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Harmonized Outcome Measures for Use in Asthma Patient Registries and Clinical Practice

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Abstract:

Background: Asthma, a common chronic airway disorder, affects an estimated 25 million people in the United States and 330 million people worldwide. Although many asthma patient registries exist, the ability to link and compare data across registries is hindered by a lack of harmonization in the outcome measures collected by each registry.

Objectives: The purpose of this project was to develop a minimum set of patient and provider relevant standardized outcome measures that could be collected in asthma patient registries and clinical practice.

Methods: Asthma registries were identified through multiple sources and invited to join the workgroup and submit outcome measures. Additional measures were identified through literature searches and reviews of quality measures and consensus statements. Outcome measures were categorized using the Agency for Healthcare Research and Quality's supported Outcome Measures Framework (OMF). A minimum set of broadly relevant measures was identified. Measure definitions were harmonized through in-person and virtual meetings.

Results: Forty-six outcome measures, including those identified from 13 registries, were curated and harmonized into a minimum set of 21 measures in the OMF categories of survival, clinical response, events of interest, patient-reported outcomes, resource utilization, and experience of care. The harmonized definitions build on existing consensus statements and are appropriate for adult and pediatric patients.

Conclusions: The harmonized measures represent a minimum set of outcomes that are relevant in asthma research and clinical practice. Routine and consistent collection of these measures in registries and in other systems would support creation of a national research infrastructure to efficiently address new questions and improve patient management and outcomes.

Key Messages:

- o Asthma patient registries collect a wealth of data on asthma treatment patterns and outcomes, but the ability to compare, link, and aggregate data across registries and other systems is hindered by variability in the selection and definition of outcome measures.
- o Consistent and routine collection of a minimum set of 21 standardized outcome measures that are relevant to asthma patients, providers, and other stakeholders would create the foundation for a national research infrastructure that could efficiently address new questions and improve patient management and outcomes.

Capsule Summary:

A minimum set of patient outcome measures was developed through a consensus-based process for use in asthma research and clinical practice. Measure definitions were mapped to standardized terminologies to support implementation in electronic health records.

Keywords:

asthma, patient registry, outcome measure, patient outcome, data standard, common data element, harmonization

Abbreviations:

ACQ	Asthma Control Questionnaire
ACT	Asthma Control Test
AHRQ	Agency for Healthcare Research and Quality

103	ATAQ	Asthma Therapy Assessment Questionnaire
104	C-ACT	Childhood Asthma Control Test
105	ED	Emergency department
106	EHRs	Electronic health records
107	FEV	Forced expiratory volume
108	FDA	Food and Drug Administration
109	FVC	Forced vital capacity
110	NIH	National Institutes of Health
111	OMF	Outcome Measures Framework
112	PRO	Patient reported outcome
113	ROPR	Registry of Patient Registries
114	SABAs	Short-acting beta agonists
115	TRACK	Test of Respiratory and Asthma Control in Kids
116	WPAI	Work Productivity and Activity Impairment Questionnaire
117		

Introduction

Asthma is a common chronic airway disorder that affects an estimated 25 million people, including 6 million children, in the United States, and 330 million people worldwide.¹⁻³ In 2015, 1.7 million emergency department (ED) visits and 11 million physician office visits listed asthma as the primary diagnosis.¹ Asthma can be fatal in some cases.⁴ The economic burden of asthma, including absenteeism and mortality, is estimated at \$81 billion per year in the United States.⁵

While asthma cannot be cured, effective treatments are available to control symptoms and reduce the risk of future exacerbations. In recent years, new treatments have become available for severe asthma² and specific asthma phenotypes,⁶ and new tools such as electronic inhaled medication sensors and digital health management programs are available to support medication adherence and patient self-management.⁷⁻⁹ With these advances have come new questions about how to personalize asthma treatment to improve individual patient outcomes across disease phenotypes.¹⁰ Questions also remain about the long-term effects of available treatments and the most effective methods for addressing racial, ethnic, and socioeconomic disparities in asthma outcomes.¹¹⁻¹³

To address these questions and improve patient outcomes, it is critical to build a robust infrastructure to consistently and efficiently collect high-quality data on outcome measures that are relevant to patients and clinicians as part of routine clinical practice. Longitudinal observational studies such as patient registries already capture a wealth of data on asthma treatment patterns and outcomes and could serve as the foundation of this infrastructure. A patient registry is defined as ‘an organized system that uses observational study methods to collect uniform data (clinical and other) to evaluate specified outcomes for a population defined by a particular disease, condition, or exposure and that serves one or more pre-determined

scientific, clinical, or policy purposes.¹⁴ As observational studies, patient registries capture data that reflect routine clinical practice.

Linkage of data across registries and related data collection efforts would offer the opportunity to address new research questions efficiently, drawing on large populations of diverse patients. However, because each effort has unique objectives and methodologies, they often focus on different outcome measures. Even when the same outcome is captured (e.g., exacerbation), different definitions of the measure may be used, reflecting the lack of harmonization of outcome measure definitions across professional societies and research funding agencies. These variations make linkages and comparisons across data sources challenging, thus reducing the utility of these resources for answering new research questions.

To address these issues, the U.S. Department of Health & Human Services, led by the Agency for Healthcare Research and Quality (AHRQ) and in collaboration with the Food & Drug Administration (FDA) and the National Library of Medicine, has supported the development of the Outcome Measures Framework (OMF). The OMF is a conceptual model for classifying outcomes that are relevant to patients and providers across most conditions.¹⁵ The OMF is designed to serve as a content model for developing harmonized outcome measures in specific disease areas; the framework was developed with input from over 400 stakeholders and refined through analyses of outcome measures used in existing registries.

Our goal was to develop a minimum set of standardized outcome measures for use in asthma patient registries and in clinical practice in the United States. The objectives were to 1) test the utility of the OMF for categorizing asthma outcomes and for supporting harmonization of outcomes across treatment pathways; 2) identify a minimum set of outcome measures that could be captured in asthma patient registries and clinical practice; 3) agree on harmonized definitions

for each outcome in the minimum measure set; and 4) map the harmonized definitions to standardized terminologies to support consistent implementation and collection of the outcome measures within electronic health records (EHRs) as part of routine clinical practice.

Methods

Existing asthma registries and asthma-related data collection efforts were identified through a multi-step process including searches of the Registry of Patient Registries (RoPR)¹⁶ and ClinicalTrials.gov;¹⁷ reviews of the Qualified Clinical Data Registries list maintained by the Centers for Medicare and Medicaid Services, Post-Marketing Commitment studies listed on the FDA website, and projects funded by the Patient-Centered Outcomes Research Institute (PCORI); and searches of the published medical literature using PubMed and Google Scholar and the ‘gray literature’ including conference abstracts.

All identified registries meeting definitional criteria for a patient outcomes-focused registry¹⁴ and collecting data in the United States were invited to participate as voluntary members of the registry workgroup. In addition, a stakeholder group, including clinicians, researchers, and representatives from medical specialty associations, health systems, community health centers, regulatory agencies, funding agencies, payers, patient advocacy organizations, measure developers, and measure endorsement organizations, was formed.

Outcome measure specifications were obtained from the participating registries, the published literature, and additional resources such as the COMET (Core Outcome Measures in Effectiveness Trials) Initiative database¹⁸ and the National Quality Forum database.¹⁹ The registry workgroup met virtually and in-person five times over a six-month period to develop the harmonized measures. First, the group categorized all identified measures using the OMF

categories of survival, clinical response, events of interest, patient-reported, resource utilization, and experience of care. Within each category, measures representing similar concepts were identified and grouped accordingly. Workgroup members rated the priority of each measure concept, and the workgroup used the weighted average of the ratings as a basis for the development of the minimum measure set. The minimum measure set is intended for use as a core set of outcomes that will be collected in all future asthma registries and would also be suitable for use in clinical practice; some studies may collect additional outcomes using other definitions to meet specific purposes. For each measure in the minimum set, definitions were reviewed, and detailed comparisons highlighting differences in definitions were prepared. Through iterative meetings, the workgroup discussed the clinical significance of the differences, reasons for the differences, and possible approaches to harmonization (e.g., recommending use of an existing definition, modifying an existing definition to incorporate concepts from other definitions) until consensus was reached.

The combined registry workgroup and stakeholder group met to reach consensus on the minimum measure set and harmonized narrative definitions. Clinical informaticists mapped these narrative definitions to standardized terminologies (primarily ICD-10 and SNOMED) to produce a library of common data definitions suitable for implementation within EHRs. For each measure, the recommended reporting period, initial population for measurement, outcome-focused population, and data criteria and value sets were defined. Where possible, existing common data elements and value sets were used. The narrative definitions and standardized definitions were posted for public comment. Following public comment, the measure set was finalized.

Results

Twenty-one registries were identified, and 13 registry sponsors agreed to participate. Participating registries represented multiple purposes, patient populations, and care settings (Table I). Five participating registries focus on severe asthma, while the others capture data on patients with mild, moderate, or severe asthma. Three participating registries enroll pediatric patients only, five enroll adults only, and three enroll adults and children. Appendix A describes registries that declined to participate. The registries that declined are similar to the participating registries in terms of number of patients enrolled, patient populations, and areas of focus.

Thirteen stakeholders participated, representing patient advocacy organizations (Asthma and Allergy Foundation of America, COPD Foundation, Allergy & Asthma Network), professional societies (American Thoracic Society, American Academy of Allergy, Asthma, and Immunology, American College of Chest Physicians), industry (Propeller Health), health systems (Montefiore), the National Institute of Allergy and Infectious Diseases, the National Library of Medicine, and the National Quality Forum.

Forty-six outcome measures were identified from registries and other sources and curated according to the OMF. Of these, 17 (37%) were categorized as resource utilization, such as asthma-related ED visits or hospitalizations. The remaining measures were categorized as patient reported (30%), clinical response (20%), events of interest (7%), survival (4%), and experience of care (2%). The project team identified ten consensus statements with relevant outcome measure definitions for asthma.³³⁻⁴²

Twenty-one measures are included in the minimum measure set. The minimum measure set is intended to be feasible to collect in all registries, so burden of collection and reporting are important considerations. These measures are suitable for use in both adult and pediatric patients

with asthma. Measure definitions and sources are listed in Table II; the rationale for selection of the measures and definitions is described below. It is important to note that these measures are intended to track patient outcomes over time to support patient management, inform clinical decision-making, and facilitate clinical research. While it is possible that these measures could be adapted for use in quality measurement programs, the measures presented here are not intended for use as measures of quality. In addition, some measures appear in multiple categories to reflect the importance of the measure in different contexts. For example, hospitalization is included in the ‘events of interest’ category because it is a significant event from a patient perspective and in the ‘resource utilization’ category because of the cost implication. The inclusion of a measure in multiple categories does not imply duplicate data collection, but rather a different way of viewing the same data.

Survival

Asthma-related death, the single survival measure included, is relatively rare and may be difficult to capture in some circumstances, such as when a registry patient is lost to follow-up or when the cause of death cannot be ascertained. Despite these difficulties, the workgroup recommends capturing asthma-related deaths whenever feasible, in concordance with the National Institutes of Health (NIH) consensus statements on asthma outcomes.⁴⁰

Clinical Response

Six clinical response measures are included in the minimum set. Exacerbation was identified as an important outcome, but multiple definitions have been developed through consensus-based efforts^{37, 41, 42} and by individual registries. Of note, the definitions use different criteria to identify treatments that are indicative of an exacerbation (e.g., any change in treatment; any use of systemic corticosteroids or an increase in maintenance dose or use for at

least three days). The harmonized definition includes prescribed systemic steroids (defined as two or more days of oral steroids or a steroid injection) or an increase in a maintenance dose of steroids to reflect potential variability in practice patterns. Treatment-seeking behavior, such as hospitalizations, visits to the ED or urgent care centers, or unscheduled office visits resulting in a prescription for systemic corticosteroids are also indicative of an exacerbation and are included in the harmonized definition. Lastly, the workgroup included 'documentation by a provider of acute asthma exacerbation' to capture exacerbations that are managed through contact with the provider but that do not result in a new prescription for systemic corticosteroids (e.g., an exacerbation in a pediatric patient that is managed using a SABA).

Similar to exacerbations, measurement of asthma control is central to understanding clinical response in asthma. Validated asthma control instruments are widely used in research, quality improvement efforts, and clinical practice, and have established cutoff values for asthma control and minimal clinically important differences. Building on existing quality measures⁴³ and consensus statements,³³ the workgroup recommended capturing improving, worsening, and stable levels of asthma control for adults using the Asthma Control Test (ACT), Asthma Control Questionnaire (ACQ), or Asthma Therapy Assessment Questionnaire (ATAQ). For children under age 12, the workgroup recommends the Test for Respiratory and Asthma Control in Kids (TRACK), Childhood Asthma Control Test (C-ACT), Asthma Therapy Assessment Questionnaire (ATAQ), or Asthma Control Questionnaire (ACQ). Other instruments were considered but not included because they lacked validated cutoffs or minimal clinically important differences, or because the necessary usage fees would pose a burden to registries.

Lung function, as measured by pre-bronchodilator percent predicted forced expiratory volume in 1 second (FEV₁%), forced vital capacity (FVC%), and the FEV₁/FVC ratio, was

included in the minimum measure set. Most registries capture this as a secondary outcome measure, and workgroup participants noted challenges ranging from the difficulty of measuring lung function in young children to the lack of availability of equipment and trained personnel at some community health centers. However, the group emphasized that lung function is important to measure for patient treatment and management purposes. The measure is included in the minimum set, but additional work is needed to understand variability in measuring this outcome and to identify resource and training-related barriers that should be addressed to improve measurement.

Two clinical response measures are included to track changes in medication use over time as correlates for asthma control. Change in asthma controller medication use and change in quick-relief medication use should be tracked by patient/caregiver self-reports (average daily use over the past 2 weeks), physician reports, prescription fills or electronic monitoring. Each of these sources of information has strengths and limitations, and the selection of the most appropriate method(s) will depend on the purpose and design of the registry or other data collection effort. Further work is needed to develop a validated, reliable method for obtaining average daily use over the past 2 weeks.

Events of Interest

Five events of interest are captured in the minimum measure set: systemic corticosteroids for asthma, ED visit for asthma; hospitalization for asthma; near fatal asthma exacerbations; and asthma medication-related adverse events. While there is some overlap between the events of interest and other categories (clinical response, resource utilization), the workgroup identified these as important events to track individually because of their impact on patients. The definitions for these measures were taken from participating registries, with one exception. After

extensive discussion and two virtual activities, the workgroup agreed to modify the definition of near fatal asthma from the Severe Asthma Research Program to reduce the complexity of the definition and to clarify how to apply the definition in pediatric populations. The harmonized definition for near fatal asthma is, ‘an asthma exacerbation associated with severe respiratory compromise requiring intubation or noninvasive positive pressure ventilation (to prevent it from progressing to a fatal asthma exacerbation). Note, use of high flow nasal cannula in pediatrics is not considered ‘positive pressure ventilation’ for the purposes of defining near fatal asthma.’

Patient-Reported Outcomes

Asthma is a lifelong, chronic disease, and patient-reported outcomes (PROs) are important to help understand the impact of asthma on a patient’s quality of life and the patient’s experience with treatment. The registry workgroup and stakeholders both expressed strong interest in capturing PROs, but failed to identify a validated instrument that is publicly available, sensitive to change over time, and sufficiently brief to allow for routine use in clinical practice. Identifying an instrument that would be relevant across patient populations and registries was also noted as a challenge. Further work is needed in this area to develop, validate, and implement asthma-specific PROs that are meaningful to clinicians and patients.

To facilitate comparisons of burden across diseases, the workgroup recommended measuring general quality of life using a validated, commonly used instrument, such as PROMIS Global 10 or the VR-12.

The workgroup included a measure of asthma control in the patient-reported category, reflecting the fact that asthma control instruments are largely based on patient-reported data. In comparison to the ‘change in asthma control’ measure included in the clinical response category, this measure captures patients who have maintained asthma control through the measurement

period, as indicated by achieving a well-controlled score on the most recent asthma control instrument result and having fewer than two ED and/or hospitalizations in the last 12 months. This measure is already captured by some participating registries as a quality measure.⁴³

Lastly, the workgroup included medication adherence in the patient-reported category. Medication adherence is not a direct patient outcome, but adherence affects key patient outcomes. Tracking adherence over time and attempting to understand the factors that influence adherence for an individual patient are important for increasing adherence and improving patient outcomes.

Resource Utilization

Resource utilization measures capture the cost of care for a specific condition and are typically calculated using existing data sources (EHR data, claims data). In asthma, cost drivers include hospitalizations, ED visits, urgent care visits, office visits, and medications. Absenteeism from school and work are also important factors when considering the overall economic burden of asthma. The workgroup recommends measuring asthma-related unscheduled visits to the primary care provider's office, urgent care center, ED, or hospital. To capture the burden of medications and regular visits with a care provider, the workgroup recommends measuring all resource utilization related to treatment or management of asthma. These measures focus on individual health resource consumption. Family costs are an important issue in asthma and could be captured as a supplemental measure. It is important to note that these measures are intended to track resource utilization; they are not intended for use as indicators of quality.

In addition to treatment-related utilization, the workgroup recommends measuring missed school days and/or missed work days for patients and for caregivers of a patient with asthma. The Work Productivity and Activity Impairment Questionnaire (WPAI) is recommended as a

validated tool for measuring absenteeism from work related to a health problem. However, further work is needed to develop a corollary tool for measuring missed school days.

Lastly, the workgroup recommends measuring the asthma medication ratio, calculated as the number of canisters of asthma controller medication dispensed during the measurement year divided by the number of canisters of total asthma medications dispensed (controllers plus relievers) during the measurement year.⁴⁴ The workgroup cautioned that this measure is most useful in patients with persistent asthma (as opposed to patients with intermittent asthma) and may be problematic in pediatric patients, where multiple quick-reliever medication prescriptions may be filled for use in different locations (e.g., home, school, camp, daycare).

Experience of Care

Experience of care measures, unlike the outcome measures discussed above, do not capture the disease-related outcomes of treatment for an individual patient. Instead, these measures capture the patient's perspective on the process of receiving treatment. These measures may be useful for helping providers understand issues encountered by patients during treatment, such as communication challenges. Asthma is a chronic condition that affects a diverse patient population, and patients express different needs regarding the education and support necessary to manage their asthma appropriately.⁴⁵ Understanding patients' satisfaction with care may help providers build stronger partnerships with patients. However, more work is needed to develop a validated, publicly available instrument that is meaningful to patients and clinicians and could be recommended for broad use in registries and in clinical practice.

Characteristics

In addition to defining the minimum measure set, the workgroup identified asthma-specific characteristics of the participant, disease, and provider for which there is published

evidence showing a correlation with patient outcomes (Figure 1); these characteristics are important to consider for risk adjustment when measuring asthma outcomes. Further work is needed to recommend specific approaches for risk adjustment for each outcome measure included in the minimum measure set.

Standardized Library

Narrative definitions were translated into standardized terminologies to facilitate implementation within EHRs. Some challenges were encountered in translating the text definitions produced by the workgroup into standardized definitions and value sets. Of note, several outcome measures focus on change over time, such as change in medication dosage or change in pulmonary function over a 12-month period. These measures require multiple measurements in the data representations. The workgroup recommended using the first and last measurement within the parameter of “interval of interest” (generally 12 months).

Related to the outcomes occurring outside of the clinical setting (e.g., missed work/school days), condition specific instruments and/or standard terminology representing the instruments may not exist. The same challenge applies to patient-reported outcomes and patient-reported activities (e.g., medication adherence). In addition, while missed work or school days may be captured within the EHR setting, there is no reliable way to assert that the missed days are due to asthma (as opposed to another condition).

Discussion

This initiative builds on other efforts to harmonize outcomes measurement in asthma^{40, 41} and expands on those efforts in two important ways. First, some efforts have focused on harmonizing asthma outcomes for use in clinical trials and observational research studies, but

these outcomes do not always reflect the outcomes that are meaningful and feasible to capture in routine clinical practice across a wide range of provider types and practice settings.⁴⁰ The OMF standardized outcome measures for asthma are designed for use in a wide range of routine clinical practice settings as well as in research studies. These measures acknowledge and, where possible, address variations in clinical practice across the United States, such as differences in the duration of systemic corticosteroid use following an exacerbation (three days versus two days) and the challenges related to obtaining spirometry measurements in some practice settings. The measure definitions were also modified where necessary to apply to pediatric as well as adult patients.

Second, other harmonization efforts generally have not addressed the informatics components of the definitions, such as how the data could be captured in, and extracted from, an EHR. This is an important and major challenge for new registries and other research projects. For example, the ability to expand pragmatic clinical trials, such as those conducted in PCORnet, is highly dependent on EHR-derived outcomes with standard definitions. Key goals of standardization are to reduce duplicate data collection (and therefore data collection costs) by harmonizing data requirements across the learning healthcare system and to increase the utility of registry data for improving patient outcomes and facilitating shared decision-making. The OMF effort includes development of standardized definitions that could be implemented within an EHR as a core component. The potential limitations of EHR-derived data were considered during the measure harmonization process; for example, some measures (exacerbation, resource utilization) group together unscheduled physician office visits and urgent care center visits because of the difficulty of distinguishing between these types of visits in some EHR data.

The clinical implications for use of standardized outcome measures across patient registries and clinical practices are twofold. First, use of the harmonized measures provides clinicians with access to consistently defined measures that are useful for informing clinical decision-making and important to patients and caregivers. A major barrier to providing optimal multidisciplinary team-based care for pediatric and adult patients with asthma is a lack of standardized clinical measures. The use of standard definitions and the ability to easily extract these important clinical data from various sections of the EHR (e.g. medication tab for controller, quick-relief and oral steroid use, encounter tab for hospitalizations, ED visits, urgent care, asthma specialist and primary care visits, review flowsheet for asthma control tool scores, procedure tab for spirometry results, laboratory test tab for Immunoglobulin E and eosinophil counts, and letters section for asthma action plans) into one central location, would allow primary care physicians and asthma specialists to better communicate about and tailor treatment for individual patients. For difficult to control and severe asthmatics, it would allow asthma specialists to more efficiently and accurately assess a patient's asthma phenotype, and in turn, optimize selection of treatment. The use of a standardized minimum measures set also enables more efficient identification of high-risk patients across large health care systems and facilitates the targeting of additional resources toward this group.

In addition, standardized measures provide a foundation for understanding treatment patterns and outcomes for all asthmatics on a population health scale. Capturing the same outcomes consistently across health systems and within in different registries would create a national data infrastructure that could be leveraged to efficiently monitor patient outcomes, identify areas for improvement, and address new research questions.

The minimum measure set has several limitations. First, consistent capture of the minimum measure set across providers, patients, and care settings will be challenging. For some of the measures, necessary data are not currently captured as part of routine clinical care in all care settings. For example, a registry may be unable to determine if a patient's death was due to asthma. Lung function may not be measured in some care settings, and many providers do not capture quality of life measures (either general or disease-specific) as part of routine care for asthma patients. Even when a measure is captured routinely (e.g., exacerbation), it is difficult to consistently extract the same data from different systems. The development of standardized measure definitions is intended to help address both types of practical limitations by making it easier for providers to codify these data elements within the EHR to capture the data, and to facilitate automated extraction of the data for multiple uses (e.g., quality reporting, clinical research, population management). The utility of standardized measurement at the population level for benchmarking, quality improvement, and population management is well-established in health care. The minimum measure set described here builds on that foundation with a set of measures that are useful at both the population level as well as the individual patient level.

While implementing the measure set in new registries should reduce burden, a major barrier to use in existing registries is mapping existing data to the new measures and updating registry infrastructure. This requires substantial resources, and, in some cases, mapping existing data to the new measures may not be feasible. A pilot implementation of the measure set would be valuable to demonstrate the feasibility of capturing the measures consistently across care settings and the utility of the measures in terms of reducing data collection burden and providing useful information to inform clinical decision-making. In addition, asthma is a heterogeneous disease, and the measures here do not cover all special circumstances (e.g., cardiovascular

support for anaphylactic shock). These measures are intended to cover the most broadly relevant patient outcomes, and discussion of all special circumstances in asthma care are beyond the scope of this measure set.

Additional work is also needed to determine how best to incorporate PROs into asthma research and practice. While some registries captured information on asthma-related quality of life, the workgroup did not identify a tool that was considered appropriate for use in routine clinical practice across care settings and patient populations. Consistent collection of PROs within registries would provide important information on quality of life as it relates to asthma management and treatment.

Lastly, effective governance is necessary for sustainability of the minimum measure set. Regular review and updates are necessary to ensure that the measures continue to reflect current clinical practice. A transparent governance structure is also needed to develop processes for monitoring implementation of the measure set and setting and monitoring benchmarks for success.

The 21 harmonized measures represent a minimum set of outcomes that are relevant in asthma research and multiple clinical practice settings. Consistent collection of these measures in registries and in other systems would support creation of a national research infrastructure to efficiently address new questions and improve patient management and outcomes.

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References

1. Centers for Disease Control and Prevention. Asthma Data, Statistics, and Surveillance: Most Recent Asthma Data. Available at: https://www.cdc.gov/asthma/most_recent_data.htm. Accessed May 30, 2018.
2. Kim AS, Doherty TA. New and Emerging Therapies for Asthma. *Ann Allergy Asthma Immunol* 2016; 116:14-7.
3. Centers for Disease Control and Prevention. Asthma in Children. Available at: <https://www.cdc.gov/vitalsigns/childhood-asthma/>. Accessed May 31, 2018. .
4. Centers for Disease Control and Prevention. Asthma as the Underlying Cause of Death. Available at: https://www.cdc.gov/asthma/asthma_stats/asthma_underlying_death.html. Accessed May 31, 2018.
5. Nurmagambetov T, Kuwahara R, Garbe P. The Economic Burden of Asthma in the United States, 2008-2013. *Ann Am Thorac Soc* 2018; 15:348-56.
6. Fajt ML, Wenzel SE. Asthma phenotypes and the use of biologic medications in asthma and allergic disease: the next steps toward personalized care. *J Allergy Clin Immunol* 2015; 135:299-310; quiz 1.
7. Barrett MA, Humblet O, Marcus JE, Henderson K, Smith T, Eid N, et al. Effect of a mobile health, sensor-driven asthma management platform on asthma control. *Ann Allergy Asthma Immunol* 2017; 119:415-21.e1.
8. Barrett M, Combs V, Su JG, Henderson K, Tuffli M. AIR Louisville: Addressing Asthma With Technology, Crowdsourcing, Cross-Sector Collaboration, And Policy. *Health Aff (Millwood)* 2018; 37:525-34.
9. Adams SA, Leach MC, Feudtner C, Miller VA, Kenyon CC. Automated Adherence Reminders for High Risk Children With Asthma: A Research Protocol. *JMIR Res Protoc* 2017; 6:e48.
10. Levy BD, Noel PJ, Freemer MM, Cloutier MM, Georas SN, Jarjour NN, et al. Future Research Directions in Asthma. An NHLBI Working Group Report. *Am J Respir Crit Care Med* 2015; 192:1366-72.
11. Akinbami LJ, Moorman JE, Simon AE, Schoendorf KC. Trends in racial disparities for asthma outcomes among children 0 to 17 years, 2001-2010. *J Allergy Clin Immunol* 2014; 134:547-53.e5.
12. Beck AF, Huang B, Simmons JM, Moncrief T, Sauers HS, Chen C, et al. Role of financial and social hardships in asthma racial disparities. *Pediatrics* 2014; 133:431-9.
13. Keet CA, Matsui EC, McCormack MC, Peng RD. Urban residence, neighborhood poverty, race/ethnicity, and asthma morbidity among children on Medicaid. *J Allergy Clin Immunol* 2017; 140:822-7.
14. Gliklich R DN, Leavy M, eds. Registries for Evaluating Patient Outcomes: A User's Guide. Third edition. Two volumes. (Prepared by the Outcome DECIDE Center [Outcome Sciences, Inc., a Quintiles company] under Contract No. 290 2005 00351 TO7.) AHRQ Publication No. 13(14)-EHC111. Rockville, MD: Agency for Healthcare Research and Quality. April 2014. <http://www.effectivehealthcare.ahrq.gov/registries-guide-3.cfm>.
15. Gliklich RE, Leavy MB, Karl J, Campion DM, Levy D, Berliner E. A framework for creating standardized outcome measures for patient registries. *J Comp Eff Res* 2014; 3:473-80.

16. Registry of Patient Registries (RoPR). Agency for Healthcare Research and Quality. Available at: <https://patientregistry.ahrq.gov/>. Accessed March 31, 2018. .
17. ClinicalTrials.gov. National Library of Medicine. Available at: <https://clinicaltrials.gov/>. Accessed March 31, 2018. .
18. The COMET (Core Outcome Measures in Effectiveness Trials) Initiative. Accessed January 10, 2018. <http://www.comet-initiative.org/>.
19. National Quality Forum. Accessed March 31, 2018. <https://www.qualityforum.org/QPS>.
20. ClinicalTrials.gov. Longitudinal Observational Study of Severe Asthma. NCT01780142.] Available from <https://clinicaltrials.gov/ct2/show/NCT01780142>.
21. ClinicalTrials.gov. The Genetics of Severe Asthma in Children. NCT01238432.] Available from <https://clinicaltrials.gov/ct2/show/NCT01238432>.
22. Teague WG, Phillips BR, Fahy JV, Wenzel SE, Fitzpatrick AM, Moore WC, et al. Baseline Features of the Severe Asthma Research Program (SARP III) Cohort: Differences with Age. *J Allergy Clin Immunol Pract* 2018; 6:545-54.e4.
23. Afshar M, Press VG, Robison RG, Kho AN, Bandi S, Biswas A, et al. A computable phenotype for asthma case identification in adult and pediatric patients: External validation in the Chicago Area Patient-Outcomes Research Network (CAPriCORN). *J Asthma* 2017;1-8.
24. ClinicalTrials.gov. Vitamin D, Steroids, and Asthma in African American Youth (AsthMaP2). NCT01647399.] Available from <https://clinicaltrials.gov/ct2/show/NCT01647399>.
25. ClinicalTrials.gov. CSP #595 - Pulmonary Health and Deployment to Southwest Asia and Afghanistan. NCT02825654.] Available from <https://clinicaltrials.gov/ct2/show/NCT02825654>.
26. American Academy of Allergy, Asthma and Immunology. AAAAI Allergy, Asthma and Immunology Quality Clinical Data Registry (AAAI QCDR).] Available from <https://www.aaaai.org/practice-resources/practice-tools/qcdr>.
27. ClinicalTrials.gov. Mechanisms of Response to Diesel Exhaust in Subjects With Asthma. NCT01799746.] Available from <https://clinicaltrials.gov/ct2/show/NCT01799746>.
28. MN Community Measurement. .] Available from <http://mncm.org/>.
29. ClinicalTrials.gov. Observational Study of Characteristics, Treatment and Outcomes With Severe Asthma in the United States. NCT03373045.] Available from <https://clinicaltrials.gov/ct2/show/NCT03373045>.
30. ClinicalTrials.gov. Immune Interactions in Severe Asthma. NCT02566668.] Available from <https://clinicaltrials.gov/ct2/show/NCT02566668>.
31. Children's Health Foundation. Children's Health Foundation Pediatric Asthma Registry.] Available from <http://www.ch-foundation.org/improving-pediatric-practices/quality-improvement/pediatric-asthma-care-management/pediatric-asthma-registry>.
32. ClinicalTrials.gov. Bronchial Thermoplasty in Severe Persistent Asthma (PAS2). NCT01350336.] Available from <https://clinicaltrials.gov/ct2/show/NCT01350336>.
33. Cloutier MM, Schatz M, Castro M, Clark N, Kelly HW, Mangione-Smith R, et al. Asthma outcomes: composite scores of asthma control. *J Allergy Clin Immunol* 2012; 129:S24-33.

34. Krishnan JA, Lemanske RF, Jr., Canino GJ, Elward KS, Kattan M, Matsui EC, et al. Asthma outcomes: symptoms. *J Allergy Clin Immunol* 2012; 129:S124-35.
35. Wilson SR, Rand CS, Cabana MD, Foggs MB, Halterman JS, Olson L, et al. Asthma outcomes: quality of life. *J Allergy Clin Immunol* 2012; 129:S88-123.
36. Tepper RS, Wise RS, Covar R, Irvin CG, Kerckmar CM, Kraft M, et al. Asthma outcomes: pulmonary physiology. *J Allergy Clin Immunol* 2012; 129:S65-87.
37. Fuhlbrigge A, Peden D, Apter AJ, Boushey HA, Camargo CA, Jr., Gern J, et al. Asthma outcomes: exacerbations. *J Allergy Clin Immunol* 2012; 129:S34-48.
38. Akinbami LJ, Sullivan SD, Campbell JD, Grundmeier RW, Hartert TV, Lee TA, et al. Asthma outcomes: healthcare utilization and costs. *J Allergy Clin Immunol* 2012; 129:S49-64.
39. Szeffler SJ, Wenzel S, Brown R, Erzurum SC, Fahy JV, Hamilton RG, et al. Asthma outcomes: biomarkers. *J Allergy Clin Immunol* 2012; 129:S9-23.
40. Busse WW, Morgan WJ, Taggart V, Togias A. Asthma outcomes workshop: overview. *J Allergy Clin Immunol* 2012; 129:S1-8.
41. Reddel HK, Taylor DR, Bateman ED, Boulet LP, Boushey HA, Busse WW, et al. An official American Thoracic Society/European Respiratory Society statement: asthma control and exacerbations: standardizing endpoints for clinical asthma trials and clinical practice. *Am J Respir Crit Care Med* 2009; 180:59-99.
42. Global Strategy for Asthma Management and Prevention. Global Initiative for Asthma (GINA). 2017. Available at: <https://ginasthma.org/>. Accessed July 10, 2018.
43. AAAAI Allergy, Asthma & Immunology Quality Clinical Data Registry. 2017 Quality Measure Specifications. Available at: https://www.aaaai.org/Aaaai/media/MediaLibrary/PDF Documents/Practice Resources/2017-AAAI-QCDR-Measures-Specifications_final.pdf. Accessed July 10, 2018.
44. Schatz M, Zeiger RS, Vollmer WM, Mosen D, Mendoza G, Apter AJ, et al. The controller-to-total asthma medication ratio is associated with patient-centered as well as utilization outcomes. *Chest* 2006; 130:43-50.
45. Rubin BK, Zhao W, Winders TA. What do patients want from their asthma care doctors? *Paediatr Respir Rev* 2017.

612 **Table I: Participating Registries**

Registry Name	Sponsoring Organization	Primary Purpose	Patient Population
Longitudinal Observational Study of Severe Asthma ²⁰	National Heart, Lung, and Blood Institute (NHLBI)	To compare severe asthmatics with mild or moderate asthmatics, and healthy volunteers, to study the progression and outcomes of the disease and to gain a better understanding of pathogenic mechanisms that differentiate severe asthma from mild to moderate asthma.	Patients ages 18 or older with severe, moderate, or mild asthma and healthy volunteers. Estimated enrollment is 600 participants.
The Genetics of Severe Asthma in Children ²¹	Connecticut Children's Medical Center	To examine whether a child's ADR β 2 genotype is associated with the development of a near fatal asthma exacerbation.	Patients ages 4 to 18 years with asthma who are admitted to the hospital with an exacerbation or who have not been admitted to the hospital with an exacerbation; and healthy controls.
Washington University Severe Asthma Research Program III ²²	Washington University School of Medicine	To better understand the basis of airway remodeling in severe asthma and how remodeling changes over time using a well-characterized cohort of adult and pediatric subjects with severe asthma.	Patients ages 6 years and older with severe asthma, well-controlled asthma, and healthy controls.
CAPriCORN Asthma Survey ²³	Chicago Area Patient-Centered Outcomes Research Network (CAPriCORN)	To determine how people are affected by asthma and other health conditions.	Children and adults with asthma identified from electronic health records from 10 institutions participating the network.
Vitamin D, Steroids, and Asthma in African American Youth (AsthMaP2) ²⁴	Children's Research Institute	To examine the contribution of vitamin D to disparities in the chronic control and acute severity of asthma. The overall goal of this study is to provide critical epidemiological/molecular information that will inform the interpretation of ongoing and impending randomized clinical trials of vitamin D supplementation in asthma, especially with regard to urban African-American youth with asthma.	Patients ages 6 to 20 years with physician-diagnosed asthma.
CSP #595 - Pulmonary Health and Deployment to Southwest Asia and Afghanistan ²⁵	Veterans' Affairs	To assess the association of airborne exposures encountered during deployment with current measures of respiratory health among United States military Veterans who served in Iraq (Mar. 2003 – Dec. 2011) and Afghanistan (Oct. 2001-current).	United States military Veterans who served in Iraq and Afghanistan.

Registry Name	Sponsoring Organization	Primary Purpose	Patient Population
AAAAI Allergy, Asthma and Immunology Quality Clinical Data Registry ²⁶	The American Academy of Allergy, Asthma & Immunology (AAAAI)	To provide a practice improvement tool and a CMS approved registry option for the Merit Based Incentive Payment Schedule (MIPS) reporting program under the Medicare Access and CHIP Reauthorization Act (MACRA).	Patients seen by physicians specializing in allergy/immunology for routine clinical care.
Mechanisms of Response to Diesel Exhaust in Subjects With Asthma ²⁷	University of Pennsylvania Rutgers University	To determine the acute effect of diesel exhaust inhalation on airway inflammation and hyperresponsiveness (AHR) in subjects with mild to moderate stable asthma, using non-invasive measures.	Adults ages 18 to 55 years old with a history of mild/moderate asthma.
MN Community Measurement ²⁸	MN Community Measurement	To accelerate the improvement of health by publicly reporting health care information, including information about asthma in children and adults, from health care providers in Minnesota.	Children and adults seen by physicians in Minnesota for routine clinical care for asthma.
A Longitudinal Prospective Observational Study of the Characteristics, Treatment Patterns and Health Outcomes of Individuals with Severe Asthma ²⁹	AstraZeneca Duke University	To describe the epidemiology and medical management of United States adults with severe asthma who have not achieved control with high-dose inhaled corticosteroids therapy and additional controllers.	Adults with severe asthma who did not achieve control with high-dose inhaled corticosteroid therapy with additional controllers and/or require systemic corticosteroid or monoclonal antibody therapy.
Immune Interactions in Severe Asthma ³⁰	University of Pittsburgh	To obtain human lung samples by bronchoscopy from a range of asthmatics and healthy controls to address questions related to the mechanisms for the development of the complex immune processes observed in the lungs.	Individuals with severe asthma, mild/moderate asthma, and healthy controls.
Pediatric Asthma Registry ³¹	Children's Health Foundation	To identify children with asthma, assign an asthma severity classification per NHLBI guidelines, and enter encounter-based updates on key clinical actions and measures to support improved patient management and outcomes.	Children with asthma treated by pediatricians who participate in the Children's Health Foundation collaboration.
Bronchial Thermoplasty in Severe Persistent Asthma (PAS2) ³²	Boston Scientific Corporation	To demonstrate durability of the treatment effect and to evaluate the short-term and longer-term safety profile of the Alair System in the United States in the intended use population (patients 18 years and older with severe persistent asthma).	Patients 18 years and older with severe persistent asthma receiving bronchial thermoplasty treatment.

Table II. Asthma minimum measure set and harmonized definitions

OMF Category	Outcome Measure	Definition
Survival	Death (asthma-related)	Death due to asthma, reported in 12-month intervals.
Clinical Response	Exacerbation	Exacerbations of asthma are episodes characterized by an increase in symptoms of shortness of breath, cough, wheezing or chest tightness, and decrease in lung function, i.e. they represent a change from the patient's usual status that is sufficient to require a change in treatment. An exacerbation includes any of the following: a) Prescribed systemic steroids (defined as 2 or more days of oral steroids or a steroid injection) or increasing the oral steroid dose from baseline dose. b) An asthma-related hospitalization, ED visit, urgent care center visit, or unscheduled office visit requiring prescription of systemic corticosteroids. c) Documentation by provider of acute asthma exacerbation.
Clinical Response	Change in asthma control (adults – ages 12 and older)	<u>Measurement Tools</u> ACT - o Not well-controlled: ≤ 19 - o MID: Increase in score ≥ 3 points ACQ - o Not well-controlled: ≥ 1.5 - o MID: Decrease in score ≥ 0.5 points ATAQ - o Not well-controlled: ≥ 1 - o MID: Decrease in score ≥ 1 point <u>Improvement in Asthma Control:</u> Change from not well controlled to controlled OR change representing $\geq$ minimal important difference (MID) improvement in control. <u>Worsening of Asthma Control:</u> Change from controlled to not well controlled OR change representing $\geq$ minimal important difference (MID) decrease in control. <u>Stable Level of Asthma Control:</u> Patient remains stable throughout measurement period (controlled or not well-controlled) OR does not demonstrate a change in score representing $\geq$ the minimal important difference (MID). Reported in 12-month intervals. <i>Notes: Patient scores (as opposed to 'controlled' vs. 'uncontrolled' only) on the selected measurement instrument should be recorded to permit future analyses. Where multiple measurements are available, the first and last measurement in the 12-month measurement period should be used.</i>

OMF Category	Outcome Measure	Definition
Clinical Response	Change in asthma control (pediatrics - under age 12)	<u>Measurement Tools</u> TRACK - Not well-controlled: ≤ 79 - MID: Increase of ≥ 10 points C-ACT - Not well-controlled: ≤ 19 - MID: Increase of ≥ 2 points ATAQ - Not well-controlled: ≥ 0 ACQ - Not well-controlled: ≥ 1.5 - MID: Decrease of ≥ 0.5 points <u>Improvement in Asthma Control:</u> Change from not well controlled to controlled OR change representing minimal important difference (MID) improvement in control. <u>Worsening in Asthma Control:</u> Change from controlled to not well controlled OR change representing minimal important difference (MID) decrease in control. <u>Stable Level of Asthma Control:</u> Patient remains stable throughout measurement period (controlled or not well-controlled) OR does not demonstrate a change in score representing the minimal important difference (MID). Reported in 12-month intervals. <i>Notes: Patient scores (as opposed to 'controlled' vs. 'uncontrolled' only) on the selected measurement instrument should be recorded to permit future analyses. Where multiple measurements are available, the first and last measurement in the 12-month measurement period should be used.</i>
Clinical Response	Pre-bronchodilator Indices (Pre-bronchodilator FEV ₁ % & FVC% & FEV ₁ /FVC ratio)	Change in measurements over 12-month period. The goal is to have 2 measurements in a 12-month period. Two measurements within a 24-month period is also acceptable, if two measurements within 12 months are not available. <i>Notes: Recommended for patients ages 5 and above. Use first and last measurement if more than 2 measurements are available in 12-month period.</i>
Clinical Response	Change in asthma controller medication use	Measured by patient/caregiver self-report, physician report, prescription fill, or electronic medication monitoring. <i>Preferred asthma controller medications are inhaled corticosteroids. While long-acting bronchodilators alone are not, combination inhaled corticosteroid and long-acting beta agonist medications are considered controller medications. Additional controller medications include leukotriene modifiers, long-acting muscarinic antagonists, and immunomodulators.</i>

OMF Category	Outcome Measure	Definition
<i>Clinical Response</i>	Change in quick-relief asthma medication use	Measured by patient/caregiver self-report, physician report, prescription fill, or electronic monitoring. <i>Preferred asthma quick-relief medications are short-acting beta-agonists (SABAs), e.g., albuterol. An additional quick-relief medication includes ipratropium bromide.</i>
<i>Events of Interest</i>	Systemic corticosteroids for asthma	Defined as a prescription for systemic steroids filled within 7 days of a healthcare visit for asthma (i.e., with an ICD-10 code associated with asthma). Counted as number of events per patient in a 12-month reporting period.
<i>Events of Interest</i>	Asthma-specific ED visits	Defined as the number of ED visits per patient in the 12-month reporting period.
<i>Events of Interest</i>	Asthma-specific hospital admission	Defined as the number of hospital admissions due to asthma per patient in the 12-month reporting period.
<i>Events of Interest</i>	Near fatal asthma	An asthma exacerbation associated with severe respiratory compromise requiring intubation or noninvasive positive pressure ventilation (to prevent it from progressing to a fatal asthma exacerbation). <i>Note: use of high flow nasal cannula in pediatrics is not considered 'positive pressure ventilation' for the purposes of defining near fatal asthma.</i>
<i>Events of Interest</i>	Medication adverse events	Adverse events related to asthma medications.
<i>Patient Reported</i>	Asthma control	Patient who had a diagnosis of asthma and whose asthma was optimally controlled during the measurement period as defined by achieving BOTH of the following: • Asthma well-controlled as defined by the most recent asthma control tool result available during the measurement period, and • Patient not at elevated risk of exacerbation as defined by fewer than two emergency department visits and/or hospitalizations due to asthma in the last 12 months.
<i>Patient Reported</i>	Medication adherence	Measured by patient/caregiver self-report, physician report, prescription fill, or electronic medication monitoring.
<i>Patient Reported</i>	Asthma-specific quality of life	Asthma-specific quality of life should be measured using a brief, validated, publicly available instrument that is appropriate for the population of interest.
<i>Patient Reported</i>	General quality of life	General quality of life should be measured using a quality of life instrument that is validated and commonly used (e.g., PROMIS Global 10, VR-12).

OMF Category	Outcome Measure	Definition
<i>Resource Utilization</i>	Missed school days/missed work days	<u>Missed school days:</u> • Patient has had one or more missed school days due to asthma in the past 12 months, or • Number of days missed from school (preferably days missed due to asthma). <u>Missed work days:</u> • Caregiver has had one or more missed days of work due to child's asthma in the past 12 months, or patient has missed one or more days of work due to his/her own asthma. • Use Work Productivity and Activity Impairment Questionnaire (WPAI) to count work absence days.
<i>Resource Utilization</i>	Asthma medication ratio	Calculated as the number of canisters of asthma controller medication dispensed during the measurement year divided by the number of canisters of total asthma medications dispensed (controllers plus relievers) during the measurement year.
<i>Resource Utilization</i>	Unscheduled visits to primary care physician/ visits to urgent care center/ ED visits/hospital admission for asthma	Unscheduled visits to primary care physician/visits to urgent care center/ED visits/hospital admission for asthma, counted as number of visits per patient in the 12-month reporting period.
<i>Resource Utilization</i>	Treatment-related resource utilization	All resource utilization (as measured by cost) related to treatment or management of asthma, including hospitalizations, ED visits, urgent care center visits, office visits, medications, and other costs.
<i>Experience of care</i>	Patient satisfaction with care	Patients with high care satisfaction, as measured by a brief, validated, publicly available instrument.

615

616 Abbreviations: ACQ = Asthma Control Questionnaire; ACT = Asthma Control Test; ATAQ =

617 Asthma Therapy Assessment Questionnaire; C-ACT = Childhood Asthma Control Test; ED =

618 Emergency department; FEV = Forced expiratory volume; FVC = Forced vital capacity; SABAs

619 = Short-acting beta agonists; TRACK = Test of Respiratory and Asthma Control in Kids; WPAI

620 = Work Productivity and Activity Impairment Questionnaire.

ACCEPTED MANUSCRIPT

Figure 1: Outcome Measures Framework, as completed for asthma characteristics and outcomes

Figure Legend: The Outcome Measures Framework (OMF) depicts the minimum set of outcome measures recommended by the workgroup (right column), as well as the key characteristics of the participant, disease, and provider that should be captured to support risk adjustment (left column). Treatments of interest are listed in the center column.

Abbreviations: ED = emergency department; FEV = Forced expiratory volume; FVC = Forced vital capacity; GERD = Gastroesophageal reflux disease; ICU = intensive care unit.

Characteristics

Participant

- Age
- Race
- Ethnicity
- Insurance type/Health care coverage
- Gender/Gender-identity

Disease

- Asthma risk, as measured by history of near fatal attack, prior ICU stay/mechanical ventilation
- Age of onset of symptoms
- Comorbidities (e.g., depression, anxiety, GERD, rhinosinusitis, and obesity)
- Pre-bronchodilator FEV₁ & bronchodilator responsiveness
- Asthma severity classification (intermittent, mild- moderate- and severe-persistent)

Provider

Primary care (e.g., internal medicine, family medicine, pediatrics and medicine/pediatrics) and asthma specialists (e.g., allergists and immunologists and pulmonologists)

Treatment

Type

- Quick-relief medications
- Long-term control medications
- Immunotherapy
- » Immunomodulators

Intent

- Management

Outcomes

Survival

- Death (asthma-related)

Clinical Response

- Exacerbations
- Change in asthma control (adults)
- Change in asthma control (pediatrics)
- Pre-bronchodilator Indices (FEV₁%, FVC%, and FEV₁/FVC ratio)
- Change in asthma controller medication use¹
- Change in quick-relief asthma medication use¹

Events of Interest

- Systemic corticosteroids for asthma
- Asthma-specific ED visits
- Asthma-specific hospital admissions
- Near fatal asthma
- Medication adverse events

Patient Reported

- Asthma control
- Medication adherence¹
- Asthma-specific quality of life
- Generic quality of life

Resource Utilization

- Missed school days / Missed work days due to child's asthma / Missed work days as an adult
- Asthma Medication Ratio²
- Unscheduled visits to primary care physician/ visits to urgent care center/ ED visits/hospital admission for asthma
- Treatment-related resource utilization

Experience of Care

- Patient satisfaction with care

¹ Measured by patient/caregiver self-report, physician report, prescription fill, or electronic monitoring

² In pediatrics, consider the possibility of multiple medications for school, daycare, etc..

Appendix A: Invited Registries that Declined to Participate

Registry Name	Sponsoring Organization	Primary Purpose	Reason for Declining to Participate
Characterization of Adults for Asthma Microbiome Research Studies (CAARS)	University of Michigan	To characterize adult subjects regarding their history of allergy and asthma, clinical manifestations of asthma, and exposures and conditions that may influence asthma severity and control.	Registry outcomes are not clinically focused.
American Lung Association Airways Clinical Research Centers	American Lung Association	Network of clinical research centers dedicated to asthma and chronic obstructive pulmonary disease (COPD) treatment research.	Did not respond to invitations.
Tri State Physician Hospital Organization Asthma Improvement Initiative and Outcomes	Tri State Physician Hospital Organization	To improve the quality of care and outcomes for children with asthma in the region through collaboration among community-based physicians, hospital-based physicians and Cincinnati Children's Hospital Medical Center.	Time commitment.
Pediatric Physicians' Organization at Children's (PPOC) Asthma Program	Pediatric Physicians' Organization at Children's	To improve patient outcomes and quality of care in children with persistent asthma.	Scheduling conflicts.
Characterizing Asthma Sputum Elasticity in the UCSF Severe Asthma Research Program (CAESAR)	University of California, San Francisco	To characterize subjects in terms of their sputum phenotype. The purpose of this study is to learn more about the impact of having abnormally elastic sputum on asthma severity by comparing subjects with severe as well as mild/moderate asthma to healthy controls.	Does not capture clinical patient outcomes.
Severe Asthma Research Program - University of Virginia (SARP3)	University of Virginia National Heart, Lung, and Blood Institute (NHLBI)	To better understand the basis of airway remodeling in severe asthma and how remodeling changes overtime by studying a well characterized cohort of individuals with severe asthma using a multidisciplinary state-of-the-art-approach.	Time commitment; in addition, the SARP3 project is represented by another registry in the workgroup.
Observational Study of Obstructive Lung Disease (NOVELTY)	AstraZeneca	To investigate patient characteristics, treatment, burden of illness, and underlying disease mechanisms in people with	Time commitments and stage of registry (had not started recruitment yet at time of invitation).

		asthma and/or chronic obstructive pulmonary disease (COPD) using a multi-county, multi-center, prospective, longitudinal study design.	
Colorado Pediatric Collaborative Asthma Patient Registry	Colorado Pediatric Collaborative	To track, monitor, and improve the health of asthma patients.	Time commitment and change in registry personnel.