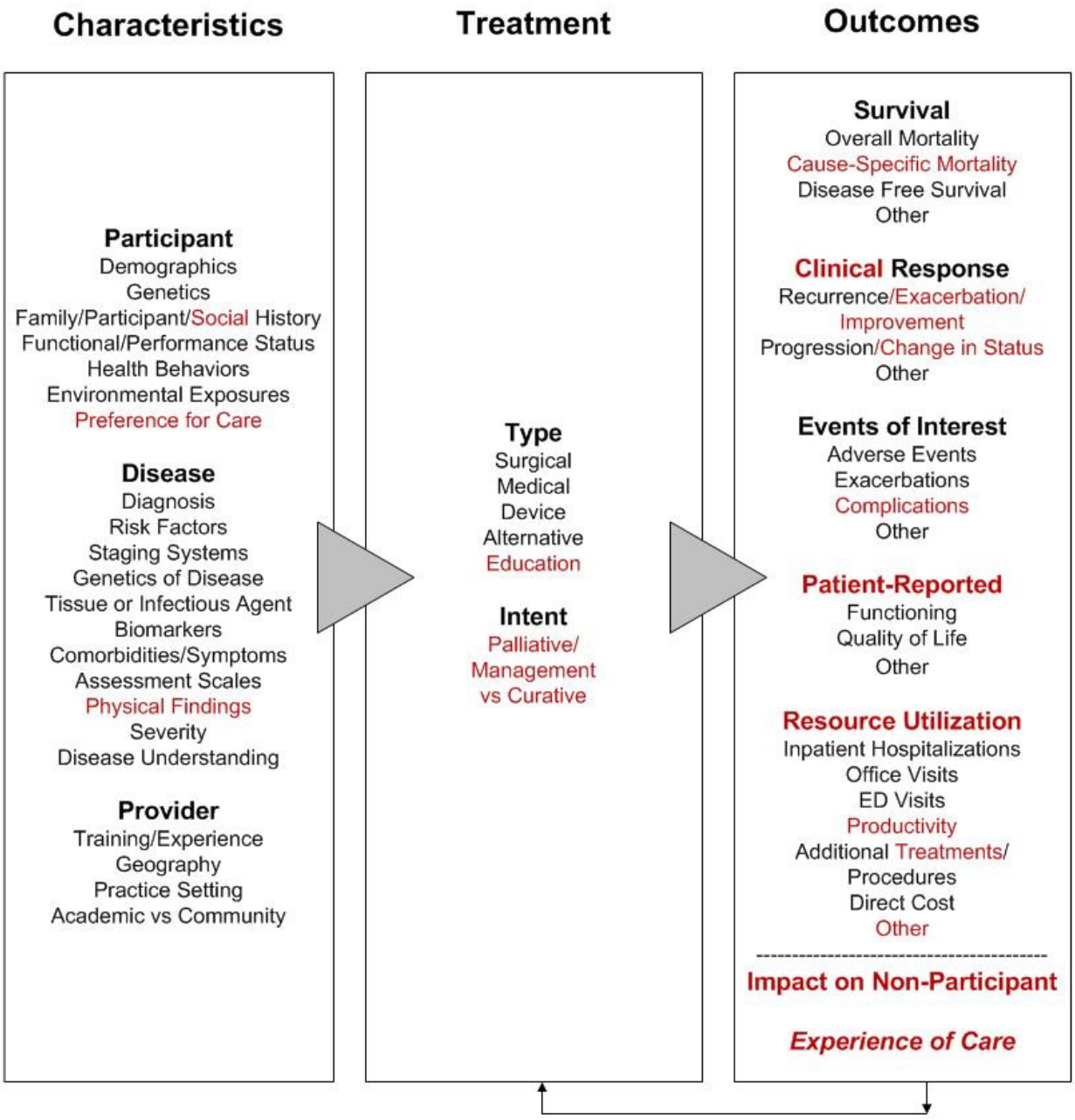
In the "Events of Interest" category, the current OMF did not explicitly name 'Complications', which is a common term for events or conditions that arise from a prior condition or from an intervention. Therefore, the reviewers suggested adding the term "Complications" to "Events of Interest" subcategory.

Health System Utilization was replaced with Resource Utilization as the category largely represented the use of health system-related resources. Included in this subclassification is productivity, ability to record additional treatments as well as procedures, and another category to capture any use of health systems resources that are not already enumerated in the OMF.

One of the critical findings in the qualitative analysis was the recognition that some outcomes of registries include endpoints related to participants who are not the enrollees in the registry at the onset. For example, pregnancy registries enroll the mother but the outcome of interest is the baby. In this case, the registry participant is the mother, and the baby is actually not a participant. Hence, "Impact on Non-participant" is listed within the OMF as an outcome related to someone other than an enrollee. Similarly, patient experience of care is being evaluated with more frequency, but represents an outcome other than the end result of the patient's treatment. Used to capture things like treatment satisfaction, waiting times, satisfaction with physician care, this category is intended to be a catch-all for metrics that are distinct from the end results for which the patient of the condition is being treated.

Figure 1 displayed below represents the current OMF[2] with the suggested clarifications and additions described above (suggested changes in red).

Figure 1. Outcome measure framework[2] modification



Outcome Measure Repository

- The structure used to develop the OMR was inspired by consultation with stakeholders, and review of other outcome measure repositories such as AHRQ's National Quality Measures Clearinghouse (NQMC) (https://www.qualitymeasures.ahrq.gov/), the National Library of Medicine (NLM) Value Set Authority Center (VSAC) (https://vsac.nlm.nih.gov/) and the National Quality Forum (NQF) (http://www.qualityforum.org/). The metadata associated with each outcome measure is designed to be comprehensive in describing the relevant attributes of an outcome

measure. It is more detailed than some of the metadata attributes collected by other outcome measure repositories, as it is designed to maximize value to users searching the OMR for relevant outcome measures. With the outcome measures described with structured attributes that can be compared, rather than more generic free-text responses which could be utilized to provide the same information, it is easier to compare and scan outcome measures when searching for relevant information. This will place some additional burden on those who enter the data to populate outcome measures using this structure, but the benefits to users searching the OMR is expected to outweigh the time requirement.

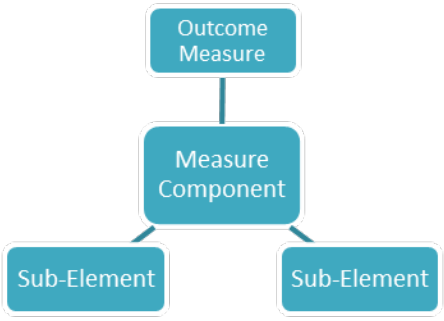
- The data elements that make up each outcome measure are captured in 'sub-elements' within the generic framework. These elements are structured to align with existing data element repositories, to reduce burden on the OMF operations team where possible.

In addition to the primary sources cited above, Appendix A contains the initiatives that were referenced when reviewing the OMF generic framework.

Information Model

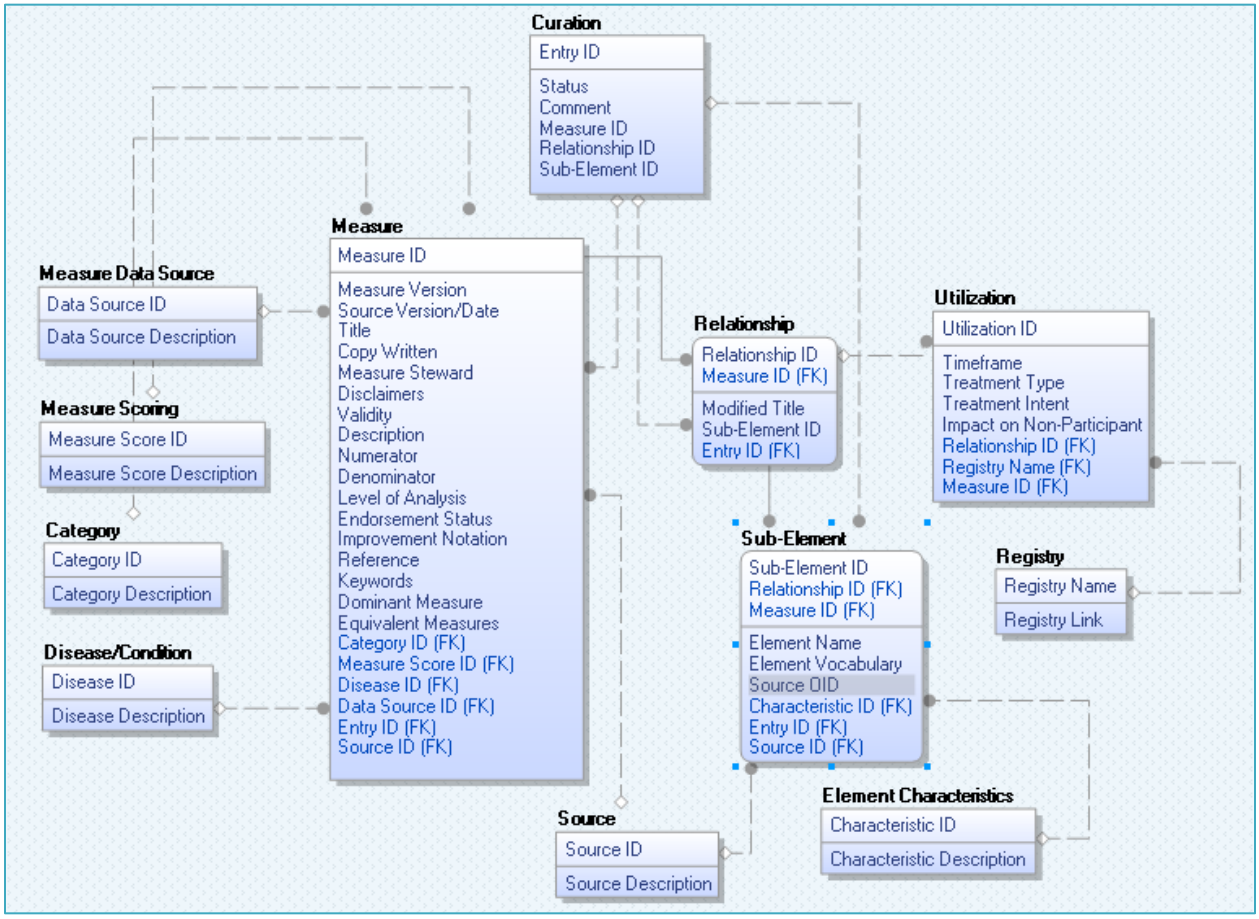
The data stored in the OMR will describe outcome measures, each of which will have sub-elements describing the data required to analyze or calculate the outcome measure. Each outcome measure will have one or more sub-elements; the relationship between these entities is shows in Figure 2 below.

Figure 2. Outcome measure and sub-element relationship



In addition to the attributes describing the outcome measure as a distinct entity, information is needed for the operations team to curate the OMF content, and for registry holders to indicate how they utilize outcome measures in their specific registry application. The relationships between these entities are described in this information model showing a detailed view of all of the component frameworks detailed in the sections below. Figure 3 is a proposed information model; the precise data model may vary depending on the technology selected when the OMR is implemented.

Figure 3. Information model for outcome measures repository



Information Model for the OMR

The recommended generic structure of outcome measures includes the metadata shown in Table 6 that will be captured for each outcome measure listed in the OMF. The attributes listed in Table 6 are described in detail in the Centers for Medicare and Medicaid Services (CMS) Measures Management System Blueprint, version 11.2.[18]

Table 6. Attributes describing an outcome measure

Field Name	Description	Properties
Measure Version	Version of entry in Outcome Measure Repository (OMR), will be populated automatically or entered by operations team.	Required
Measure ID	Unique identifier of this outcome measure within the OMR. Will be populated automatically.	Required
Measure Source	Free text entry, source of the information being entered, spell out acronyms.	Required
Source version/date	Free text entry, version identifier of the source of information (if one is available). If version identifier is not provided by the source, enter the date the information was obtained from the source.	Required
Title	Free text entry, title of the outcome provided by the source, or derived from source content, spell out acronyms.	Required
Copy Written	Yes or No, indicates whether the outcome measure is copy written.	Required

Field Name	Description	Properties
Measure Steward	Free text entry, name of copyright holder, and/or measure steward for the outcome measure. Required if Copy Written is yes.	Conditionally Required
Disclaimers	Free text entry, disclaimers related to the outcome measure.	Optional
Validity	For patient-reported outcome measures, any publication(s) describing the content validity, criterion validity, reliability, or sensitivity of the instrument in the target population should be referenced here.	Optional
Description	Free text entry, this should include the intended use of the outcome measure and a brief statement describing the patients and the specific aspect of health care to which the measure applies. This may also include the evidence basis for the measure and an explanation of how to interpret results with more detail than the 'improvement notation'.	Required
Numerator	Free text entry, numerator of calculation of this outcome measure as provided by source of information, spell out acronyms.	Optional
Denominator	Free text entry, denominator of calculation of this outcome measure as provided by source of information, spell out acronyms.	Optional
Measure Scoring	One or more of the Measure Scoring options listed below this table.	Optional
Data Source	One or more of the Data Sources listed below this table.	Required
Level of Analysis	Patient Level or Population Level	Required
Endorsement Status	If applicable for the measure, a citation or reference to any publicly available an endorsement of the measure by a group or agency.	Optional
Improvement Notation	Free text entry, example: higher score indicates better quality, higher score indicates lower quality.	Optional
Disease/Condition	One or more MeSH selections relevant for this outcome measure. See the 'Taxonomy for Grouping Outcome Measures into Families' section.	Optional
Category	One or more categories relevant for this outcome measure. See the 'Taxonomy for Grouping Outcome Measures into Families' section.	Required
Reference	Free text entry, reference to source of information in Agency for Healthcare Research and Quality (AHRQ) citation format available here: http://www.ahrq.gov/fund/refstyle.htm. In general this should contain a single reference; however, if the definition content provided by the source includes additional references, enter multiple references for a single outcome measure here.	Required
Keywords	Free text entry, keywords include relevant acronyms and related terms and phrases, and will be used in the search capability of the OMR.	Required
Dominant Measure	If selected, that indicates this is a dominant outcome measure as determined in review of clinical equivalency.	Optional
Equivalent Measures	If Dominant Measure is selected this is required. This will contain the Measure ID(s) of clinically equivalent outcome measures.	Conditionally Required

Measure Scoring

The method used to score the measure[19] should be selected from the options listed below. Scoring applies to the methods that are integral to the measure as designed by its developer for its current use. Other users may choose to analyze and display the results of measurements in additional ways.

Categorical Variable[20]

A categorical variable groups items into pre-defined, discrete, non-continuous classes (male, female), (board certified, not board certified). Categories may reflect a natural order, in which case they are called ordinal (cancer stage: I, II, III, or IV), (hospitals rankings: good, better, best).

Continuous Variable[20]

A measure score in which each individual value for the measure can fall anywhere along a continuous scale (for example, mean time to thrombolytics which aggregates the time in minutes from a case presenting with chest pain to the time of administration of thrombolytics).

Composite/Scale[21]

A composite measure is a combination of two or more individual measures into a single measure that results in a single score. The individual component measures are typically highly related to one another, both conceptually and statistically.

A scale is a statistical tool for ordering entities with respect to quantitative attributes or traits, either through the estimation of magnitudes on a continuum or the relative ordering of the entities.

Count[22]

The number of times the unit of analysis for a measure occurs.

Dichotomous[a]

A term used to describe a variable or data that can be divided into two categories (e.g., yes or no; present or absent).

Frequency Distribution[a]

A display of cases divided into mutually exclusive and contiguous groups along a continuum reflecting gradations of conformance to a quality-related criterion.

Mean/Median[23]

Mean: The mathematical average of a set of numbers, calculated by adding two or more scores and dividing the total by the number of scores.

Median: The number separating the higher half of a sample from the lower half. The median of a finite list of numbers can be found by arranging all the observations from lowest value to highest value and picking the middle one. If there is an even number of observations, the median is not unique, so one often takes the mean of the two middle values.

Rate/Proportion[24]

A score derived by dividing the number of cases that meet a criterion for quality (the numerator) by the number of eligible cases within a given time frame (the denominator) where the

[a] A measure score in which each individual value for the measure can fall anywhere along a continuous scale (for example, mean time to thrombolytics which aggregates the time in minutes from a case presenting with chest pain to the time of administration of thrombolytics).

numerator cases are a subset of the denominator cases (e.g., percentage of eligible women with a mammogram performed in the last year).

Ratio[24]

A score that may have a value of zero or greater that is derived by dividing a count of one type of data by a count of another type of data (e.g., the number of patients with central lines who develop infection divided by the number of central line days).

Weighted Score[24]

A combination of the values of several items into a single summary value for each case where each item is differentially weighted (i.e., multiplied by an item-specific constant).

Non-Weighted Score/Composite/Scale[24]

A combination of the values of several items into a single summary value for each case.

Data Sources

This field identifies the data source(s) necessary to implement the measure. One or more of the following options[22] should be selected:

Administrative Clinical Data[22]

Data such as enrollment or eligibility information, claims information, and managed care encounters. The claims and encounters may be for hospital and other facility services, professional services, prescription drug services, laboratory services, and so on, gathered from billing codes or other coding systems. This refers to information that is collected, processed, and stored in automated information systems.

Administrative Management Data[19]

Data that describe attributes of delivery organizations, staff, equipment, non-clinical operations, and financing.

Clinical Training Documentation[19]

The recording of the details of educational and related activities intended to augment the skills and knowledge of clinical personnel.

Electronic Health/Medical Record[23]

In health informatics, an electronic medical record (EMR) is considered to be one of several types of electronic health records (EHRs), but EMR and EHR are also used interchangeably. EHRs are sometimes defined as including other systems that keep track of medical information, such as practice management software that facilitates the day-to-day operations of a medical

practice. Such software frequently allows users to capture patient demographics, schedule appointments, maintain lists of insurance payers, perform billing tasks, and generate reports.

Health Professional Survey

An investigation aimed at gathering information from health professionals to search and disseminate information relating to their professions.[25]

Example: The World Health Organization (WHO), Centers for Disease Control and Prevention (CDC), and the Canadian Public Health Association (CPHA) developed the Global Health Professional Survey (GHPS) in 2004 to collect data on tobacco use and cessation counseling among health professional students.[26]

Imaging Data[27]

Data derived from the use of radiographic, sonographic, and other technologies.

Example: PET, CT, MRI, X-ray.

Inspections/Site Visits[28]

A formal visit to a hospital or heath care facility by representatives from an accrediting organization (e.g., The Joint Commission [TJC], Centers for Medicare & Medicaid Services [CMS]) to assess the quality of care provided in the institution, as reflected by the facility's adherence to guidelines for providing such care.

Laboratory Data

Data collected from a site equipped for experimentation, observation, testing and analysis, or practice in a field of study.[29] In regards to clinical practice, laboratory data may provide information on diagnosis, prognosis, prevention, or treatment of disease based on close examination of the human body.[30]

National Public Health Data[31]

Public health data include national health status (gathered through birth and death certificates, hospital discharge diagnoses, other epidemiologic sources), communicable disease (food/water/air/waste/vector borne), environmental health risks, presence of and use of health care facilities and providers, preventive services, and other information identified by the nation as helpful for planning.

Example: Data available from the National Center for Health Statistics, such as National Health Interview Survey (NHIS) or National Health and Nutrition Examination Survey.

Patient/Individual Survey[32]

An instrument that assesses patients' perspectives on any of the following: their health and the care they receive, including the level of patients' satisfaction, or patients' understanding of their health status.

Pharmacy Data[33]

A database that provides information on prescription and/or dispensing of drug and non-drug products that may be obtained from a pharmacy (retail or health care institution-based). The information provided may include clinical attributes such as the product's ingredients (e.g., ampicillin), drug classes (e.g., antibiotics, penicillin), strength (e.g., 500mg), and form (e.g., capsule). Non-clinical information provided may include manufacturer (e.g., Merck), packaging (e.g., 500 per bottle), and price (e.g., $2 per 500).

Region, County, or City Public Health Data

Public health data include community health status on a region/county/city level (gathered through birth and death certificates, hospital discharge diagnoses, local surveys, other epidemiologic sources), communicable disease (food/water/air/waste/vector borne), environmental health risks, presence of and use of health care facilities and providers, preventive services, and other information identified by the local community as helpful for planning.[31]

Example: The City of Baltimore Department of Public Health maintains a variety of health data files.[34]

Registry Data[35]

Data derived from 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 predetermined scientific, clinical, or policy purposes.[1]

Example: Cystic Fibrosis Foundation Patient Registry (see: http://www.cff.org/LivingWithCF/CareCenterNetwork/PatientRegistry/ External Web Site Policy)

State/Province Public Health Data

Public health data include community health status on a state/province level (gathered through birth and death certificates, hospital discharge diagnoses, statewide and local surveys, other epidemiologic sources), communicable disease (food/water/air/waste/vector borne), environmental health risks, presence of and use of health care facilities and providers, preventive services, and other information identified by the community as helpful for planning.[31]

Example: Behavioral Risk Factor Surveillance System is the world's largest, on-going telephone health survey system, tracking health conditions and risk behaviors in the United States yearly since 1984. Currently, data are collected monthly in all 50 states, the District of Columbia, Puerto Rico, the U.S. Virgin Islands, and Guam.[36]

Other[32]

Other data sources not described by the options listed here.

Sub-Element Framework

In addition to the metadata associated with each outcome measure in the generic measure framework, certain attributes will describe the sub-elements in more details. The following attributes listed in Table 7 are related to outcome measure curation.

Table 7. Attributes related to sub-elements

Sub-Element Attribute Name	Description	Properties
Sub-Element ID	Unique identifier of this sub-element within the OMR. Will be populated automatically.	Required
Element Name	Free text name of the sub-element.	Required
Element Characteristics	One or more element characteristics listed below this table. A glossary for these characteristics is provided in Appendix B.	Required
Source OID	Identifier in integrated system sub-element is sourced from another repository, for example NLM's VSAC. The format of this attribute should be confirmed during feasibility assessment, once systems to be integrated with are confirmed in order to properly validate data entered into this field.	Optional
Element Vocabulary	One or more vocabularies relevant to describe this sub-element. Options will include (https://www.nlm.nih.gov/healthit/dec/): AdministrativeGender, AdministrativeSex, CDCREC, CDT, CPT, CVX, HCPCS, ICD9CM, ICD10CM, ICD10PCS, LOINC, RXNORM, SNOMEDCT, SOP	Optional
Element Source	Free text entry, source of the information being entered for this sub-element, spell out acronyms.	Optional
Measures	One or more selections of the Measure ID associated with an outcome measure that utilizes this sub-element.	Required

Element Characteristics

The list of element characteristics were developed in the course of the RoPR project, in consultation with stakeholders, and in review of the National Library of Medicine's Data Element Catalog for Clinical Quality Measure (CQM) (https://www.nlm.nih.gov/healthit/dec/).

- Assessment Scale
- Attribute
- Biomarker
- Communication
- Comorbidity/Symptom
- Condition/Diagnosis/Problem
- Device
- Disease Severity

- Disease Understanding
- Diagnostic Study
- Encounter
- Environmental Exposure
- Family/Participant/Social History
- Functional Status
- Genetics
- Health Status
- Individual Characteristic
- Intervention
- Laboratory Test
- Medication
- Participant Demographic
- Participant Preference for Care
- Physical Exam
- Practice Setting
- Procedure
- Provider Geography
- Provider Training/Experience
- Risk Category/Assessment
- Staging Systems
- Substance
- Tissue or Infectious Agent
- Transfer of Care

Outcome Measure and Sub-Element Relationship Framework

The attributes describing an outcome measure may be interpreted differently based on the sub-elements utilized in a particular definition. For example, if myocardial infarction is defined based on an ICD10-CM selection in one data element, but by an EKG result within a certain threshold in another data element, that would affect the ability to pool the data from two datasets but it

would not change the text of the description of the outcome measure as defined in the Information Model for the OMR. For this reason, to prevent needing to re-enter outcome measures within the OMR, a separate entity to relate the measure and its sub-elements will be an important part of the recommended OMR. These attributes shown in Table 8 would be entered for each distinct collection of sub-elements that comprise one variation in the definition of the outcome measure (Measure Attributes + Sub-Element Attributes).

Table 8. Attributes related to outcome measure and sub-element relationships

Relationship Attribute Name	Description	Properties
Modified Title	If modified, e.g., geriatric or pediatric	Required
Measure ID	One instance of the unique identifier of the outcome measure within the OMF.	Required
Sub-Element ID	One or more sub-elements associated with this instance of the outcome measure. The unique identifier of this sub-element within the OMF will be utilized.	Required

Examples of outcomes measures have been provided in Appendix C and provide contextual data regarding the varying levels of complexities. Straightforward outcome measure such as hypertension are presented as an outcome measure entered into the OMR, as are relatively more complex endpoints such as major adverse cardiac events (MACE).

Outcome Measure Curation Metadata Within Outcome Measure Repository

In addition to the metadata associated with each outcome measure and sub-elements in the generic measure framework, certain attributes shown in Table 9 relate to governance and curation of the outcome measure content set.

Table 9. Attributes related to outcome measure curation

Attribute Name	Description
Status	Draft, Reviewed, Approved. Set by the operations team during the curation process. This status may apply to the outcome measure, a sub-element, or the definition of outcome measure and sub-element relationships.
Comment	Comment added by the OMR staff while working on the outcome measure. The public should have access to the comments to allow full transparency.

Measure Utilization Metadata Within Outcome Measure Repository

The registry owners who indicate that an outcome measure is utilized in their registry may make use of additional metadata. The engagement of registry owners would benefit from a feasibility assessment to verify the acceptable burden of data collection, particularly in the case of quality improvement registries that may have several hundred relevant outcome measures. Engaging with a broad set of registry stakeholders will verify how much detail is reasonable for data collection, and its corresponding value to users viewing what outcome measures are in use in patient registries. It is expected that a registry owner would provide the information shown in Table 10 for each outcome measure that is relevant for their registry. If they are selecting multiple outcome measures for the same registry at one time, it would be preferable for the registry owner to only enter the Registry Name and Registry Link attributes once, to reduce the

burden of data entry. The other attributes should be collected for each outcome measure of interest, as the responses may vary. The attributes shown in Table 10 are related to a registry owner indicating usage of an outcome measure.

Table 10. Attributes related to usage

Attribute Name	Description	Properties
Utilization	Indicates outcome measure is utilized in a patient registry.	Required
Registry Name	Free text entry, name of registry.	Required
Time frame	Free text entry, include the type of event date that initiates the timeframe, and describe the timeframe(s) over which the measure is calculated. Examples: 30 days post-operation, 6 months post-discharge, full registry duration	Required
Treatment Type	One selection from the following list: Surgical, Medical, Device, Alternative, Education	Optional
Treatment Intent	One selection from the following: Palliative/Management, Curative	Optional
Impact on Non-Participant	Yes or No – select whether this is being used to evaluate Impact on Non-Participant (e.g., impact on child if pregnant mother was in registry, second hand smoke exposure)	Required
Registry Link	Hyperlink to relevant source of information about the registry.	Optional

Operational Policies and Procedures

Taxonomy for Grouping Outcome Measures Into Families

Outcome measures will be more easily searchable both for the operations team and for registry owners or other interested stakeholders if they can be categorized or grouped into families. After review of the categorization of outcome measures in AHRQ's National Quality Measure Clearinghouse (NQMC), and patient registries listed in ClinicalTrials.gov and the RoPR), the National Library of Medicine (NLM) Medical Subject Headings (MeSH) high-level conditions were identified as a consistent categorization technique among these reference points.

The Medical Subject Heading (MeSH) entries for diseases are:

- Bacterial and Fungal Diseases
- Behaviors and Mental Disorders
- Blood and Lymph Conditions
- Cancers and other Neoplasms
- Digestive System Diseases
- Diseases or Abnormalities at or before Birth
- Ear, Nose, and Throat Diseases
- Eye Diseases
- Gland and Hormone Related Diseases
- Heart and Blood Diseases
- Immune System Diseases
- Mouth and Tooth Diseases
- Muscle, Bone and Cartilage Diseases
- Nervous System Diseases
- Nutritional and Metabolic Diseases
- Occupational Diseases
- Parasitic Diseases
- Respiratory Tract (Lung and Bronchial) Diseases
- Skin and Connective Tissue Diseases
- Substance Related Disorders
- Symptoms and General Pathology
- Urinary Tract, Sexual Organs, and Pregnancy Conditions
- Viral Diseases
- Wounds and Injuries

Each outcome measure in the OMR can be associated with one or more MeSH disease selections. The top level disease selections will be utilized rather than requiring the operations team to drill into the MeSH tree in detail, in order to ease the burden of populating the OMR.

Though more detailed MeSH disease selections may provide value to users searching the OMR, it would be very time consuming to identify, populate, and maintain detailed MeSH disease selections for a robust catalog of outcome measures. In addition, much of the benefit to users can be mimicked with little or no burden on the operations team by providing Natural Language Process (NLP) capabilities within the OMR search. See the 'Search Function and use of NLP' section for more information.

The MeSH disease selections only address outcome measures that are disease specific. The following categories were developed in the course of the RoPR project, in consultation with stakeholders, to address measures that are not disease specific. Each outcome measure will require one of more selections of category as part of its definition:

- Survival (e.g., overall mortality, cause specific mortality, disease free survival)
- Clinical Response (e.g., recurrence/exacerbation/improvement, progression/change in status)
- Events of Interest (e.g., adverse events, exacerbations, complications)
- Patient-Reported (e.g., functioning, quality of life)
- Resource Utilization (e.g., inpatient hospitalizations, office visits, ED visits, productivity, additional treatments/procedures, direct cost)
- Experience of Care (e.g., is the patient satisfied with their care)

Use of Existing Data Dictionaries To Limit Duplication of Efforts

There are multiple data dictionaries containing outcome measures, with differing objectives and priority condition areas. The staff working within the OMR proposes to partner with these data dictionaries rather than re-creating existing content. These partnerships may involve data transfers of outcome measure or sub-element definitions, so that data does not need to be manually re-entered within the OMR. Within the OMR, the source attribution would be provided and the data dictionary would be cited. Examples of potential partner dictionaries for both outcome measures and sub-elements include:

- AHRQ National Quality Measures Clearinghouse
- NQF Quality Positioning System for Measures Included in the NQF Endorsement Process
- NLM Value Set Authority Center (VSAC) for Managing Value Sets
- Encore CoreGPS, or other EHR tools to obtain sub-elements mapped to measures

If possible an automated integration of these data dictionaries to populate the OMR would be preferred. Such a relationship should undergo feasibility assessment, as partnership and data use agreements may be necessary with these or any other partner data dictionary source.

In addition it may be possible to partner with sources of information that indicate utilization of a given measure in an existing patient registry. Examples may include registry records in the RoPR, or ClinicalTrials.gov records, if sufficient specificity is available within the repository of information, and any considerations regarding indicating something automatically on behalf of registry owners have been fully considered and addressed during a feasibility assessment.

Linkage to Existing Registries Collating the Same Measures or Measure Content

As discussed in the Information Model for the OMR section, registries that are collating the same measures listed in the OMR should be referenced in the OMR. This would permit other registry owners, those conducting harmonization efforts, or those considering creating a new measure to understand how much usage the existing measure set has. Just because an outcome measure is utilized in an existing registry does not necessarily indicate that it is the 'preferred' outcome measure by the registry owner. In some cases it is not feasible to modify data collection to capture preferred data for a measure. In such cases, registries utilize an alternate measure definition. Therefore, there will be some risk to concluding there is limited adoption of optimal measures among existing registries. Some registries may be unable to modify the variable set already being collected to facilitate the adoption of a new preferred or standard measure. In some cases where prospective data collection may be cost prohibitive, it may be possible to integrate with EHR or other registry tools such as Encore CoreGPS, which is designed to map EHR data elements with NQF endorsed clinical quality measures.

Process for Updating and Archiving Definitions

Frequency Requirements

The OMR operations team should release new outcome measures and updates to existing measures regularly, ideally on a quarterly basis. This will provide time to actively curate and review candidate measures and sub-elements or their proposed updates, while also providing regular updates to the OMR user community.

Access to Changes and Engagement of Registry Owners

A record of updates included in each OMF release should be available for reference by interested stakeholders. If the clinical intent of an outcome measure is modified, then it may be necessary to issue a new OMF identifier for that outcome measure, to ensure that an updated version does not inadvertently attribute any previous registry utilization to the revised outcome measure content. However, if an outcome measure is modified with edits that do not change its clinical intent it should retain the same OMR ID, but just receive a new version identifier. This will minimize the burden placed on registry owners as they would not need to re-select the outcome measures associated with their registry, except in cases of modification to clinical intent (which is expected to be rare).

OMR Governance

Governance Model

The Data Governance Institute (DGI) defines data governance as "a system of decision rights and accountabilities for information-related processes, executed according to agreed-upon models which describe who can take what actions with what information, and when, under what circumstances, using what methods.[37] "The DGI identifies ten Rules of Engagement, each of which must be defined, and twelve processes for governing data. Each of these rules is listed below with a description of its application to the OMF Governance.

1. Mission and Vision

   The OMR will display information on outcome measures currently used in registries, with the short-term goal of reducing variation in outcome measures. Characterizing the outcome measures currently in use will support long-term efforts to develop standard outcome measures by identifying areas of common ground where standards may be developed relatively quickly and areas that will require additional work.

2. Goals, Governance Metrics and Success Measures, and Funding Strategies

   Goals include content addressing outcomes for a limited set of clinical domains in the first two years of operation with harmonized content.
   Success is defined as clear display and definition of all measure data content without requiring searches for information outside the database with less than 10% overlap in definitions at the end of two years.

3. Data Rules and Definitions

   Data must be defined using clear algorithms and, where applicable, value sets. Each data element must include information about its clinical focus, what is included, what is excluded, and its scope.

4. Decision Rights

   Each measure and data element entered must indicate its steward, i.e., the organization responsible for creating and maintaining it. All decisions to update or modify each element are the responsibility of its steward. Stewards agree to routine maintenance and to collaborate and attempt to harmonize their content with other stewards with similar content.

5. Accountabilities

   The measure and data stewards are accountable to manage their own content.

6. Controls

The OMR Staff will assure that tools exist to support the activities of data entry and harmonization.

7. People and Organizational Bodies

   Data Stakeholders: Data stakeholders include all those with interest in the related clinical condition or procedure.

   A Data Governance Office: A Steering Committee will establish and coordinate the policies and procedures of the OMR.

   Data Stewards: Owners (steward) of data elements and measures are the organizations responsible for their development and maintenance.

8. Processes: Proactive, Reactive, and Ongoing Data Governance

   Governance is maintained on a community level based on collaboration and harmonization among data and measure stewards. The Scientific Advisory Committee is responsible to adjudicate any disputes or unresolved issues and assure adequate maintenance of all content.

Processes for Governing Data

The remainder of this section will address the processes for governing data (http://www.datagovernance.com/the-dgi-framework/), including:

1. Aligning Policies, Requirements and Controls
2. Establishing Decision Rights
3. Establishing Accountability
4. Performing Stewardship
5. Managing Change
6. Defining Data
7. Issue Resolution
8. Specifying Data Quality Requirements
9. Building Governance into Technology
10. Stakeholder Care and Support
11. Stakeholder Communications
12. Measuring and Reporting Value

Following is a list of existing organizations representing three type of governance models: Fully curated, Community-Sourced, and Hybrid-Community Curated.

Examples of Existing Governance Models

Fully Curated Governance Model

Condition-specific registries managed by clinical specialty societies are often good examples of fully curated governance models. The clinical specialty societies develop content and create definitions and data collection methods based on evidence and/or expert consensus. Similarly, research organizations develop content based on careful study and validation. Examples include the Society for Thoracic Surgery National Database and the Patient Reported Outcome Measurement Information System (PROMIS).

Society of Thoracic Surgeons (STS)

Participation in the Society of Thoracic Surgeons (STS) National Database requires users to sign participation agreements that govern use of the information included in the database. Individual participants own their own patient data and, therefore, may use their own information included in the database as needed. The STS rules of engagement require that an appropriate Institutional Review Board review any particular research hypothesis and study methods for scientific merit and ethical propriety.[38] Participants or industry representatives can submit *ad hoc* queries to STS for data analysis. STS approves such requests based on the merits and intended use of the information (e.g., evaluating quality and patient safety, promoting medical research, or analyzing national trends in practice patterns). The STS Council on Quality, Research and Patient Safety and its Workforce on National Databases is responsible for the development and enhancement of the adult cardiac, general thoracic, and congenital heart surgery databases. Reporting to the Board of Directors, this council is governed by an Operating Board and a Chair and a representative of the Executive Committee. The Workforce members serve for three year terms.[39]

Patient Reported Outcome Measurement Information System (PROMIS)

The Patient-Reported Outcomes Measurement Information System (PROMIS) is a network of clinicians, clinical researchers, and measurement experts organized around six primary research sites.[40] A steering committee (SC), comprised of the seven principal grantees and five NIH scientists governs and assumes ultimate responsibility for the priorities and direction of the network. An independent scientific advisory board (SAB) provides oversight, makes recommendations that support the exchange of research tools and resources, encourages the adoption of common policies on data sharing, leads the creation of item banks and also solicits input and feedback from stakeholders. NIH appoints the SAB and consists of 11 experts from academia, government, and industry.

A statistical coordinating center (SCC) provides a secure, customizable, coordinated data management system for collection, storage, and analysis of data collected by the primary research sites. The SCC also coordinates, facilitates, and maintains information exchange and dissemination, standardizes protocols, study procedures and forms and develops end-user training materials for clinicians. A panel of 22 clinical research and health outcomes experts, the Advisory Panel on Health Outcomes, advises the SCC on relevance and feasibility for clinical research.

Community-Sourced Governance Model

Two examples of community-based governance include (a) management of openEHR content for defining content, or archetypes for use across EHR systems, and (b) the National Library of Medicine (NLM) Value Set Authority Center (VSAC). Each includes some oversight, and the community involvement is briefly described below.

openEHR

openEHR is a virtual community working on interoperability and computability in e-health. Its main focus is electronic patient records (EHRs) and systems.[41] The goal is to standardize health information for computing such that all health data for a person is stored in a lifetime electronic health record that is vendor-independent, enabling analytic functions like clinical decision support to improve health. The Australia National E-Health Transaction Authority applies governance, although development of clinical content descriptions, or archetypes, for openEHR is community-based. Garde, *et al.*, notes that clinical information is constantly evolving with respect to breadth (i.e., new knowledge), depth (i.e., finer-grained detail), and complexity (i.e., new relationships). Therefore, governance comprises "all tasks related to establishing or influencing formal and informal organizational mechanisms and structures in order to systematically influence the building, dissemination, and maintaining of knowledge within and between domains." A community model addresses concept overlaps (e.g., a cardiovascular assessment for a cardiologist may be applicable to a cardiovascular surgeon) and, therefore, achieves standardization. Definitions must be easily accessible, evidence-based and maintained and systematically updated when knowledge changes. Good governance can remove ambiguity among definitions and encourage understanding of inter-relationships.[42]

National Library of Medicine Value Set Authority Center

The National Library of Medicine (NLM) Value Set Authority Center (VSAC) established rules for content authors and stewards.[43] Authors create, edit and submit value sets to designated stewards. Stewards approve, reject and publish submitted value sets. VSAC governance is more of a community model. The site provides definitions of roles and functions and also tools to enable collaboration and harmonization of concepts. VSAC Administrators arrange VSAC users into two roles, steward groups and author groups. Authors have permissions to create, edit and delete their own draft value sets, as well as to submit value sets to their assigned Stewards for approval, and withdraw value sets from approval. Stewards have permissions to approve, reject, and publish value sets that their assigned author groups create and submit. Stewards provide overall coordination and management of the value sets created by Authors under a specific program or for a specific purpose. Stewards should adhere to the goals of their stewarding organization with regard to the content and maintenance of the value set. VSAC also publishes best practice recommendations regarding development and entry of content into the database. Criteria include clinical validity, complete and correct metadata, non-redundancy, completeness and accuracy of content, alignment with standards, naming conventions.[44]

New to the VSAC site is the "collaboration management" tool, allowing users to create interactive discussions with stewards of similar or competing value sets to allow harmonization. Harmonization efforts can lead to consolidating one or more value sets. Such efforts can also

clarify that the definitional metadata was insufficient to describe the intent of the content; such clarification may result in better description of the value set title and metadata rather than consolidation.

Hybrid Community-Curated Governance Model

Two hybrid governance models address information from a wide-range of stakeholders and incorporate public comment and consensus to publish standards for measurement. Descriptions follow for the National Quality Forum Consensus Development Process (CDP) and the Agency for Healthcare Research and Quality National Quality Measures Clearinghouse (NQMC).

National Quality Forum Consensus Development Process

The National Quality Forum (NQF) defined policies and processes for evaluating clinical quality measures as part of the Consensus Development Process (CDP).[45] The CDP includes a nomination process for clinically relevant Steering Committee membership, a call for submission of measures (standards), Steering Committee review, public and member comment, voting, and approval by a subcommittee of the Board of Directors, the Consensus Standards Approval Committee (CSAC) which make final endorsement decisions. The CSAC enforces harmonization of measures or measure content for those that address identical clinical concerns. A separate Appeals Board evaluates disputes. The CSAC, all Steering Committees and all other activities performed by NQF include representation from each of the eight member councils: Consumers, Health Plans, Health Professionals, Provider Organizations, Public /Community Health Agencies, Purchasers, Quality Measurement, Research and Improvement, and Suppliers and Industry.

In addition to the CDP process, NQF coordinates three other measurement-related organizations, each with its own governance structure:

1. The “Measure Incubator” facilitates development of outcome measures, especially taking advantage of data collected through EHRs.[46] An Incubator Advisory Council (IAC) governs the Measure Incubator process, addressing conflicts of interest and advising on funding, project selection and consistency. The IAC includes seven industry leaders in measure development and quality management, as well as business leadership.
2. The National Priorities Partnership (NPP), encompassing 52 major national organizations, identifies areas important to improve health in a safe, equitable and value-driven health care system based on the National Quality Strategy (NQS). Managed by its own governance structure, the NPP advises HHS on the NQS and identifies areas with measurement gaps.[47]
3. The Measure Applications Partnership (MAP) is a public-private partnership created to provide input to the Department of Health and Human Services (HHS) on the selection of performance measures for public reporting and performance-based payment programs.[48] Annually, the MAP solicits public comment on measures under consideration for implementation by HHS programs in the subsequent year.[49]

AHRQ National Quality Measures Clearinghouse (NQMC)

AHRQ manages the National Quality Measures Clearinghouse (NQMC).[50] The NQMC provides search capabilities for users to find healthcare quality measures. NQMC provides structured, standardized summaries containing information about measures and their development, using the NQMC Template of Measure Attributes. The NQMC/NGC (National Guideline Clearinghouse) Editorial Board is composed of health care professionals with collective expertise in evidence-based quality measures and clinical practice guidelines. The Editorial Board works with AHRQ to govern content and as a resource for feedback and guidance on developments in health care, providing expert commentaries on topics germane to the quality measures and guidelines. An NQMC/NGC Expert Panel is composed of health care professionals with collective expertise in all aspects of evidence-based health, clinical practice guidelines, quality measurement and reporting, health care policy and administration, and health informatics. The Expert Panel provides feedback and guidance to NQMC and NGC on broad project areas.[51] NQMC provides: a Domain Framework and Inclusion Criteria; a Template of Measure Attributes; a Glossary clarifying definitions and examples of terms used to describe common properties of health care measures used in the NQMC structured summaries; and a Classification Scheme to facilitate searching and information retrieval as well as advising on content development and naming conventions.

Promotion of Collaboration Within OMR

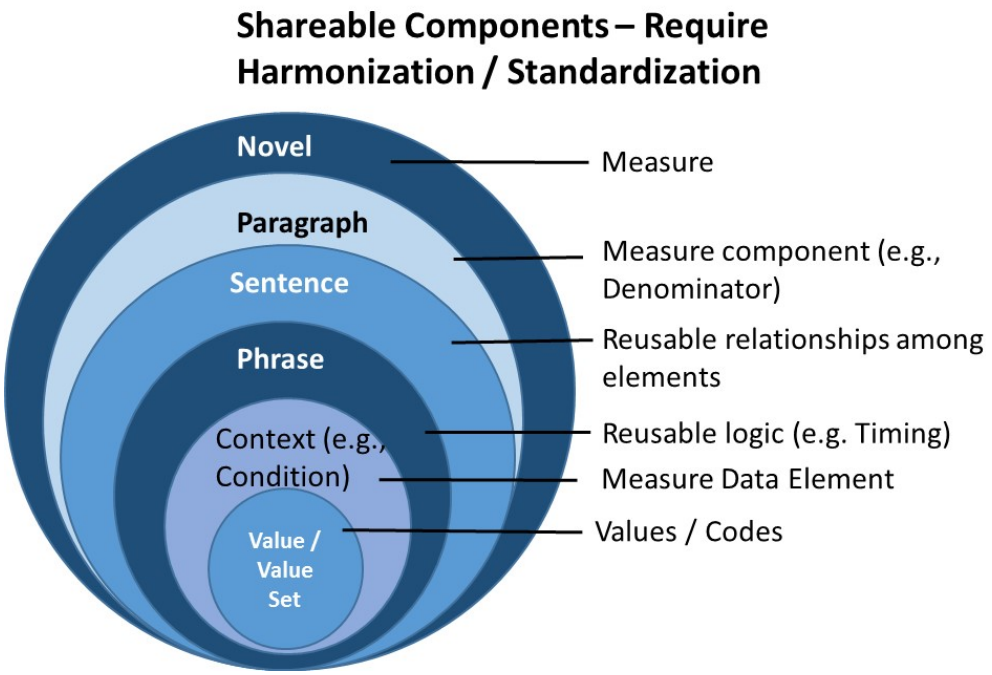
To support its mission, the OMR must be a dynamic resource for clinicians, healthcare organizations, researchers, purchasers of healthcare services, payer organizations, and all persons seeking information to evaluate care they receive. The resource must also provide information that is clear, unambiguous, and with sufficient detail for users to differentiate one measure from another. The goal is to allow users to determine which measure(s) might be appropriate for their individual needs. To meet this goal, measures must include very discrete information about the definition of each component (e.g., numerator, denominator, etc.), and further, the definition of the elements in those components. As an example, a measure about acute myocardial infarction (AMI) may, on the surface, seem comparable to other measures of AMI. However, if one measure defines AMI as one of a list of diagnoses entered on a problem list by a physician, and another defines an AMI based on achievement of a threshold of electrocardiograph changes, troponin and myocardial-specific creatinine kinase (CK) levels, the two measures may not be defining the same patients in the denominator. Further, using the same AMI definition example, if one measure uses different thresholds of test results for troponin and CK levels, the populations may also vary. Therefore, to allow users to clearly differentiate measures and to avoid confusion, the OMR must contain sufficient information about the measures at the atomic level (I.e., referencing specific codes, or value sets used for each data element, and where applicable, the specific thresholds, units of measure, and calculation logic employed). While such detail may seem overly complex to include in a single database, existing infrastructure in electronic measurement landscape provides a model for moving forward. Moreover, clear description of the data element detail allows measure developers to collaborate and, where possible, agree on standard definitions; where consensus is not possible, the collaboration enables measure developers to more clearly describe the differences in the definition and naming of their data elements. Existing models for such collaboration also exist today.

The National Library of Medicine (NLM) Value Set Authority Center (VSAC) currently provides such collaboration tools for authoring and maintaining value sets used in electronic

clinical quality measures (eCQMs) developed for U.S. government programs. The tools enable value set stewards to navigate code systems (e.g., LOINC and SNOMED-CT) and tools also alert the value set stewards about updates to the code systems used (i.e., on publication of a new version), highlighting the content in each value set impacted by the update. The tool thus gives value set stewards the ability to manage and version their content. The NLM VSAC also provides a collaboration space allowing measure developers with questions or suggestions about existing value sets to query the respective value set steward. Such queries may result in (a) addition or removal of concepts from existing value sets, or (b) greater documentation of the purpose, inclusion and exclusion criteria for the value set to reduce potential ambiguity. Cases of continued conflict in definition could require escalation to other forums to review.

Rather than duplicating existing infrastructure, the OMR should use and extend the NLM-VSAC collaboration space. Ideally, such community-driven collaboration will extend to include review at the value set, the clause, or phrase level (e.g., the AMI definition described above that incorporates observation values), and the measure component level (e.g., a denominator that includes the AMI definition during a specified time frame and other population restrictions) (see Figure 4). Also, to enable harmonization and collaboration at each level of abstraction, the OMR tools will need to provide reference libraries of existing and harmonized value sets, clauses and measure components. Using the AMI example, the same, harmonized value sets may describe the referenced laboratory tests with LOINC codes, there may be several harmonized AMI "clauses" (e.g., posterior AMI, anterior AMI, etc.) and several harmonized AMI "populations" available in a library of reusable measure components at each level of abstraction.

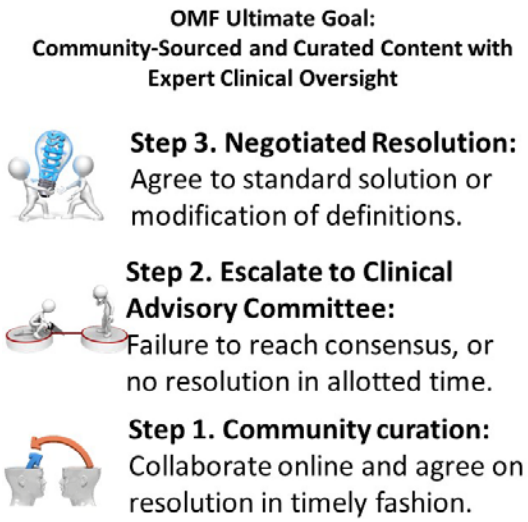
Figure 4. Use of shareable components in across measures



Each level of measure abstraction will evolve over time and each requires updating and potential harmonization with corresponding versions of the underlying code systems and/or clinical evidence. Comments and requests in a community collaboration environment must be

continuous, and the infrastructure to perform such collaboration requires tools to track the frequency of requests, the time from request to resolution, and the successful outcome of resolution (i.e., consensus has or has not been reached). The tools must be able to escalate to OMR staff all cases in which resolution has not occurred in acceptable time frames, or when consensus has not been reached (i.e., 80% of collaborating parties have not approved the resolution). The OMR staff may then decide to work with the parties involved to understand the issues and encourage a resolution, or, where resolution is not forthcoming, refer the issue to the Clinical Advisory Committee for review and recommendation (see Figure 5).

Figure 5. Hybrid curation model



The initial objective of the OMR is to collect sufficient information to characterize the types of outcome measures that are currently used in patient registries. The long-term objective of the OMR is to support efforts to standardize outcome measures and to facilitate access to that information. The OMR will display information on the outcome measures currently used in registries, with the short-term goal of reducing variation in outcome measures. Characterizing the outcome measures currently in use will support long-term efforts to develop standard outcome measures by identifying areas of common ground where standards may be developed relatively quickly and areas that will require additional work.

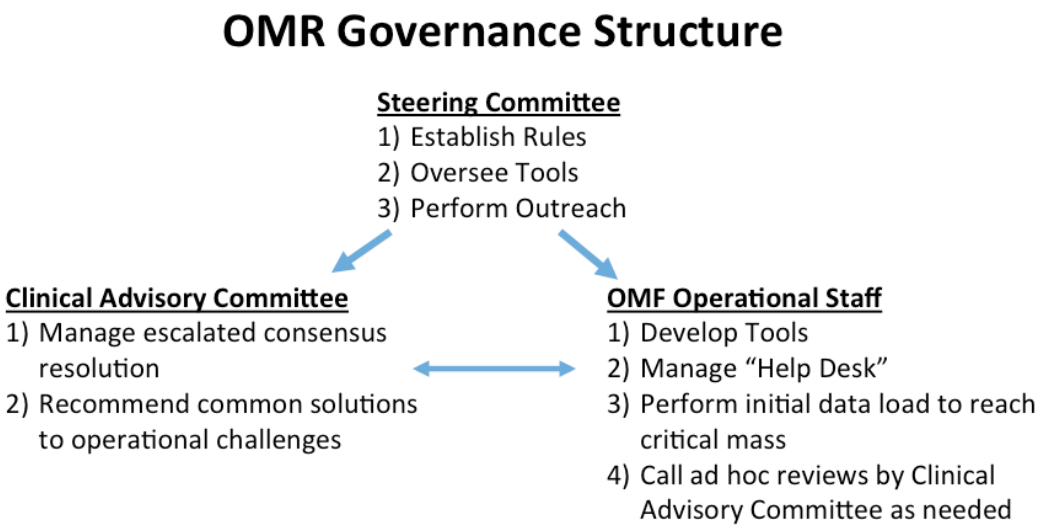
More importantly, the OMF conceptual model can serve as a content model for developing standard outcome measures in specific disease areas. While existing outcome measures may fit into the conceptual model, a long-term goal of the OMR is to encourage groups that are developing outcome measures to use the conceptual framework to define new measures. The increasing recognition of the value of outcome measures has led to a need for more outcome measures across a broad range of conditions. By promoting the use of the OMF conceptual framework, it will be possible to simplify the task of aggregating measures across multiple conditions while encouraging researchers and others to think of outcome measures in a standardized way, both of which will support the long-term goals of the OMR.

Composition of the OMR Governance

A hybrid community-curated model for managing OMR governance is proposed here. Combining the NLM-VSAC community-based efforts and the NQF CDP and MAP process, input from the community is important to identify when harmonization is necessary, and further, tools to enable harmonization among the various measure stewards will enhance collaboration and improve clarification of the content. Similar to these existing organizational processes, administration and maintenance of the OMR will require a Steering Committee to provide high-level policy and structure and a broad-based Clinical Advisory Committee with clinical expertise to meets its goals and objectives, and dedicated management staff. The responsibilities of these groups are described in Figure 6 further below. The organizational structure may be modified to incorporate a role for the funding source(s), once a funding plan has been identified for the OMR.

Scope of Responsibilities

Figure 6. OMR governance structure



Steering Committee

The OMR governance structure should include a broad set of stakeholders, similar to the either NQF categories to encompass consumers, health plans, health professionals, provider organizations, public and community health agencies, purchasers, quality measurement, research and improvement experts, and suppliers and industry (including software vendors and pharmaceutical companies). By including stakeholders in the governance structure, the OMR will be able to ensure that it meets the needs of multiple potential user groups especially in addressing the outcome categories. Potential users include those who provide the measure information (e.g., registry owners) and registry seekers, who may search the OMR to identify outcomes or outcome measures of interest for new research, for managing a group of patients based on their preferences, or consumers seeking information about their conditions or

procedures. Groups seeking to develop data standards for specific disease areas may also use the OMR to understand how data are defined as collected in existing measures and registries.

A Steering Committee that includes a broad set of stakeholder representatives will allow the OMR to be responsive to user needs while still achieving its primary goals and objectives. The Steering Committee will be responsible for making strategic and executive decisions for the OMR, covering three major areas:

1. Establishing rules to ensure that the content of the OMR remains relevant and useful to registry holders and registry seekers, and maintaining the balance between the need for detailed information and the burden on users. This primary focus will address the needs and ease of use for registry users. The Steering Committee will assure content is clearly defined and also promote the objectives of the OMR and disseminate information about its purpose and use, in order to encourage submission of patient and population outcome measures.
2. Providing oversight for tools that enable community collaboration and curation and that provide sufficient measures to evaluate the success of the process. The Steering Committee will decide on timing of update releases for the OMR and should give priority to users' interests when contemplating changes or revisions.
3. Performing outreach to assure coverage of appropriate clinical domains in the database.

The Steering Committee should include stakeholders with clinical expertise, experience in registry design and conduct, and information technology system design. Members should be selected from community nominations and appointed for a fixed renewable term of three years, consistent with common practice. A staggered term is desirable so that not all committee members rotate off at the same time. The Steering Committee should develop bylaws to govern its activities and a regular schedule for meetings (e.g., quarterly). The Steering Committee will work closely with the Clinical Advisory Committee and the OMR staff.

The Steering committee will be comprised by seven members. The contracts/project officer for the OMF project shall serve as the Chair of the Steering Committee. Representatives from the following disciplines shall comprise the membership of the Steering Committee: one (1) from a member representing a group involved in harmonization efforts, one (1) registry owner focusing on quality improvement program, one (1) registry owner representing a registry operated within an academic setting, one (1) potential user of the OMF [a research naïve setting new to setting up a registry who has not yet been involved in harmonization efforts], one (1) technical expert, and one (1) member representing technical solutions and hosting efforts.

Clinical Advisory Committee

The OMR will contain clinical content for a wide range of disease areas. Clinical expertise will be necessary to determine clinical equivalency for similar definitions and to assess whether some submitted items are appropriate for inclusion in the OMR. The OMR Staff will solicit nominations of clinical experts in various clinical domains and maintain a list of advisors including physicians, nurses and other clinicians involved in each relevant domain to provide guidance on many topics; however, additional guidance may be needed for particularly complex questions. The Clinical Advisory Committee will include experts from a broad range of clinical

areas who will provide guidance to the OMR Staff and the Steering Committee on clinical issues and decisions that affect the clinical content of the OMF. The OMR Staff will consult with Committee members individually or in small groups on a regular basis to discuss specific clinical questions related to those members' areas of expertise. Discussions with the full committee will occur less frequently.

It is envisioned that the Clinical Advisory Committee will be comprised of approximately twelve members. These members will represent relevant aspects of clinical practice including not only physicians, but representatives of nursing, payers, consumers and patients. The goal of this team will be to manage the curation activity. Each member will be specifically responsible for a division of labor to make the resourcing on the OMR curation activities manageable. One member of the OMR Staff will likely be responsible for the content entry for each clinical domain as it comes into the OMR database. From there, 2-3 members of the OMR Staff will lead activities on clinical equivalency projections, consulting members of the Clinical Advisory Committee as needed. A member of the Clinical Advisory Committee will serve as technical advisor, with expertise in database structure and informatics. The group will be led by a scientific advisor who serves as a direct counterpart to the Steering Committee. All other members will share responsibilities on data curation activities.

OMR Staff

The OMR Staff will be responsible for the day-to-day operations of the OMR. The staff will require technical resources to maintain the OMR database, clinical resources to review submitted content, project management staff to manage relationships with third-party systems (e.g., the RoPR), and support staff to interact with users. The operations will also coordinate the activities of the Steering Committee and Clinical Advisory Committee and consult with these groups as needed. Tasks include:

1. Provide tools to the measure development community to develop and collaborate on value sets, measure clauses and measure components. Such tools may include infrastructure developed external to the OMR tools, and yet available for use as reference by OMR.
2. Evaluate new submissions to the OMR and approve inclusion of all submissions that meet basic criteria (i.e., sufficient metadata, mapping to OMF outcome criteria, steward agreement to participate in collaboration and to maintain currency of measure clinical content).
3. Monitor the output of the community collaboration tools and report to the Steering Committee and the Clinical Advisory Committee monthly regarding active collaboration, resolved issues (and resolution type – i.e., those items modified or those with more clearly defined metadata to reduce potential ambiguity), unresolved issues including the time unresolved and the number referred for resolution.
4. Advance harmonization of outcome measures and measure components by investigating harmonization issues not resolved by community curation and escalate issues that cannot be resolved to the Clinical Advisory Committee, inviting members with specific expertise to review the relevant clinical domain.
5. Maintain a list of members of the Clinical Advisory Committee assuring coverage of common, high-volume clinical domains in cooperation with the Steering Committee and AHRQ. To maintain membership with 3-year terms and maintain some consistency, the

first set of members will be assigned 1, 2 or 3 year terms, each subsequent term to be awarded for 3 years. The OMR staff will submit a public call for membership in the Clinical Advisory Committee for relevant domains and submit a recommendation for appointment to the Steering Committee for appointment.

Interactions Between the Steering Committee and Clinical Advisory Committee

The interaction between the steering committee and operations team should be iterative and cyclical. That is, members of the OMF Staff will be expected to provide regular updates to the Steering Committee on lessons learned from the OMR on a quarterly basis.

In turn, the Steering Committee may use this information to make or endorse recommended modifications as necessary to the OMR. These interactions will be most successful if both parties offer an exchange of information suited to the improvement of the overall OMR, either from a clinical or operational perspective.

OMR Data Management

Submissions to the OMR

Organizations requesting rights to enter measures or registry information into the OMR must meet a set of criteria and be approved by the OMR Staff. The Clinical Advisory Committee will review appeals for measures not meeting criteria as determined by the OMR Staff. The Steering Committee will represent a second level of appeal. Such rights should not be withheld without reason and decisions should be based on whether the applicant meets the following conditions:

1. Demonstrates evidence of clinical expertise
2. Includes multi-disciplinary representation in measure development
3. Uses policies and procedures to evaluate relevant clinical evidence
4. Considers evidence ranking and strength of recommendations
5. Evaluates measures for feasibility, reliability and validity in active clinical settings
6. Includes regular review processes to maintain currency of measures and content
7. Maintains transparency of processes and incorporates input from identified stakeholders
8. Expresses willingness to collaborate with other stewards to harmonize data elements and measures as necessary
9. Participates in data and measure harmonization processes in other settings
10. Demonstrates or able to access clinical vocabulary expertise
11. Agrees to share data and measure definitions

Management of Data Entered Into the OMR

Table 11 addresses how specific governance processes will be managed using this hybrid curated model. Procedures and policies are the responsibility of the Steering Committee and the OMR Staff. The OMR staff will monitor and provide oversight for content entered. The OMR staff will also coordinate activities for the Steering Committee, the Clinical Advisory Committee and registry owners entering and using the OMR. Registry Owners will manage most of the content including stewardship, data definitions, issue resolution and managing change. The OMR Staff will review the harmonized content and address any disputes occurring during the change or harmonization processes. The Clinical Advisory Committee assists in resolving disputes.

Table 11. OMR governance processes

Activity	Steering Committee	Clinical Advisory Committee	Registry Owners
Aligning Policies, Requirements and Controls	√		
Establishing Rules of Participation	√		
Establishing Accountability			
Performing Stewardship			√
Managing Change			√
Defining Data		Advisory	√
Issue Resolution		Advisory	√
Specifying Data Quality Requirements	√	Advisory	
Building Governance into Technology	√		
Stakeholder Care and Support	√		

Activity	Steering Committee	Clinical Advisory Committee	Registry Owners
Stakeholder Communications	√		
Measuring and Reporting Value	√		

Governance Procedures

As noted above, the Steering Committee will be responsible for strategic and executive decisions regarding the OMR. The Steering Committee will consult with the OMR Staff before making any decisions that will affect the clinical content of the system. The Steering Committee should develop bylaws to specify its decision-making process (e.g., simple majority vote, two-thirds vote). Decisions made by the Steering Committee and the rationale for the decisions should be communicated promptly to the Clinical Advisory Committee and the OMR Staff.

Transparency

Transparency is an important component of a multi-stakeholder system such as the OMF. Information on the governance procedures, as well as the Steering Committee and Clinical Advisory Committee, should be publically available. A clear process will be adopted for developing the agenda and discussion topics for Steering Committee meetings, and meeting minutes should be retained for future reference. A summary of the discussion points and decisions should be publically available. In addition, procedures for selecting members of the Steering Committee and managing existing and new conflicts of interest should be transparent.

Inclusion/Exclusion Criteria

The OMR will include any patient or population outcome measure that is or was developed for used in a patient registry and is submitted to the OMR with all required information. The OMR focuses specifically on outcomes, and not process measures used for quality improvement. Data elements used to evaluate outcomes are to be included in the OMR along with the method for determining the outcomes. Data elements used solely for evaluating processes and/or quality improvement do not represent valid content for the OMR.

To be considered complete, an outcome measure submitted to the OMR must include the complete set of metadata to assure comparisons and complete understanding for users. Metadata requirements are listed in the metadata section. Outcome measures that are published elsewhere (e.g., the National Quality Measures Clearinghouse) may be listed in the OMR. In these cases, the original source of the measure should be cited.

Additional information for an outcome measure may be required when OMR administrators enter content into the system to improve search ability and ease of use. This content is detailed in the OMR Maintenance Guide and includes Conditions, Categories, and Keywords (OMR administrators may add keywords to an item, in addition to the keywords identified by the submitter).

Clinical Equivalency

Some outcome measures submitted to the OMR may be clinically equivalent to other content in the OMR. The OMR must display sufficient metadata definition to allow differentiation or to determine if harmonization is necessary. Definitions that are worded differently but refer to the same concept are considered clinically equivalent definitions. Users seeking to enter clinically equivalent definitions into the OMR should reuse existing definitions, or request collaboration with the current owner (steward) of the existing definition. The OMR should include tools to identify such potential duplicates and to track community-curated harmonization processes. OMR staff should regularly review the outcomes of community curation regarding these potential duplicates and share unresolved disputes with the Clinical Advisory Committee, requesting committee recommendations when harmonization is unsuccessful or exceeds committee-defined time limits.

Review for clinical equivalency should include consideration of the following factors:

- Scope: definitions may differ in scope (e.g., inclusion of existing and acute myocardial infarction versus inclusion of acute myocardial infarction only). Only definitions with the same scope should be considered clinically equivalent.
- Bidirectional equivalency: if one item is a broad definition and a second item describes a subset of that broad definition, the definitions are not equivalent. Clinically equivalent definitions must be equivalent in both directions.
- Supporting evidence: two definitions may refer to the same event, but may require different evidence to make the determination. For example, one definition may rely on findings from a laboratory test, while another is based on a physical examination; such definitions may or may not be clinically equivalent.

When two definitions are determined to be clinically equivalent, the collaborating stewards must designate the dominant, or the harmonized definition. A dominant definition must be designated in two scenarios:

1. Two new items are submitted and reviewed for inclusion in the OMR in the same review cycle. The items are determined to be clinically equivalent. Based on collaboration between the two stewards, one will be added to the OMR as the dominant entry, or a harmonized definition will be substituted. The other definition will not be added. In this scenario, the stewards agree on a compromise definition.
2. A single new item is submitted and reviewed for inclusion in the OMR. The item is determined to be clinically equivalent to an existing item in the OMR. The steward desiring the new item is responsible for collaborating with the steward for the existing item. In cases where the two stewards can agree on one of the existing definitions or a compromised solution (i.e., enhanced definition), the OMR is updated with the resulting definition. In some cases the enhanced specificity of the definition from one steward is sufficiently different than the definition from the other steward; in such cases, both terms and definitions can be included in the OMR. In cases of disputes that cannot be resolved, the Operations Team will review the issue with the Clinical Advisory Committee to recommend a resolution. Any items that are replaced persist in the database but are

archived as no longer relevant. Dates for archiving and entry of changes to the OMR may be scheduled to accommodate existing measure programs.

OMR Procedures

The OMR procedures describe the process for adding new content to the OMR. As a hybrid community-curated system, the OMR will require dedicated maintenance resources to review and add new entries to the OMR and update or archive existing entries as needed.

Submission of New Content

New outcome measures will be submitted to the OMR for inclusion in the system. It is anticipated that new items will be submitted in one of two scenarios:

1. Users of the OMR in a third-party system, such as the RoPR, do not find a specific outcome measure in the OMR that is collected in their registry. They submit the item to the OMR for possible inclusion.
2. A professional association or other organization develops a standard set of outcome measures for use in a particular disease area that are appropriate for patient registries. The organization may submit these items to the OMR for possible inclusion by contacting the OMR administrators.

Items may be submitted to the OMR using a standardized online form containing all required metadata elements or by email. When implemented in a third-party system, the OMR will include a link to "Submit new outcome measures." The link will allow users to complete an online form that collects the required elements of a patient or population outcome measure submission. The complete form can be submitted online to the OMR administrators. The form will be appropriate for submission of individual outcome measures. Users wishing to submit multiple patient or population outcome measures will be instructed to contact the OMR staff. The OMR staff can provide a standard format (e.g., an Excel spreadsheet or similar file) for submission of multiple items.

Content Submitted by OMR Committees

Members of the OMR Steering Committee or Clinical Advisory Committee may submit content. It is recommended that these be submitted for consideration in the same standardized format. This content will be reviewed along with content submitted by external stakeholders.

Review of Submitted Content

Content that is submitted through the online form or emailed to the OMR staff will go through a formal review process. The goals of the review process are to ensure that only relevant, complete, and unique entries are added as new items in the OMR. To improve efficiency, submitted items will be batched and will move through the review cycle together. The Steering Committee will develop the review process, involving the kinds of steps outlined below:

1. OMR Staff review the submissions to determine if they are patient or population outcome measures.

2. OMR Staff review the submissions for completeness (see the Inclusion/Exclusion Criteria section above). Incomplete submissions are returned to the submitters for additional information.
3. OMR Staff review complete submissions against existing entries in the OMR and against other items in the same batch. Duplicate submissions are identified, and the operations team sends a notification to the submitter to explain that the content already exists in the OMR.
4. OMR Staff with clinical expertise review the complete, unique submissions for relevance (e.g., whether it is used in a patient registry) and clinical equivalency. Clinical experts may reject items that do not represent patient or population outcome measures or that are not used in a patient registry. They may also identify an item as clinically equivalent, in which case a dominant entry must be selected (see the Clinical Equivalency section above).
5. OMR Staff with clinical expertise approve submissions for entry into the OMR. Questionable items may be referred to the Operations Team for adjudication (e.g., if there is a question related to clinical equivalency, selection of the dominant entry).

Addition of New Content to OMR

Once new entries have been approved, they will be added to the OMR and updates will be released to third-party systems. A regular update schedule should be established to minimize disruptions for third-party systems. The update schedule should balance the need for timely updates with the burden of updates for third-party systems. Submitters of approved items should be notified when the new entries are available in the OMR.

Revision of Existing Content

In general, once an entry has been added to the OMR it should not change. However, there are three scenarios in which changes may be necessary. These are described below:

1. Minor content updates are necessary. For example, new keywords should be added, or a reference should be updated. OMR operations team can make these changes.
2. A new version of an existing item becomes available. For example, a widely used definition of an outcome may be revised. If the new definitions are equivalent, the entry for the existing item should be updated to the current version.
3. An item must be archived. While every effort will be made to identify and remove duplicate entries during the review process, it is possible that a duplicate item could be added to the OMR. If this occurs, the duplicate item should be archived in the system.

In any of these scenarios, the changes should be reviewed and approved by the OMR Clinical Advisory Committee and incorporated into a scheduled release.

Conflicts of Interest

Members of the OMR Steering Committee, the OMR Clinical Advisory Committee, and the OMR Staff must abide by U.S. Government Health and Human Services conflict of interest policies to avoid potential bias in decision making.

Intellectual Property Rights

Due to the cost and effort in developing content, publishers, specialty societies, terminology developers and standard development organizations often indicate intellectual property (IP) restrictions on the use of the content they develop and publish. Such restrictions can limit the extent to which measure developers will share detailed content in a publically available database. Therefore, participant providing data for the OMR must be assured their use of the content in benchmarking clinical performance and other products, including maintenance of certification efforts remain in the domain of the content provider. The participants must agree, however, that the measure specifications and definitions are available for transparency. The measures will often contain copyright information as part of the metadata, such copyright information indicates stewardship and reduces the likelihood that other users will claim ownership of the content. The OMR participation agreement must include a disclaimer that information entered is at the licensee's own risk to avoid risk and expense to the OMR.

In some cases, vocabulary content requires licensure. Assuring that all users of the OMR have a license to use the National Library of Medicine (NLM) Unified Medical Language System® (UMLS) Metathesaurus.[52] The license assures the user has the appropriate authority to use the underlying terminologies and will use the content appropriately. Thus, intellectual property rights to the terminologies will be managed without requiring separate agreements.

Measure and/or registry developers who maintain IP rights to their content may provide web links to the definitions on their own sites where they can assure users meet their individual licensure requirements. However, participation by such measure developers should be discouraged since it reduces the likelihood of collaboration and harmonization.

Search Function and Use of Natural Language Processing

A robust search capability of the OMR catalog will be beneficial to all users of the OMR, including the operations team who could easily review to verify a duplicate measure has not been submitted, harmonization teams, registry owners, and other interested stakeholders. Searching would be available based on the metadata associated with each outcome measure, including the disease/condition, category, and keywords. Natural language processing (NLP), wherein a computer scans free-text entries for themes or identifiers that may distill large volumes of data more quickly than a human could read them, will be useful in certain circumstances. NLP may be utilized to suggest to the operations team what registries listed in repositories such as ClinicalTrials.gov are utilizing a given outcome measure. NLP may suggest to a user searching the OMR what related outcome measures may be of interest to them, or it could provide context information such as 'frequency of mention' of terms relevant to that outcome measure in articles listed in PubMed or another reputable publication source.

As the OMR content becomes more robust due to population by the operations team, and as NLP technology continues to evolve and improve, more opportunities and benefits may arise. Users submitting candidate outcome measures for inclusion in the OMR may be informed that a similar (or identical) measure is already available and be prompted to participate in harmonization efforts. Such concepts should undergo a feasibility assessment for implementation when the

OMR catalog attains a critical mass and user submissions begin to place burden on the operations team due to review for potential duplicates.

Approvals To Host a New Web Site

Creating a new public Web site to house the OMR content may provide the most flexibility and value to the potential users, but there are approval considerations. Hosting a new Web site for AHRQ involves pursuit and obtainment of an Authorization to Operate for that system. If registry owners are asked to identify outcome measures that they utilize, either via an integration with the Registry of Patient Registries Web site (https://patientregistry.ahrq.gov/) or other Web site such as ClinicalTrials.gov, then Office of Management and Budget approval to ask these questions of the general public may be required. Such approvals should be considered in a feasibility assessment of implementing the OMR as a standalone Web site, a locally hosted repository of information for the operations team and potentially be shared with harmonization teams, or a solution integrated with an existing government approved or government run web application.

Conclusion

This analysis has provided useful information related to the burden of data entry within the clinicaltrials.gov site. Additionally, the qualitative analysis provided confirmation that the originally published framework withstands the application of four different condition areas, indicating that the framework functions well with little modification necessary. The information model has been developed and is presented here as a means for providing application and organization of the various elements and sub-elements of the data architecture. Additionally, the governance structure for the maintenance of such a database has been described here with respect to role clarity and responsibilities for each party.

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Appendix A. Relevant Initiatives

Name of Initiative	Type of Initiative	Objectives / Work Product
General/Multicondition Initiatives		
Clinical Data Interchange Standards Consortium (CDISC) Clinical Data Acquisition Standards Harmonization (CDASH)	Data harmonization	Provides basic recommended data elements for 18 domains (e.g., demographics, adverse events) that are common to most therapeutic areas and most phases of clinical research.[1]
National Institute of Neurological Disorders and Stroke (NINDS) Common Data Elements (CDE) Project	Data harmonization; Repository	Develops data standards for use in clinical research within the neurological community and maintains a catalog of these data standards.[2,3,4]
Core Outcome Measures in Effectiveness Trials (COMET)	Data harmonization; Repository	Collects resources relevant to core outcome measure sets to facilitate the exchange of information and foster new research.[5,6,]
Agency for Healthcare Research and Quality (AHRQ) Common Formats	Data harmonization, Repository	Provides common definitions and reporting formats for to help providers uniformly report patient safety events. Also includes metadata registry with data element attributes and technical specifications.[7]
European Clinical Research Infrastructures Network (ECRIN) Database	Repository	Provides database of outcomes related to specific medical devices, taken primarily from health technology assessments (HTAs) and other relevant publications, such as systematic reviews and horizon scans.[8]
Global Rare Diseases Patient Registry and Data Repository (GRDR)	Data harmonization	Aims to build global data sets of patients with rare diseases;[9] developed common data elements in ten categories for use in rare disease registries.[10]
HHS Measure Inventory	Repository	Provides database of measures currently being used by the agencies of the U.S. Department of Health and Human Services (HHS) for quality measurement, improvement, and reporting.[11]
International Consortium for Health Outcomes Measurement (ICHOM)	Data harmonization	Develops standard sets of outcome measures for specific condition areas, resulting in published standard sets for multiple conditions.[12]
National Quality Forum (NQF)	Endorsement body; Repository	Endorses consensus standards for performance measurement and provides searchable catalog of quality measures.[13]
National Quality Measures Clearinghouse (NQMC)	Repository	Provides database of evidence-based health care quality measures and measure sets.[14]
National Quality Registry Network (NQRN)	Data harmonization (planned)	Network of private and public registries and stakeholders interested in advancing the development and use of registries to evaluate and improve patient outcomes; plans to address data harmonization for registries.[15]
The National Patient-Centered Clinical Research Network (PCORnet)	Data harmonization (planned)	Developing a national infrastructure for patient-centered clinical research, using multiple data sources from multiple networks, which will require inter-network data harmonization. [16,17]

Name of Initiative	Type of Initiative	Objectives / Work Product
Consensus Measures for Phenotypes and eXposures (PhenX)	Measure development; Repository	Develops standardized measures of phenotypes and exposures for use in Genome-wide Association Studies (GWAS) and other research; provides a searchable catalog of measures.[18]
Patient Registry Item Specifications and Metadata for Rare Diseases (PRISM)	Repository	Developed library of questions used in rare disease registries to support re-use and eventually facilitate standardization efforts.[19,20]
Patient Reported Outcomes Measurement Information System (PROMIS)	Measure development; Repository	Develops standardized measures of patient–reported health status for physical, mental, and social well-being.[21]
TREAT-NMD Registry of Outcome Measures (ROM)	Repository	Provides database of outcome measures suitable for inclusion in neuromuscular disease studies.[22]
NIH Toolbox for Assessment of Neurological and Behavioral Function	Measure development	Developed standard measures that can be used to assess cognitive, sensory, motor and emotional function across diverse study designs and settings.[23]
United States Health Information Knowledgebase (USHIK)	Infrastructure	Provides database of health care-related metadata, specifications, and standards.[24]
National Library of Medicine (NLM) Value Set Authority Center (VSAC)	Infrastructure	Serves the central repository for the official versions of value sets that support Meaningful Use 2014 Clinical Quality Measures (CQMs).[25]

Name of Initiative	Type of Initiative	Objectives / Work Product
Condition-Specific Initiatives		
Bleeding Academic Research Consortium	Data harmonization	Developed standardizing bleeding definitions for cardiovascular disease clinical trials.[26]
American College of Cardiology/American Heart Association Task Force on Clinical Data Standards	Data harmonization	Develops data standards for multiple areas (e.g., heart failure, cardiac imaging, atrial fibrillation, electrophysiological procedures).[27,28 ,29 ,30]
National Cancer Institute (NCI) Cancer Data Standards Repository (caDSR)	Repository	Provides a repository of common data elements (CDEs), metadata, and data standards used in cancer research.[31]
Diabetes Data Strategy (Diabe-DS)	Data harmonization	Created common data elements for Type 1 diabetes using a disease-specific domain analysis model.[32]
Division of Tuberculosis Elimination, Centers for Disease Control and Prevention	Data harmonization	Developed standardized treatment outcomes for multi-drug resistant tuberculosis.[33]
European Hematology Association (EHA) Scientific Working Group on Thrombocytopenias	Data harmonization	Developed standardized data definitions for treatment response for Primary Immune Thrombocytopenic Purpura (ITP).[34]
Federal Interagency Traumatic Brain Injury Research (FITBIR)	Data harmonization; Repository	Provides data dictionary based NINDS CDE project, with ability for investigators to submit alternate terms and translation rules for the same element.[35]

Name of Initiative	Type of Initiative	Objectives / Work Product
Grid-Enabled Measures (GEM)	Infrastructure	Facilitates virtual community of investigators to promote the use of standardized measures that are tied to theoretically-based constructs and facilitate the ability to share resulting harmonized data.[36]
Harmonizing Outcome Measures for Eczema (HOME)	Data harmonization	"Roadmap" for the development and implementation of core sets of outcome measurements.[37,38]
North American Association of Central Cancer Registries	Data harmonization	Develops and promotes the use of uniform data standards for cancer registries.[39]
National Cardiovascular Research Infrastructure (NCRI)	Data harmonization	Developed harmonized cardiovascular data definitions for clinical research, patient registries, and patient care by using existing data elements and creating new data elements, when necessary.[40]
National Database of Autism Research (NDAR)	Repository	Provides a data dictionary with pre-defined data structures, as well as tools to support the development of community data standards.[41]
Outcome Measures in Rheumatology (OMERACT)	Data harmonization	Develops core sets of outcome measures for use in rheumatic diseases using a documented, reproducible process.[42]

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Appendix B. Glossary

This glossary provides draft definitions for the terms used in the Outcome Measures Framework. It is anticipated that the steering committee for the Outcome Measure Repository may review the glossary and revise terms, if needed, as more experience is gained with the framework.

Participant

A person who takes part in something.

> Reference: Oxford Dictionaries (http://www.oxforddictionaries.com/us/definition/american_english/participant)

Demographics

Statistical data relating to the population and particular groups within it.

> Reference: Oxford Dictionaries (http://www.oxforddictionaries.com/us/definition/american_english/demographics)

Genetics

The genetic properties or features of an organism, characteristic, etc.

> Reference: Oxford Dictionaries: http://www.oxforddictionaries.com/us/definition/american_english/genetics

Or the study of genes and heredity. Heredity is the passing of genetic information and traits (such as eye color and an increased chance of getting a certain disease) from parents to offspring.

> Reference: NCI Glossary http://www.cancer.gov/publications/dictionaries/cancer-terms?cdrid=444994

Family/Participant/Social History

Participant: Past Medical History (PMH): Prior illnesses, their treatments and sequelae.

> Reference: Medlexicon: http://www.medilexicon.com/medicaldictionary.php?t=41172

Social History: Marital status, past and present occupations, travel, hobbies, stresses, diet, habits, and use of tobacco, alcohol, or drugs.

Family History (FH): A record of the relationships among family members along with their medical histories. This includes current and past illnesses. A family history may show a pattern of certain diseases in a family. Also called family medical history.

Reference: NCI Glossary http://www.cancer.gov/publications/dictionaries/cancer-terms?cdrid=302456

Functional/Performance Status

Functional Status: An individual's ability to perform normal daily activities required to meet basic needs, fulfill usual roles, and maintain health and well-being. Functional status subsumes related concepts of interest: functional capacity and functional performance. While functional capacity represents an individual's maximum capacity to perform daily activities in the physical, psychological, social, and spiritual domains of life, functional performance refers to the activities people actually do during the course of their daily lives. A maximal exercise test measures physical functional capacity, while a self-report of activities of daily living measures functional performance.

Functional status can be influenced by biological or physiological impairment, symptoms, mood, and other factors. It is also likely to be influenced by health perceptions. For example, a person whom most would judge to be well but who views himself as ill may have a low level of functional performance in relation to his capacity.

Reference: American Thoracic Society: http://qol.thoracic.org/sections/key-concepts/functional-status.html

Performance Status: A measure of how well a patient is able to perform ordinary tasks and carry out daily activities.

Health Behaviors

Actions taken by a participant that impacts health and well-being. Examples: alcohol use, injection drug use (needles), unprotected sex, and smoking.

Reference: American Thoracic Society: http://qol.thoracic.org/sections/key-concepts/functional-status.html

Environmental Exposures

An exposure is defined as the event when a person comes into contact with a toxic material. Coming into contact with a toxic material is a highly dynamic process that varies from person to person (depending on behavior, location, and life style) and from one toxic substance to another. The determination of the degree of toxicity is the domain of toxicology, and occurs almost exclusively in the laboratory. For the OMF, exposures may potentially encompass any type of contact with the environment, including weather, altitude, air, water, flora, fauna, etc.

Reference: http://www.nature.com/jes/journal/v15/n6/full/7500463a.html

Preference for Care

Patient inputs to the care process that impact the care provided

Reference: Brennan PF, Strombom I. Improving Health Care by Understanding Patient Preferences: The Role of Computer Technology. *Journal of the American Medical Informatics Association : JAMIA*. 1998;5(3):257-262. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC61299/.

Diagnosis

The process of identifying a disease, condition, or injury from its signs and symptoms. A health history, physical exam, and tests, such as blood tests, imaging tests, and biopsies, may be used to help make a diagnosis.

Reference: NCI Glossary: http://www.cancer.gov/publications/dictionaries/cancer-terms?cdrid=46450

Risk Factors

A risk factor is any attribute, characteristic or exposure of an individual that increases the likelihood of developing a disease or injury. Some examples of the more important risk factors are underweight, unsafe sex, high blood pressure, tobacco and alcohol consumption, and unsafe water, sanitation and hygiene.

Reference: World Health Organization: http://www.who.int/topics/risk_factors/en/

Staging System

A system that is used to describe the extent of cancer in the body. Staging is usually based on the size of the tumor and whether the cancer has spread from where it started to nearby areas, lymph nodes, or other parts of the body

Reference: NCI Glossary: http://www.cancer.gov/publications/dictionaries/cancer-terms?search=staging

Genetics of Disease

Per the World Health Organization, ""Dysfunctional gene behavior is commonly termed as a mutation. These mutations are responsible for causing illnesses. Moreover, if the gene mutations exist in the egg or sperm cell, children can inherit the defective gene from their parents. Diseases can occur due to a defect in a single gene or in a set of genes. According to the degree of gene mutation, diseases are categorized into the following:

Chromosomal diseases: occur when the entire chromosome, or large segments of a chromosome, is missing, duplicated or otherwise altered. Down syndrome is a prominent example of a chromosomal abnormality.

Single-gene disorders: occur when an alteration occurs in a gene causing one gene to stop working. An example of a single gene disorder is sickle-cell anemia.

Multifactorial disorders: occur as the result of mutations in multiple genes, frequently coupled with environmental causes. An example of a multifactorial disorder is diabetes.

Mitochondrial disorders: are rare disorders caused by mutations in non-chromosomal DNA located within the mitochondria. (The mitochondria are subcellular organelles.) These disorders can be found to affect any part of the body including the brain and the muscles.

Genes are also known to play a role in the occurrence of infectious diseases like tuberculosis and AIDS as well as some non-communicable diseases like cancer and diabetes.

> Reference: World Health Organization. Genes and human disease. Available at: http://www.who.int/genomics/public/geneticdiseases/en/.

Tissue or Infectious Agent

Tissue: A group or layer of cells that work together to perform a specific function.

> Reference: Tissue: NCI Glossary: http://www.cancer.gov/publications/dictionaries/cancer-terms?search=tissue

Infectious Agent: The agents that cause disease fall into five groups: viruses, bacteria, fungi, protozoa, and helminthes (worms). Protozoa and worms are usually grouped together as parasites, and are the subject of the discipline of parasitology, whereas viruses, bacteria, and fungi are the subject of microbiology.

> Reference: Infectious Agent: Immunobiology: The Immune System in Health and Disease. 5th edition. http://www.ncbi.nlm.nih.gov/books/NBK27114

Biomarkers

A biological molecule found in blood, other body fluids, or tissues that is a sign of a normal or abnormal process, or of a condition or disease. A biomarker may be used to see how well the body responds to a treatment for a disease or condition. Also called molecular marker and signature molecule.

> Reference: NCI Glossary: http://www.cancer.gov/publications/dictionaries/cancer-terms?cdrid=45618

Comorbidity/symptoms

Comorbidity: The condition of having two or more diseases at the same time.

> Reference: Comorbidity: NCI Glossary www.cancer.gov/publications/dictionaries/cancer-terms?cdrid=256556

Symptom: A physical or mental problem that a person experiences that may indicate a disease or condition. Symptoms cannot be seen and do not show up on medical tests. Some examples of symptoms are headache, fatigue, nausea, and pain.

> Symptoms: NCI Glossary: http://www.cancer.gov/publications/dictionaries/cancer-terms?search=symptom

Assessment/Scales

Assessment: In healthcare, a process used to learn about a patient's condition. This may include a complete medical history, medical tests, a physical exam, a test of learning skills, tests to find out if the patient is able to carry out the tasks of daily living, a mental health evaluation, and a review of social support and community resources available to the patient

> Reference: Assessment: NCI Glossary: http://www.cancer.gov/publications/dictionaries/cancer-terms?cdrid=430407

Scales: Tools that enable evaluation of health based on findings and/or responses to specific questions.

Physical Findings

Examination by means such as visual inspection, palpation, percussion, and auscultation to collect information for diagnosis.

> Reference: Medilexicon: http://www.medilexicon.com/medicaldictionary.php?t=30839

Severity

The degree of illness and risk of disease manifested by patients, based either on clinical data from the medical records or on hospital discharge/billing data. Outcome comparisons usually are interpreted in terms of severity of illness to ensure meaningful data interpretations are made.

> Reference: Medilexicon: http://www.medilexicon.com/medicaldictionary.php?t=43516

Disease Understanding

Health Literacy has been defined as the cognitive and social skills which determine the motivation and ability of individuals to gain access to, understand and use information in ways which promote and maintain good health. Health Literacy means more than being able to read pamphlets and successfully make appointments. By improving people's access to health information and their capacity to use it effectively, health literacy is critical to empowerment.

> Reference: WHO: http://www.who.int/healthpromotion/conferences/7gchp/track2/en/

Health literacy is the degree to which individuals have the capacity to obtain, process, and understand basic health information and services needed to make appropriate health decisions.

Reference: AHRQ http://www.ahrq.gov/professionals/quality-patient-safety/quality-resources/tools/literacy/index.html

Training/Experience

Training is based on education and technical exercises. As a reference, the World Health Organization defines health worker category definitions that include basic training references. The United States Agency for International Development (USAID) addressed evaluation of competence and capabilities of healthcare providers. The subject requires clear definition and a measureable taxonomy especially regarding experience, or competency.

Reference: World Health Organization. Health worker definitions. Available at: http://www.optimizemnh.org/health-worker-category-definitions.php. US Agency for International Development (USAID). Measuring the Competence of Healthcare Providers (Kak N, Burkhalter B, Cooper MA, editors). 2001. Available at: https://www.usaidassist.org/sites/assist/files/measuring_the_competence_of_hc_providers_qap_2001.pdf.

Geography

Healthcare provider location, especially with respect to access to care. Healthy People 2020 defines a number of measures dealing with ability to access care.

Reference: Office of Disease Prevention and Health Promotion. Healthy People 2020. Available at: https://www.healthypeople.gov/2020/topics-objectives/topic/Access-to-Health-Services.

Practice setting: Academic Vs. Community

Practice setting can include the intensity of care provided at various locations. Examples include academic inpatient, community inpatient, long term post-acute care (LTPAC), rehabilitation, skilled nursing, extended care, outpatient (such as hospital services not including admission), short stay surgical care, ambulatory, home, and others.

Surgical

A procedure to remove or repair a part of the body or to find out whether disease is present. An operation.

Reference: NCI Glossary: http://www.cancer.gov/publications/dictionaries/cancer-terms?cdrid=45570

Medication

A legal drug that is used to prevent, treat, or relieve symptoms of a disease or abnormal condition.

Reference: NIC Glossary: http://www.cancer.gov/publications/dictionaries/cancer-terms?cdrid=463717

Non-Medication

Treatment that does not include medication or a surgical procedure. This category may include lifestyle change, counseling, physical therapy, occupational therapy, and others that are based on scientific research and are currently accepted and widely used.

Device

An object that has a specific use. In medicine, wheelchairs, pumps, and artificial limbs are examples of devices.

Reference: NCI Glossary: http://www.cancer.gov/publications/dictionaries/cancer-terms?cdrid=635288

Alternative

Treatments that are used instead of standard treatments. Standard treatments are based on the results of scientific research and are currently accepted and widely used. Less research has been done for most types of alternative medicine. Alternative medicine may include special diets, megadose vitamins, herbal preparations, special teas, and magnet therapy. For example, a special diet may be used instead of anticancer drugs as a treatment for cancer.

Reference: NCI Glossary: http://www.cancer.gov/publications/dictionaries/cancer-terms?cdrid=44921

Education

Health education is any combination of learning experiences designed to help individuals and communities improve their health, by increasing their knowledge or influencing their attitudes.

Reference: World Health Organization. Health education. 2016. Available at: http://www.who.int/topics/health_education/en/

Palliative vs. Management vs. Curative

Palliative: Treatment given to relieve the symptoms and reduce the suffering caused by cancer and other life-threatening diseases. Palliative cancer therapies are given together with other cancer treatments, from the time of diagnosis, through treatment, survivorship, recurrent or advanced disease, and at the end of life.

Reference: Palliative: NCI Glossary: http://www.cancer.gov/publications/dictionaries/cancer-terms?search=Palliative

Management:

Curative (surgery): Surgery to remove all malignant (cancerous) tissue, which is meant to cure the disease. This includes removing part or all of the cancerous organ or tissue and a small amount of healthy tissue around it. Nearby lymph nodes may also be removed. Curative surgery works best for localized cancer. Chemotherapy or radiation therapy may be given before surgery to shrink the tumor or after surgery to kill any cancer cells that remain.

> Reference: Curative (surgery): NCI Glossary
> http://www.cancer.gov/publications/dictionaries/cancer-terms?cdrid=688838

Outcomes

A specific result or effect that can be measured. Examples of outcomes include decreased pain, reduced tumor size, and improvement of disease.

> Reference: NCI Glossary: http://www.cancer.gov/publications/dictionaries/cancer-terms?cdrid=467853

Survival

The percentage of people in a study or treatment group who are still alive for a certain period of time after they were diagnosed with or started treatment for a disease, such as cancer. The survival rate is often stated as a five-year survival rate, which is the percentage of people in a study or treatment group who are alive five years after their diagnosis or the start of treatment.

> Reference: Survival Rate: NCI Glossary:
> http://www.cancer.gov/publications/dictionaries/cancer-terms?cdrid=44301

Overall mortality

Refers to the state of being mortal (destined to die). In medicine, a term also used for death rate, or the number of deaths in a certain group of people in a certain period of time. Mortality may be reported for people who have a certain disease, live in one area of the country, or who are of a certain gender, age, or ethnic group.

> Reference: Mortality: NCI Glossary:
> http://www.cancer.gov/publications/dictionaries/cancer-terms?cdrid=496502

Cause-Specific Mortality

The cause-specific mortality rate is the mortality rate from a specified cause for a population. The numerator is the number of deaths attributed to a specific cause. The denominator remains the size of the population at the midpoint of the time period. The fraction is usually expressed per 100,000 population. In the United States in 2003, a total of 108,256 deaths were attributed to accidents (unintentional injuries), yielding a cause-specific mortality rate of 37.2 per 100,000 population.

Reference: Cause-Specific Mortality Rate: Centers for Disease Control and Prevention: http://www.cdc.gov/ophss/csels/dsepd/ss1978/lesson3/section3.html

Disease-free survival

Cause-Specific Survival (NCI): The length of time from either the date of diagnosis or the start of treatment for a disease, such as cancer, to the date of death from the disease. Patients who die from causes unrelated to the disease are not counted in this measurement. In a clinical trial, measuring the cause-specific survival is one way to see how well a new treatment works. Also called CSS.

Reference: Cause-Specific Survival: NCI Glossary: http://www.cancer.gov/publications/dictionaries/cancer-terms?cdrid=655264

Recurrence or Exacerbation

Recurrence: Cancer that has recurred (come back), usually after a period of time during which the cancer could not be detected. The cancer may come back to the same place as the original (primary) tumor or to another place in the body. Also called recurrent cancer.

Reference: NCI Glossary: http://www.cancer.gov/publications/dictionaries/cancer-terms?cdrid=45861

Progression / Change in Status

In medicine, the course of a disease, such as cancer, as it becomes worse or spreads in the body.

Reference: NCI Glossary: http://www.cancer.gov/publications/dictionaries/cancer-terms?search=progression

Adverse Events

An unexpected medical problem that happens during treatment with a drug or other therapy. Adverse events do not have to be caused by the drug or therapy, and they may be mild, moderate, or severe. Also called adverse effect.

Reference: NCI Glossary: http://www.cancer.gov/publications/dictionaries/cancer-terms?cdrid=444960

Exacerbations

Exacerbation: A worsening. In medicine, exacerbation may refer to an increase in the severity of a disease or its signs and symptoms. For example, an exacerbation of asthma might occur as a serious effect of air pollution, leading to shortness of breath.

Reference: http://www.medicinenet.com/script/main/art.asp?articlekey=24661

Complications

In medicine, a medical problem that occurs during a disease, or after a procedure or treatment. The complication may be caused by the disease, procedure, or treatment or may be unrelated to them.

> Reference: NCI Glossary: http://www.cancer.gov/publications/dictionaries/cancer-terms?cdrid=463706

Impact on Others

Patient/Caregiver Reported

Any report of the status of a patient's health condition that comes directly from the patient, without interpretation of the patient's response by a clinician or anyone else.

> Reference: National Quality Forum. Patient-Reported Outcomes. Available at: https://www.qualityforum.org/Projects/n-r/Patient-Reported_Outcomes/Patient-Reported_Outcomes.aspx.

Functioning

Physical, behavioral, cognitive or social performance that can be evaluated and may change over time. Functioning can be specified as body functions related to body structured, activities and participation, and can be influenced by environmental factors.

> References:
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> World Health Organization. International Classification of Functioning, Disability and Health (CF). Available at: http://www.who.int/classifications/icf/en/.
>
> American Physical Therapy Association. Physical Therapy Outcomes Registry. Available at: http://www.ptoutcomes.com/home.aspx.
>
> Terwee CB, Bot SDM, de Boer MR, *et al.* Quality criteria were proposed for measurement properties of health status questionnaires, *J Clin Epidemiol.* 60(2007):34-42. Available at: https://www.researchgate.net/profile/Caroline_Terwee/publication/6637555_Quality_criteria_were_proposed_for_measurement_properties_of_health_status_questionnaires/links/0c960515006c8237c6000000.pdf.

Health-Related Quality of Life

Health-related quality of life (HRQoL) is a multi-dimensional concept that includes domains related to physical, mental, emotional, and social functioning. It goes beyond direct measures of population health, life expectancy, and causes of death, and focuses on the impact health status has on quality of life. Numerous measures have been developed, including disease-specific

quality of life measures that quantify the functional effect of a medical condition and/or its consequent therapy upon a patient's quality of life. Still other measures evaluate quality of life that can address outcomes regardless of condition. Such cross-cutting measures help to evaluate patients with multiple chronic conditions. A related concept of HRQoL is well-being, which assesses the positive aspects of a person's life, such as positive emotions and life satisfaction.

> Reference: Office of Disease Prevention and Health Promotion. Healthy People.gov: Health-Related Quality of Life and Well-Being. Available at: https://www.healthypeople.gov/2020/about/foundation-health-measures/Health-Related-Quality-of-Life-and-Well-Being.

Experience of Care

The Consumer Assessment of Healthcare Providers and Systems (CAHPS) surveys address patients' experience as their perception of access, communication, coordination of care, provider and staff courtesy, helpfulness and respect, and customer service. In addition to patient surveys, experience of care may be addressed by evaluating objective criteria such as frequency of visits, time between encounters and distance to care sites.

> Reference: Agency for Healthcare Research and Quality. Consumer Assessment of Healthcare Providers and Systems (CAHPS) Program. Available at: https://cahps.ahrq.gov/about-cahps/cahps-program/index.html.

Productivity

Ability to accomplish anticipated tasks and goals in a defined period of time. Productivity may be work-related but may also apply to capabilities related to daily living unrelated to employment.

> Reference: Centers for Disease Control. Workplace Health Promotion: Glossary Terms. Available at: http://www.cdc.gov/workplacehealthpromotion/glossary/index.html#P9.

Presenteeism - the measurable extent to which health symptoms, conditions, and diseases adversely affect the work productivity of individuals who choose to remain at work.

> Reference: Chapman LS. Presenteeism and its role in worksite health promotion. Am J Health Promot. 2005;19(4): suppl 1-8.

Productivity (Health-Related) – a measure of worker output impacted by the worker's health status.

> Reference: Sears LE, Shi Y, Coberly CR, Pope JE. Overall well-being as a predictor of health care productivity, and retention outcomes in a large employer group, *Population Health Management.* 2013(16):397-405. Available at: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3870481/pdf/pop.2012.0114.pdf.

Resource Utilization

Health care resource use measures reflect the amount or cost of resources used to create a specific product of the health care system. The specific product could be a visit or procedure, all services related to a health condition, all services during a period of time, or a health outcome. "Efficiency" measures are a subset of resource use measures that compare the production of products of a specified level of quality.1, 106 Most resource use measures in use are not efficiency measures by this definition because they do not explicitly incorporate a measurement of the quality of the product.

> Reference: AHRQ: http://www.ahrq.gov/professionals/quality-patient-safety/quality-resources/tools/perfmeasguide/perfmeaspt3.html

Inpatient Hospitalization

A patient whose care requires a stay in a hospital.

> Reference: http://www.medicinenet.com/script/main/art.asp?articlekey=39152

Office Visits

Per the National Ambulatory Medical Care Survey (NAMCS) and the National Hospital Ambulatory Medical Care Survey (NHAMCS): Ambulatory medical care is the predominant method of providing health care services in the United States, and although it occurs in a wide range of settings, the largest proportion of ambulatory care takes place in physician offices. NAMCS was inaugurated in 1973 to gather, analyze, and disseminate information about the health care provided by office-based physicians. NAMCS is complemented by NHAMCS, which was first conducted in 1992 to expand the scope of data collection to the medical services provided in EDs, OPDs, and ambulatory surgery locations (both hospital-based and freestanding). Hospital-based ambulatory surgery locations were added to NHAMCS in 2009, and freestanding centers were added in 2010. Together, NAMCS and NHAMCS data provide an important tool for tracking ambulatory health care utilization in the United States.

> Reference: Centers for Disease Control and Prevention. National Center for Health Statistics: Survey Content for the National Ambulatory Medical Care Survey (NAMCS) and the National Hospital Ambulatory Medical Care Survey (NHAMCS). 2012. Available at: http://www.cdc.gov/nchs/data/ahcd/body_namcsopd.pdf.

Emergency Department Visits

Emergency Department Visits are defined as care provided in a hospital setting known as an "Emergency Department." The Emergency Medical Treatment & Labor Act (EMTALA) enacted in 1986 addresses such hospital settings: Medicare-participating hospitals that offer emergency services to provide a medical screening examination (MSE) when a request is made for examination or treatment for an emergency medical condition (EMC), including active labor, regardless of an individual's ability to pay. Hospitals are then required to provide stabilizing treatment for patients with EMCs.

Reference: Centers for Medicare and Medicaid Services. Emergency Medical Treatment and Labor Act (EMTALA). Available at: https://www.cms.gov/Regulations-and-Guidance/Legislation/EMTALA/.

Per the American College of Emergency Physicians, Emergency medicine is the medical specialty dedicated to the diagnosis and treatment of unforeseen illness or injury. It encompasses a unique body of knowledge as set forth in the "Model of the Clinical Practice of Emergency Medicine." The practice of emergency medicine includes the initial evaluation, diagnosis, treatment, coordination of care among multiple providers, and disposition of any patient requiring expeditious medical, surgical, or psychiatric care. Emergency medicine is not defined by location, but may be practiced in a variety of settings including hospital-based and freestanding emergency departments (EDs), urgent care clinics, observation medicine units, emergency medical response vehicles, at disaster sites, or via telemedicine.

Reference: American College of Emergency Physicians. Definition of Emergency Medicine. June 2015. Available at: https://www.acep.org/Clinical---Practice-Management/Definition-of-Emergency-Medicine/.

Additional Treatments / Procedures

Treatment generally means the provision, coordination, or management of health care and related services among health care providers or by a health care provider with a third party, consultation between health care providers regarding a patient, or the referral of a patient from one health care provider to another. In the context of the OMF, "additional" treatments or procedures address those services required beyond the initial services provided for the primary condition.

Reference: US Department of Health and Human Services. Health Information Privacy: Uses and Disclosures for Treatment, Payment, and Health Care Operations (45 CFR 164.506). Available at: http://www.hhs.gov/hipaa/for-professionals/privacy/guidance/disclosures-treatment-payment-health-care-operations/index.html

Direct Cost

Those costs associated with providing patient care for services, equipment, medication, etc. In contrast, indirect costs are those not directly attributable to the delivery of care (examples: transportation to receive healthcare services, loss of productivity and related income loss for the patient and/or caregiver, etc.).

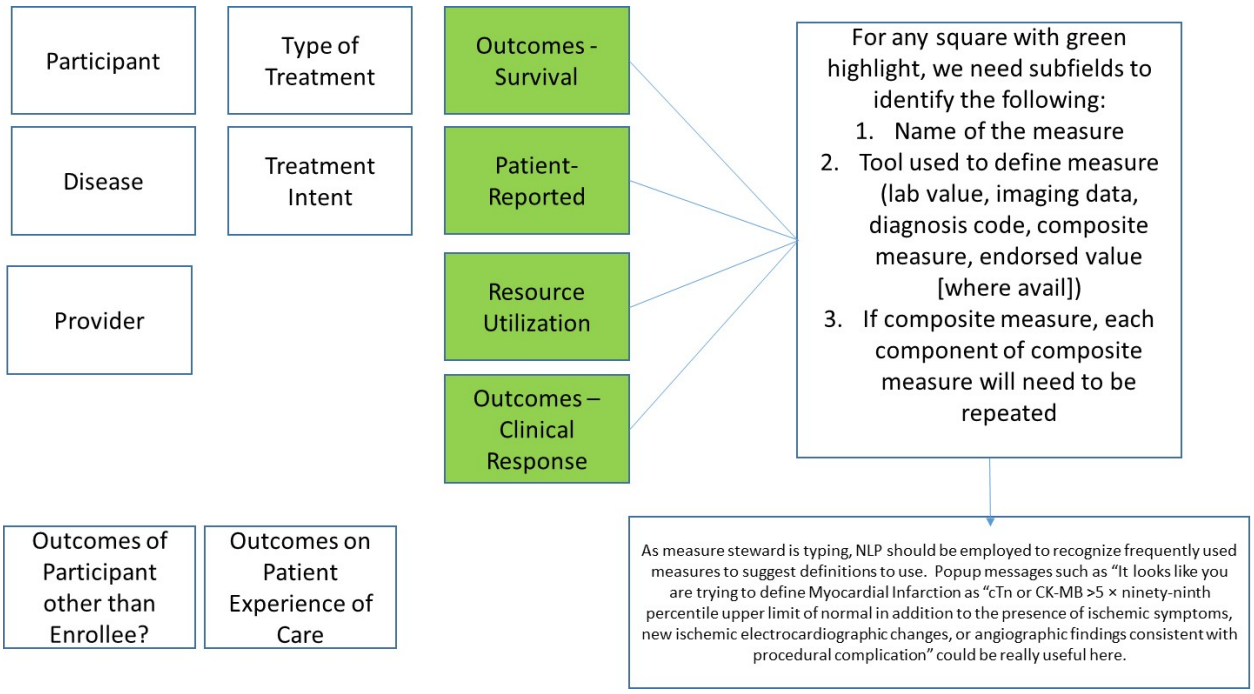
Reference: Derived from: The Advisory Board Company. What's the Difference between 'cost' and 'cost'? 2013. Available at: https://www.advisory.com/research/financial-leadership-council/at-the-margins/2013/06/difference-between-cost-and-cost.

Appendix C. Examples of OMR Outcome Measure Entry

In order to store data efficiently so that registry stewards or users of the data in the future can readily identify outcomes in the OMR, the following example has been created to demonstrate the storage of such data.

Figure C-1 below demonstrates a conceptual model where data will be entered and stored into the database.

Figure C-1. Outcome measure entry



Source: Kip KE, Hollabaugh K, Marroquin OC, Williams DO. The problem with composite end points in cardiovascular studies the story of major adverse cardiac events and percutaneous coronary intervention. Journal of the American College of Cardiology. 2008 Feb 19;51(7):701-7. Used with permission.

There are a multitude of different outcomes that may be measured in each study. In this Appendix, several examples will be given for various outcomes, ranging from simplistic measures to more complex measures representing composite scores of multiple outcomes.

Example: Hypertension

Hypertension may be entered into the OMR as Outcomes-Clinical Response. Within the dropdown menu of "outcome" may appear "Outcomes – Clinical Response". From there, a second categorization of "Complication" may be selected. At the point of the lowest level term, an open text field will allow the user to enter the endpoint of interest: in this case, hypertension.

Hypertension would be entered in a free text field. As measure steward is typing, NLP could be employed to recognize frequently used measures to suggest definitions to use. Popup messages such as "It looks like you are trying to define hypertension. Would you like to use the standard definition of systolic bp >140 mm HG or diastolic bp >90 mm HG?" may prove useful in seeking to harmonize data. In the even there is a new outcome that is to be entered, this would be an option.

As the OMR evolves, standards in data definition may change and will require the periodic review of data measures stored within the OMR, consistent with the governance structure defined here within.

Complex Outcome Measure: Major Adverse Cardiac Events

For a complex measure that is known throughout therapeutic areas for having various definitions, this process becomes more convoluted and will be explained here. Major Adverse Cardiac Events is defined as a composite measure representing both *safety* and *effectiveness* of a treatment process. As recently as 2008, the American College of Cardiology have maintained that there is no single definition, though it is generally thought to represent procedural, short term, and long term evaluations.[1] The table below represents the various definitions of MACE used in clinical trials over several years. It is evident that not only is the definition of MACE not standardized across these clinical trials, but various studies define each of the various components differently to meet MACE criteria (see **Figure** C-2 taken from the study cited).

Specifically in the example shown, studies in the Drug Eluting Stent (DES) registry list myocardial infarction (MI) but define MI differently; some include just Q-Wave MI, others include stent thrombosis (ST), target lesion revascularization (TLR), target vessel revascularization (TVR), emergent (or non-specified) coronary artery bypass graft (CABG), percutaneous intervention, restenosis, acute coronary syndrome (ACS). This MACE example, show how the OMR may be misinterpreted without a clear and granular indication of the details used to define each element ("MI" in the example). For the success of the OMR, the data structure must be optimized to house the components of the outcome measure as well as the definitions of each subcomponent. Furthermore, the scoring of the overall MACE endpoint must be able to be captured within the OMR.

The history of the MACE endpoint, including the heterogeneity noted above, has been the subject of multiple discussions on the coding of this significant outcome measure. The US Food and Drug Administration has worked toward adjudication of endpoints for MACE in recent years.[2] This conference noted a need for data standards, particularly in the endpoint of MACE. The motivation behind such standardization, according to the Agency was to provide endpoint definitions so that events are clearly characterized by objective criteria and reported uniformly. The inclusion/exclusion of various criteria such as hospitalization for unstable angina under the MACE umbrella has led published task force position papers on the call for standardization.[3] Many of these efforts have been led in response to clinical trial standardization, but have implications in observational research as well. The OMR serves as a feasible starting point for the harmonization of these types of endpoints.

Figure C-2. Major adverse cardiac events endpoint in cardiovascular research

Table 1 RCTs of BMS Versus DES With MACE as an Outcome

Reference Year (Ref. #) Journal	Trial Name	Composite Name	Death	Cardiac Death	MI	Q-Wave MI	ST	TLR	TVR	CABG (Emergent)	CABG	Stroke
Morice et al. 2002 (11) *N Engl J Med*	RAVEL	MACE, P	✓		✓				✓		✓	
Grube et al. 2003 (12) *Circulation*	TAXUS-I	MACE, P	✓			✓	✓		✓			
Colombo et al. 2003 (13) *Circulation*	TAXUS-II	MACE, S		✓	✓				✓			
Moses et al. 2003 (14) *N Engl J Med*	SIRIUS	MACE P & S	✓S	✓P	✓P		✓S	✓S	✓P			
Schofer et al. 2003 (10) *Lancet*	E-SIRIUS	MACE, S	✓		✓			✓		✓		
Ardissino et al. 2004 (15) *JAMA*	SES-SMART	MACE and CVA, S		✓	✓			✓			✓	✓
Gershlick et al. 2004 (16) *Circulation*	ELUTES	MACE, S	✓		✓		✓	✓				
Grube et al. 2004 (17) *J Am Coll Cardiol*	SCORE	MACE, S		✓	✓			✓				
Grube et al. 2004 (18) *Circulation*	FUTURE I	MACE, P	✓		✓			✓ within 30 days			✓TVR	
Lansky et al. 2004 (19) *Circulation*	DELIVER	Composite, P	✓		✓			✓				
Schampaert et al. 2004 (20) *J Am Coll Cardiol*	C-SIRUS	MACE, S	✓		✓			✓		✓		
Stone et al. 2004 (21) *N Engl J Med*	TAXUS-IV	MACE, P		✓	✓				✓			
Kaiser et al. 2005 (22) *Lancet*	BASKET Cost Effectiveness	MACE, P		✓	✓				✓			
Kelbaek et al. 2006 (23) *J Am Coll Cardiol*	SCANDSTENT	MACE, S	✓		✓			✓				
Sabate et al. 2005 (24) *Circulation*	DIABETES	MACE, S		✓	✓		✓	✓				
Stone et al. 2005 (25) *JAMA*	TAXUS-V	MACE, S		✓	✓				✓			
Fajadet et al. 2006 (26) *Circulation*	ENDEAVOR-II	Composite MACE, S	✓S	✓P	✓P	✓S		✓S	✓P	✓S		
Suttorp et al. 2006 (27) *Circulation*	PRISON-II	MACE, S		✓	✓			✓				
Tsuchiya et al. 2006 (28) *J Am Coll Cardiol*	FUTURE-I FUTURE-II (pooled)	MACE, P		✓	✓			✓			✓TVR	
Vermeersch et al. 2006 (29) *J Am Coll Cardiol*	RRISC	MACE, S	✓		✓				✓			

The MACE endpoint provides an example of a critical aspect that must be considered when entering a composite outcome measure into the OMR. Not only will the various components of the composite need careful attention, but the definitions of the underlying sub-elements of the components must also be captured. The OMR will support this via a multi-level entry process whereby each specific sub-element can be entered so that every critical portion of the composite has been captured. This will ensure the user community of the OMR access to a well-described endpoint that can then be used in the future in an effort to standardize outcomes such as MACE.

Appendix C References

1. Kip, KE, Hollabaugh, K, Marroquin, OC et al. The problem with composite endpoints in cardiovascular studies: the story of major adverse cardiac events and percutaneous coronary intervention. J Am Coll Cardiol 2008;51:701–7.
2. FDA Endpoint Adjudication conference. Center for Drug Evaluation and Research. May 6, 2015.
3. Hicks KA, Tcheng, JE, Bozkurt, B, et al. Standardized definitions for cardiovascular and stroke endpoint events in clinical trials. J Am Coll Cardiol. 2015;66(4):403-469.