Heterogeneity in Asthma Care in a Statewide Collaborative: the Ohio Pediatric Asthma Repository

Jocelyn M. Biagini Myers, PhD[a], Jeffrey M. Simmons, MD, MSc[b], Carolyn M. Kercsmar, MD[c], Lisa J. Martin, PhD[d], Valentina V. Pilipenko, PhD[d], Stephen R. Austin, BS[a], Mark A. Lindsey, BS[a], Katharine M. Amalfitano, BS[a], Theresa W. Guilbert, MD, MS[c], Karen S. McCoy, MD[e], Shalini G. Forbis, MD, MPH[f], John T. McBride, MD[g], Kristie R. Ross, MD, MS[h], Pierre A. Vauthy, MD[i], Gurjit K. Khurana Hershey, MD, PhD[a]

abstract

BACKGROUND AND OBJECTIVE: Asthma heterogeneity causes difficulty in studying and treating the disease. We built a comprehensive statewide repository linking questionnaire and medical record data with health outcomes to characterize the variability of clinical practices at Ohio children's hospitals for the treatment of hospitalized asthma.

METHODS: Children hospitalized at 6 participating Ohio children's hospitals for asthma exacerbation or reactive airway disease aged 2 to 17 were eligible. Medical, social, and environmental histories and past asthma admissions were collected from questionnaires and the medical record.

RESULTS: From December 2012 to September 2013, 1012 children were enrolled. There were significant differences in the population served, emergency department and inpatient practices, intensive care unit usage, discharge criteria, and length of stay across the sites (all $P < .0001$, total $n = 1012$). Public insurance was highest in Cleveland and Cincinnati (72 and 65%). In the emergency department, Cincinnati and Akron had the highest intravenous magnesium sulfate use (37% and 33%); Columbus administered the most intramuscular epinephrine (15%). Cleveland and Columbus had the highest intensive care unit admittance (44% and 41%) and proportion of long-stay patients (95% and 85%). Moderate/severe asthma severity classification was associated with discharge prescription for inhaled corticosteroids (odds ratio = 2.7; 95% confidence interval: 1.6–4.5; $P = .004$) but not stay length.

CONCLUSIONS: These data highlight the need for standardization of treatment practices for inpatient asthma care. There is considerable opportunity for personalized care plans that incorporate a patient's asthma impairment, risk, and treatment response history into hospital practices for asthma exacerbation treatment. The Ohio Pediatric Asthma Repository is a unique statewide resource in which to conduct observational, comparative effectiveness, and ultimately intervention studies for pediatric asthma.

Divisions of [a]Asthma Research, [b]Hospital Medicine, [c]Pulmonary Medicine, and [d]Human Genetics, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio; [e]Division of Pediatric Pulmonology, Nationwide Children's Hospital, Columbus, Ohio; [f]Department of Pediatrics, Dayton Children's Hospital, Dayton, Ohio; [g]Department of Pulmonary Medicine, Akron Children's Hospital, Akron, Ohio; [h]Department of Pediatrics-Pulmonary, Rainbow Babies and Children's Hospital, Cleveland, Ohio; and [i]Department of Pediatric Pulmonary Medicine, ProMedica Toledo Children's Hospital, Toledo, Ohio

Dr Biagini Myers contributed to the conception and design of the study, subject recruitment, acquisition of data and design of the data collection instruments, oversaw the data analyses, interpreted the analyses, drafted the initial manuscript, and reviewed and revised the manuscript; Drs Simmons and Kercsmar contributed to the conception and design of the study and data acquisition, interpreted the data analyses, and reviewed and revised the manuscript; Dr Martin oversaw the data analyses and contributed to the interpretation of the data analyses and reviewed and revised the manuscript; Dr Pilipenko carried out all the data analyses, contributed to the interpretation of the data analyses, and reviewed and revised the manuscript; Dr Guilbert contributed to data acquisition and interpretation of analyses and reviewed and revised the manuscript; Mr Austin and Mr Lindsey coordinated the memorandum of understanding, designed the data collection instruments, supervised the recruitment of subjects, data acquisition, and data management at all 6 sites, contributed to the initial draft of the manuscript, and reviewed and revised the manuscript; Ms Amalfitano contributed to the data analyses and the initial draft of the manuscript and reviewed and revised the manuscript; Dr Guilbert interpreted the data analyses and reviewed and revised the manuscript;

WHAT'S KNOWN ON THIS SUBJECT: Asthma is heterogeneous and 40% to 70% of patients fail to achieve control with current treatment strategies. To delineate relevant subphenotypes of asthma, identify key factors, and test novel interventions, comprehensive repositories linking clinical, environmental, and biologic data are required.

WHAT THIS STUDY ADDS: This is the first statewide repository for inpatient pediatric asthma. The data collected will better define asthma phenotypes, identify care practices associated with the best health outcomes, and inform personalized care plans to reduce reutilization and readmission for pediatric asthma.

Downloaded from pediatrics.aappublications.org at University of Liverpool Library on February 20, 2015

Asthma, a chronic inflammatory disorder of the airways, is estimated to affect 25 million people in the United States, costing $56 billion per year in medical expenses, lost school and work days, and early deaths.[1] Asthma is 1 of the most common diseases of childhood, affecting 7.1 million US children, resulting in 7 million ambulatory visits, 774 000 emergency department (ED) visits, 200 000 hospital admissions, and $14.4 million in lost school days annually.[2,3] In 2008, 15.2% of Ohio children were diagnosed with asthma, and hospitalization rates for asthma in Ohio were 39% to 150% above the Healthy People 2010 targets.[4]

Asthma is heterogeneous in terms of phenotypes and natural history,[5,6] which contributes to difficulty in studying and treating the disease. Forty to seventy percent of asthmatics fail to achieve control of their disease with current treatment strategies.[7] Nearly two-thirds of asthmatic children reported ≥1 exacerbation in the previous 12 months, and 6-month hospital readmission rates are as high as 40%,[8] highlighting suboptimal management of asthma in this group.[2] Even children with generally well-controlled asthma are vulnerable to exacerbations, particularly during acute respiratory illnesses.[9] Therefore, to delineate relevant phenotypes and subphenotypes of asthma, identify key social, environmental, and personal factors, and test novel interventions, comprehensive repositories linking clinical, environmental, and ultimately biologic data are required.

To meet this challenge, the Ohio Children's Hospital Association, in conjunction with the Ohio Department of Job and Family Services, developed the Ohio Pediatric Asthma Repository (OPAR). The objectives of OPAR are (1) to build a comprehensive biorepository linking clinical, demographic, adherence, environmental, and health outcomes data with biologic specimens; and (2) to compare effectiveness of treatment strategies employed at Ohio children's hospitals for acute asthma exacerbation. This article presents the necessary infrastructure to build OPAR, as well as a comparison of the populations served and variability in emergency, inpatient, and discharge practices for children hospitalized with acute asthma exacerbation at Ohio children's hospitals. OPAR presents a unique opportunity to delineate how patient-level and system-level factors impact outcomes while minimizing physician-provider variability.

METHODS

Subject Identification, Eligibility Criteria, and Informed Consent

Participants in OPAR were hospitalized at Cincinnati Children's Hospital Medical Center (CCHMC, Coordinating Center), Nationwide Children's Hospital, Dayton Children's Hospital, Akron Children's Hospital, University Hospitals Rainbow Babies and Children's Hospital in Cleveland, and ProMedica Toledo Children's Hospital. The OPAR study utilizes a central institutional review board (IRB) structure whereby each participating site's IRB agreed to rely on the CCHMC IRB. Recruitment began at CCHMC in December 2012 and all other sites by March 2013. All participants aged 2 to 17 years admitted for asthma, wheezing, or reactive airway disease were eligible. Subjects without a discharge diagnosis of asthma or those with cystic fibrosis, hyper immunoglobulin E syndrome, cancer, or sickle cell crisis were excluded. The participant's legally authorized representative (LAR) signed a parental permission form; assent was obtained from children older than 7.

Questionnaires and Clinical Data Collection

Questionnaires used in this study, completed by the participant's LAR, were modified from the published New Visit Questionnaire currently used by the Greater Cincinnati Pediatric Clinic Repository.[10] Data collected by the questionnaires are described in the online Supplemental Information. Information from the admission including times of admission/discharge to hospital units, measurement tools used, drugs administered, provider specialty, discharge diagnoses, and follow-up is collected from the medical chart. Length of stay (LOS) was defined as the time the disposition was set for admission (or admission time for those directly admitted) until the time that clinical discharge criteria were met.

Data Validation, Flow, Reporting, and Sharing

The data processes are graphically depicted in Fig 1 and are described in the online Supplemental Information.

Statistical Analyses

Variability among the populations and hospital practices were analyzed employing the χ^2 test or Fisher's exact test for categorical variables and analysis of variance or Kruskal-Wallis test for continuous variables. A Bonferroni correction for the 7 domains evaluated (demographics, housing characteristics, environmental exposures, asthma severity, ED practices, inpatient practices, and discharge practices) was applied ($P \leq .0071$; 0.05/7). Statistical analyses were performed by using JMP Genomics 6.0 and SAS 9.3 (SAS Institute, Inc, Cary, NC). Secondhand smoke (SHS) exposure was defined by a previously described questionnaire.[11] Asthma severity classification (impairment) was assigned as intermittent, mild persistent, moderate persistent, or severe persistent by using the Expert Panel Report-3 (EPR-3)[12] criteria. High risk for asthma admission was defined as hospitalization for asthma in the past 12 months. For the mixed model analyses of asthma impairment and risk, we used the SAS procedure

Downloaded from pediatrics.aappublications.org at University of Liverpool Library on February 20, 2015

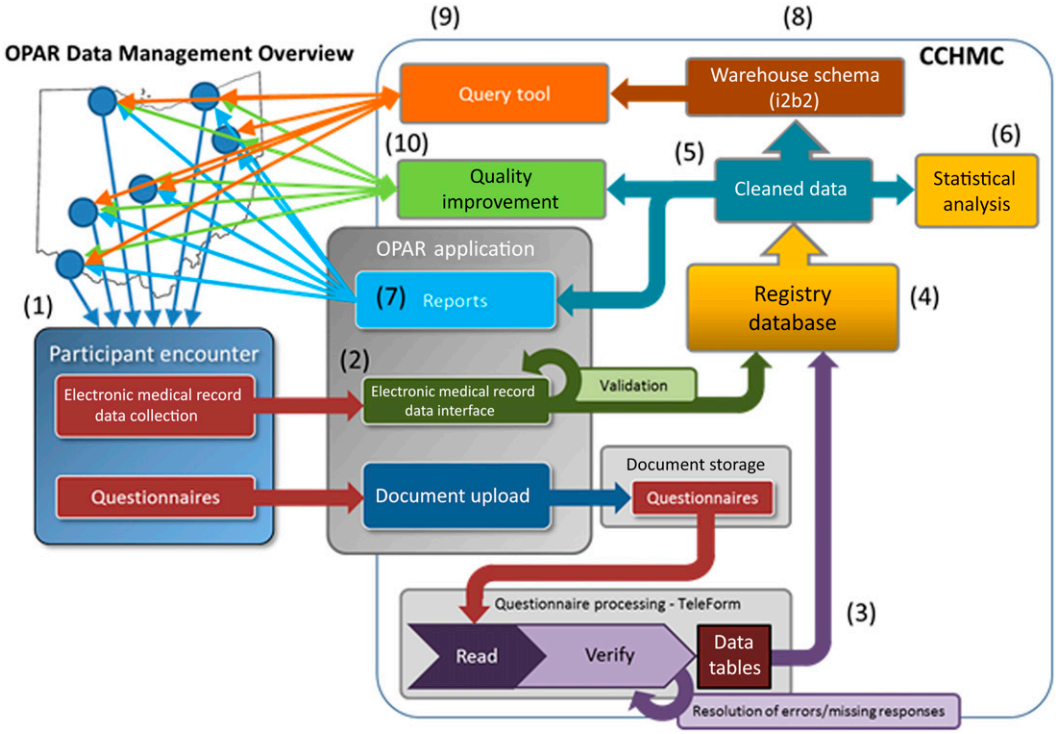

FIGURE 1

OPAR data management overview. Data from (1) the participant encounter, (2) electronic medical record (EMR) data collection, and (3) questionnaires filled out by the family and verified by TeleForm are uploaded to the database. (4) Data are transferred to the CCHMC internal network, (5) validated and cleaned, and then submitted to the data analysis team for (6) analysis of clean data. Data are then shared by (7) reporting of clean data via Web, (8) SHRINE/i2b2 warehousing of clean data, and (9) i2b2 query tool. (10) Cleaned data can also be used for quality improvement in the future.

GLIMMIX "between/within" method for computing the denominator degrees of freedom for tests of fixed effects; hospital was assigned as a random effect.[13]

RESULTS

Demographics, Family, and Housing Characteristics of the Populations

As of September 2013, 1012 unique children were enrolled. The mean proportion of eligible participants enrolled was 68% (53% to 81%). Nonparticipants did not differ from participants by age or gender. We had information on race and insurance type for both participants and nonparticipants at the Cincinnati and Cleveland sites; there were no differences observed for either variable. Race ($P < .0001$), insurance type ($P < .0001$), income level ($P = .0006$), and mother's education level ($P = .005$) exhibited significant variability across the sites (Table 1). Overall, the populations served by Cleveland, Cincinnati, and Columbus were predominantly African-American, had public insurance, and lower incomes; the populations served by Toledo, Akron, and Dayton were predominantly white with higher incomes. There was no significant variability across the sites in participant age, gender, father's education, number of siblings, personal history of atopy (parental report of physician diagnosis of environmental allergy or report of previous positive skin test to environmental allergen[s]), or family history (mother, father, or siblings) of asthma or environmental allergies.

There was significant variation across the sites in the proportion of subjects with more than 1 residence ($P < .0001$), as well as the type ($P = .0002$) and location ($P < .0001$) of the primary home (Table 1). The location and type of the second home, as well as the time spent between the 2 homes, did not vary across sites (data not shown). The proportion living in a poverty area (census tracts with poverty rates of 20% or more[14]), high school graduation rates, and households where no vehicle is available also significantly varied across the sites (Table 1; all $P < .0001$).

Environmental and Home Exposures

The proportion owning a dog ($P < .0001$) and reporting roaches in the home ($P = .003$) varied among all sites. Toledo had the most households with dogs (50%), whereas Cleveland had the least (24%). Eleven percent of the Cincinnati homes revealed roaches compared with none in Toledo or Akron. Sites did not vary significantly in rates of SHS exposure, cat ownership, and rodents in the home.

Differences in ED Practices

There was significant variability across all 6 sites in the use of

Downloaded from pediatrics.aappublications.org at University of Liverpool Library on February 20, 2015

TABLE 1 Demographics, Family, and Housing Characteristics and Census Tract Demographics of Population Hospitalized for Asthma Exacerbation at 6 Ohio Children's Hospitals

	Cincinnati, n = 366	Columbus, n = 169	Dayton, n = 116	Akron, n = 103	Cleveland, n = 198	Toledo, n = 60	P
Age							
$\bar{x} \pm \sigma$	7.0 ± 3.9	7.2 ± 4.0	7.2 ± 3.9	7.1 ± 4.0	7.3 ± 4.2	7.2 ± 4.6	.95
Range	2.0–17.6	2.0–17.7	2.1–17.9	2.0–17.9	2.0–17.4	2.1–16.9	
Male gender, %	63.1	59.8	55.2	52.4	66. 7	50.0	.05
Race, %							<.0001
White	34.7	37.9	43.3	50.6	18.3	57.4	
African-American	51.0	49.0	39.4	34.9	68.0	27.8	
Other	14.3	13.1	17.3	14.5	13.7	14.8	
Hispanic ethnicity, %	3.4	3.6	2.0	0.0	8.3	9.5	.01
Insurance type, %							<.0001
Private	24.0	26.0	37.1	23.3	19.2	31.7	
Public	69.7	57.4	54.3	57.3	73.7	53.3	
Other/unknown	6.3	16.6	8.6	19.4	7.1	15.0	
Income, %							.0006
<29 000	46.3	36.2	34.0	42.9	60.7	46.3	
30 000–49 000	32.2	39.2	37.1	25.7	27.7	19.5	
50 000–89 000	11.9	12.3	16.5	18.6	4.5	24.4	
90 000+	9.7	12.3	12.4	12.9	7.1	9.8	
Mother's education level, %							.005
< High school	8.2	5.9	7.8	11.3	14.6	2.6	
High school or GED	28.8	27.2	23.5	28.2	34.5	15.4	
Some college/4-y degree	58.1	58.8	55.9	50.7	47.4	69.2	
Postgraduate work+	4.9	8.1	12.8	9.9	3.5	12.8	
Father's education level, %							.20
< High school	11.6	6.5	10.5	13.3	12.3	29.0	
High school or GED	40.9	37.6	31.6	46.7	45.3	29.0	
Some college/4-y degree	41.5	50.5	48.7	35.6	37.7	35.5	
Postgraduate work+	6.1	5.4	9.2	4.4	4.7	6.5	
Number of siblings, %							.24
0	10.1	12.0	5.5	7.1	11.2	9.8	
1–2	21.1	29.6	26.6	27.4	22.5	35.3	
3–4	24.3	19.0	17.4	17.9	17.4	21.6	
5+	16.5	11.3	16.5	11.9	12.9	7.8	
Personal history of atopy, %[a]	55.5	55.5	56.9	44.7	51.8	42.3	.27
Family history of asthma, %[b]	68.9	62.6	70.6	72.6	70.1	79.0	.30
Family history of allergy, %[b,c]	64.7	68.7	77.9	76.3	73.4	65.4	.06
No. of primary homes, %	n = 281	n = 152	n = 108	n = 77	n = 189	n = 44	<.0001
1	69.8	52.0	52.8	54.6	46.0	31.8	
2	30.3	48.0	47.2	45.5	54.0	68.2	
Type of home 1, %	n = 260	N = 142	n = 105	n = 72	n = 178	n = 40	.0002
Single house	62.3	71.1	81.9	76.4	62.9	80.0	
Multi house 2+ units	36.5	26.8	18.1	18.1	36.0	20.0	
Mobile home	1.2	2.1	0.0	5.6	1.1	0.0	
Location of home 1, %	n = 276	n = 147	n = 105	n = 76	n = 182	n = 40	<.0001
City	60.1	64.6	53.3	63.2	70.9	65.0	
Suburb	34.4	25.9	34.3	15.8	26.4	17.5	
Rural	5.4	9.5	12.4	21.1	2.8	17.5	
Living in poverty area, %[d]	46.0	49.4	32.7	44.2	62.4	39.1	<.0001
< High school education, %[d]							<.0001
<10%	24.0	31.9	40.7	38.4	20.4	45.7	
10%–19%	42.3	28.1	37.2	37.2	35.0	34.8	
20%–29%	25.7	30.0	17.7	20.9	25.8	10.9	
≥30%	8.0	10.0	4.4	3.5	18.8	8.7	
No vehicle available, %[d]							<.0001
<10%	42.9	56.3	62.8	57.0	36.6	69.6	
10%–30%	36.9	37.5	31.0	40.7	37.1	28.3	
>30%	37.2	17.0	12.0	9.1	19.8	4.9	

[a] Defined as history of positive environmental skin test or report of doctor-diagnosed environmental allergies.
[b] Mother, father, or sibling.
[c] Defined as environmental allergies/hay fever.
[d] Denotes census demographics.

Downloaded from pediatrics.aappublications.org at University of Liverpool Library on February 20, 2015

magnesium, intramuscular epinephrine, albuterol spacing, and asthma pathway utilization in the ED ($P < .0001$ for all, Fig 2A). Magnesium was administered to >30% of participants in Cincinnati and Akron compared with <6% at Toledo and Dayton. Columbus administered intramuscular epinephrine to 15% of participants compared with <3% at all other sites. All sites except Cincinnati and Columbus regularly use an ED asthma pathway. The majority of initial albuterol spacing is continuous or back to back except in Cleveland where 71% received treatment more than every 30 minutes. Supplemental oxygen is most often administered in Columbus (53%) and Akron (51%, data not shown). One patient required endotracheal intubation in the Toledo ED.

Differences in Inpatient Practices

Although all sites use an inpatient standardized care pathway, admission source, intensive care unit (ICU) admittance, ipratropium administration, supplemental oxygen administration, short-acting β agonist (SABA) administration, and provider type varied significantly across the sites ($P < .0001$ for all; Fig 2B). Cleveland (44%) and Columbus (41%) had the highest proportion of patients admitted to the ICU during their admission. Four patients required endotracheal intubation across the 6 sites; this is not a criterion for ICU admission. Ipratropium was administered to 86% of patients in Cleveland compared with <8% in Cincinnati, Dayton, and Toledo. SABAs were primarily administered by metered dose inhaler at Dayton (93%), whereas nebulized treatments were almost exclusively used at Columbus, Cleveland, and Toledo. Most patients at each site were treated by either a hospitalist or a combination of providers. Cincinnati, Columbus, and Dayton had almost exclusive admissions from the ED (or internal urgent care in Cincinnati), whereas Akron, Toledo, and Cleveland had 30% to 42% of patients directly admitted (from an outside urgent care, hospital, or physician office; data not shown). Columbus administered supplemental oxygen to 63% of participants compared with 23% in Dayton.

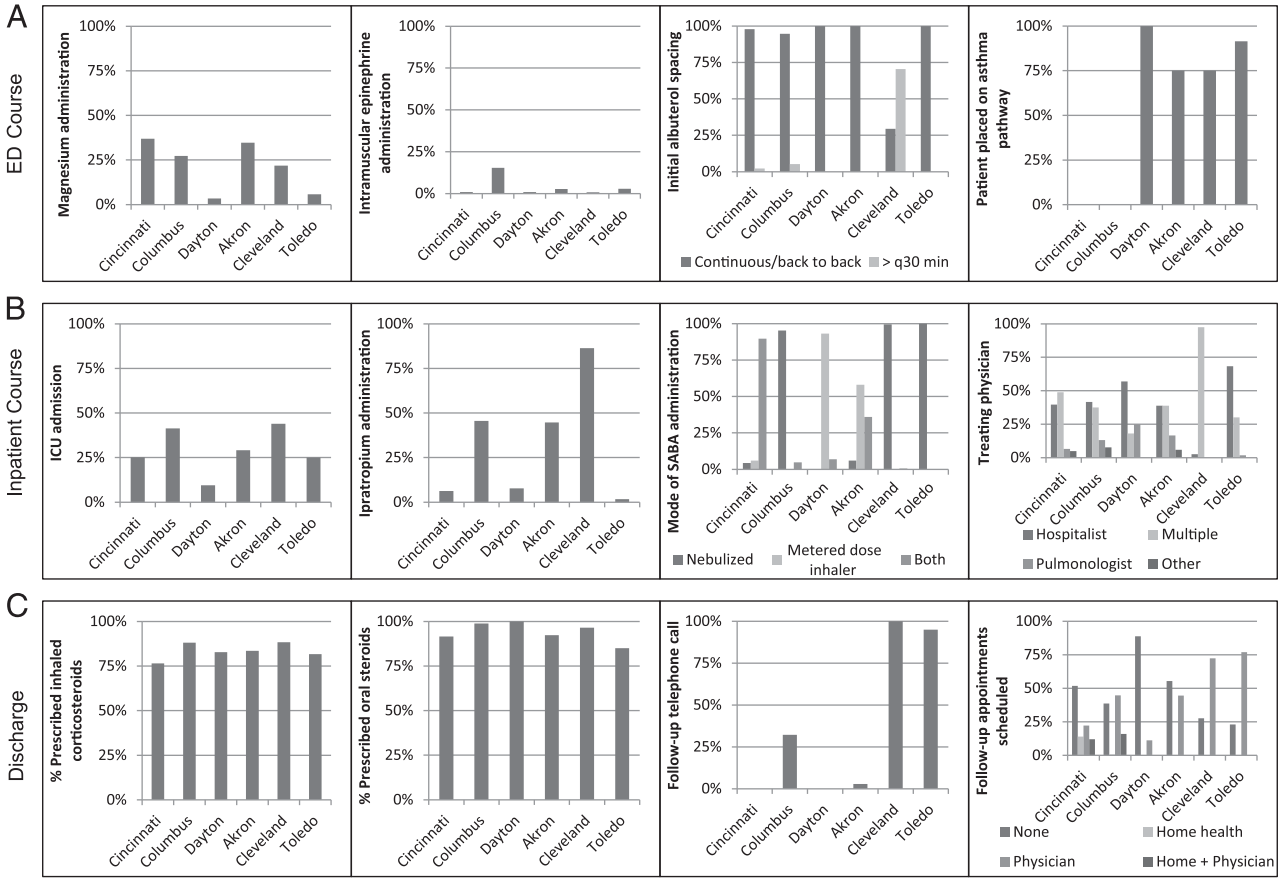

FIGURE 2

Differences in ED, inpatient, and discharge practices. The 6 sites had significant variability in (A) ED magnesium administration, intramuscular epinephrine administration, initial albuterol spacing, and asthma pathway use (all $P < .0001$); (B) inpatient ICU admission, ipratropium administration, mode of SABA administration, and treating physician (all $P < .0001$); and (C) discharge prescription of inhaled corticosteroids ($P = .0035$), prescription of oral steroids, follow-up telephone call, and follow-up appointments scheduled (all $P < .0001$).

Downloaded from pediatrics.aappublications.org at University of Liverpool Library on February 20, 2015

Differences in Discharge Practices

The sites varied significantly in albuterol spacing for discharge ($P < .0001$, data not shown), oral steroids ($P < .0001$) and inhaled corticosteroids prescribed ($P = .0035$), follow-up appointments scheduled ($P < .0001$), and telephone calls after discharge ($P < .0001$; Fig 2C). At 88%, Cleveland and Columbus had the highest proportion of children prescribed inhaled corticosteroids at discharge. Almost every patient from Cleveland (100%) or Toledo (95%) received a follow-up telephone call compared with 0% in Cincinnati and Dayton. Over 70% of patients in Cleveland and Toledo had a follow-up appointment with a physician scheduled at discharge compared with 11% in Dayton. Only Cincinnati and Columbus scheduled appointments with home health. Cincinnati, Columbus, Akron, and Toledo primarily used every 4 hours ×1 or 2 albuterol spacing as discharge criteria, whereas Dayton and Cleveland use every 6 hours ×1 or 2 (data not shown).

Health Care Utilization, Previous ICU Admission, Asthma Severity, and LOS

Asthma severity classification varied significantly across sites ($P = .006$; Fig 3A) although when dichotomized as intermittent/mild or moderate/severe, the variability is no longer significant (Fig 3B; $P = .05$). Utilization of the ED/urgent care, primary care physician visits, hospitalizations, and ICU admissions in the previous 12 months did not vary among the sites (data not shown). When the analysis was stratified by present ICU admission, previous ICU admission was significantly associated with current ICU admission in Cincinnati ($P < .0001$), Columbus ($P = .0015$), Dayton ($P = .002$), and Akron ($P = .0001$; data not shown). Asthma severity classification, previous hospitalization, and ED and primary care physician visits for asthma in the past 12 months were not associated with present ICU admission (data not shown).

The LOS varied significantly across the 6 sites (Fig 3 C and D; $P < .0001$). At 58.1 hours, Cleveland had the longest average LOS, whereas Dayton had the shortest (24.5 hours; Fig 3C). When dichotomized into short (<24 hours) and long (≥24 hours) stays, Cleveland and Columbus had the largest proportion of long stays (95% and 85%, respectively), whereas Dayton and Akron had the fewest (31% and 47%, respectively; Fig 3D).

To determine if asthma severity classification or risk were associated with clinical practices, we employed a mixed model. Across all hospitals, patients with moderate/severe asthma severity classification were almost 3 times more likely to receive a prescription for inhaled corticosteroids during discharge (odds ratio = 2.7; 95% confidence interval: 1.6–4.5; $P = .0039$); there were no associations with ED magnesium administration and supplemental oxygen, inpatient ipratropium administration and supplemental oxygen, ICU admittance, and prescription of oral corticosteroids at discharge (data not shown). Asthma severity ($P = .07$; Fig 4A) and risk ($P = .63$; Fig 4B), as well as the combination of severity and risk ($P > .11$; Fig 4C) were not significantly associated with of LOS.

DISCUSSION

OPAR is a unique and innovative resource that links the 6 Ohio children's hospitals with the goal of improving the health of children with asthma. To our knowledge, this is the first statewide repository for inpatient pediatric asthma. The long-term objective is to identify the practices and phenotypes associated with the best health outcomes so that best practices can be implemented across these hospitals and similar hospitals across the United States. These data will allow for observational and comparative effectiveness studies, and ultimately testing of novel interventions and new management strategies for hospitalized pediatric asthma. These data demonstrate that there are significant differences in the populations served, ED and inpatient practices, ICU usage, discharge criteria, and LOS among the sites, highlighting the opportunity for understanding care practices linked to best outcomes and implementation of best practices for inpatient asthma care.

The degree of variability in the clinical practices observed was somewhat unexpected. These variations in practice are certainly due, in part, to the severity of the individual exacerbation, but are also likely due to institutional policy differences. For example, we observed wide variation in ICU admittance (9% in Dayton to 44% in Cleveland). However, Dayton had the second highest proportion of baseline moderate/severe asthmatics, suggesting that the policies governing what constitutes an ICU admission at each site are a contributing factor. Indeed, ICU admission criteria (albuterol spacing, clinical scores, need for adjunctive therapy, and/or physician assessment) at Dayton are much more stringent than at Cleveland and Columbus and may contribute to the low proportion of children sent to the ICU at that site. Policy differences also hindered some comparisons. For example, each site uses a different clinical scoring system to document the exacerbation severity at admission, so site comparison was not possible. These examples highlight areas that would benefit from standardization of treatment practices for asthma care.

These data, combined with ongoing collection of biologic, genetic, and environmental samples, may provide insights into childhood asthma phenotypes and outcomes. Clinical pathways guide evidence-based

Downloaded from pediatrics.aappublications.org at University of Liverpool Library on February 20, 2015

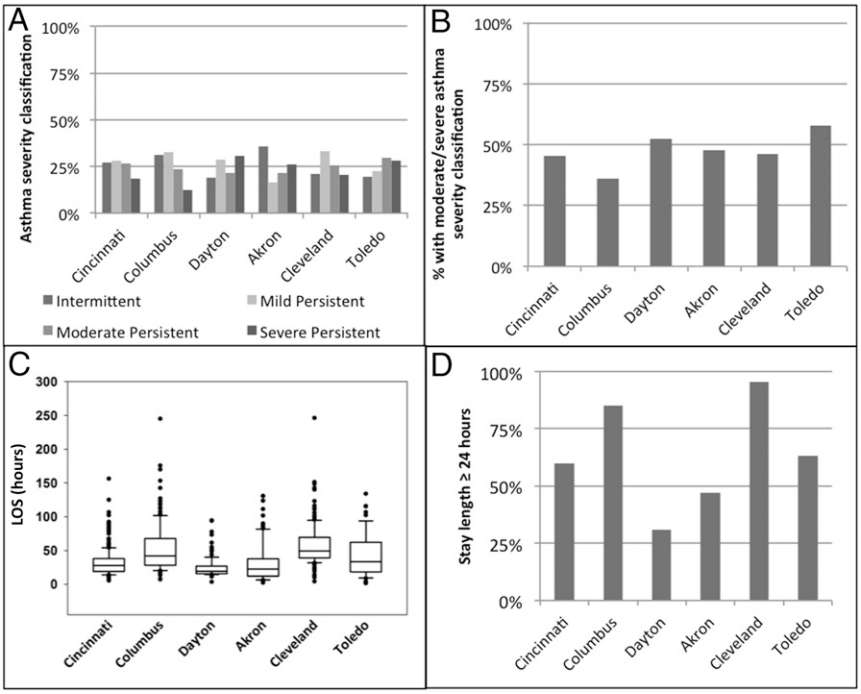

FIGURE 3

Asthma severity and LOS. A, Four-level asthma symptom severity classification varied across all sites (P = .005). B, The proportion of subjects that had moderate/severe asthma classification did not vary across the sites (P = .05). C, LOS (hours) varied significantly across all sites (P < .001). D, The proportion of subjects with long stay length (≥24 hours) varied across all sites (P < .0001).

health care by outlining a sequence for assessment and interventions for treatment.[15,16] The use of an asthma clinical pathway results in reduced hospitalization cost and LOS,[16,17] and implementation of an asthma care process model[8] or intensive care coordination services decreases pediatric asthma readmissions,[18] which highlights the need for improved asthma treatment practices for hospital care. Although the EPR-3[12] provides a basis to develop practice guidelines for asthma and suggests that clinical pathways should be developed, it is mainly focused on outpatient care.[12,16] This lack of specific guidelines leads to each institution developing their own pathways, evident by the wide-spread differences in clinical practices observed across OPAR hospitals. In the emergency setting, 70% of physicians acknowledge deviating from their institution's asthma pathway due to the patient's treatment response, their own clinical judgment, practical issues, clinical scores, and patient preference.[19] These deviations increase with asthma severity from 55% in mild asthma to 100% in severe asthma.[19] Physician-directed deviations from a given institutional pathway are often due to knowledge and understanding of the patient's history, impairment, risk, and past treatment response. A care process that integrates factors such as previous hospitalization, ICU use, LOS, medication adherence, treatment response phenotype, and psychosocial needs may be necessary to determine the intensity of hospital care, as well as to guide patient education and a home management plan of care. These steps will be necessary to ultimately reduce reutilization or rehospitalization.[8,18] Collectively, these findings support a role for personalized clinical pathways informed by the heterogeneity of the child's asthma impairment or risk, as well as the aforementioned factors.

OPAR provides a novel infrastructure to conduct comparative effectiveness studies needed to develop clinical pathways tailored to subphenotypes of asthma. In an effort to make informed health decisions regarding the manner in which diseases can be effectively prevented, monitored,

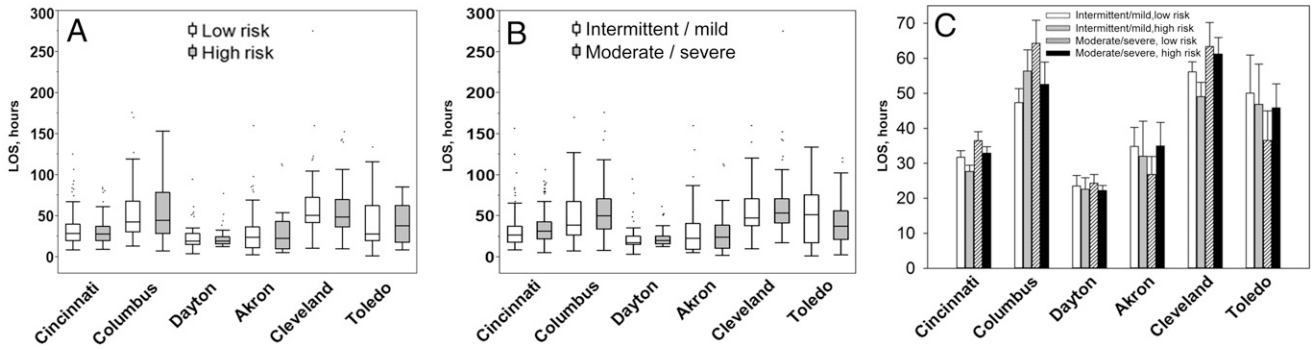

FIGURE 4

Asthma severity classification, asthma risk, and LOS. After accounting for variability between the sites, LOS did not vary with respect to asthma severity classification (P = .05), asthma risk (P = .70), or a combination of the 2 (P > .15 for all categories compared with moderate/severe, high risk).

Downloaded from pediatrics.aappublications.org at University of Liverpool Library on February 20, 2015

managed, and treated, the 2010 Patient Protection and Affordable Care Act recommends that research evaluate patient-centered outcomes and heterogeneous treatment effects as key components of comparative effectiveness research (CER), including differences in patient characteristics and models of health care delivery.[20,21] Traditional observational CER studies usually rely on administrative data that lack important clinical information, types of health care interventions, and rationale used in health care decision-making.[22] Enhanced patient registries that link administrative, clinical, and prospective patient data, such as OPAR, provide unparalleled opportunities for observational CER studies to describe standard care and to identify clinically relevant comparators.[22] Electronic medical records provide the optimal environment to develop rigorous CER studies based on these enhanced registries, allowing study designs and analytical approaches that reduce confounding and selection bias.[22]

OPAR has some limitations and challenges. Potential selection bias due to recruitment variation across the sites was minimized by conducting training visits and having broad inclusion criteria. As in many observational studies, the associations observed cannot be interpreted as causation.[23] Recall of baseline asthma severity may be impacted by the severity of the current exacerbation, although each baseline symptom question was qualified by the statement "not including the days leading up to this hospitalization." Baseline severity also could have been affected by asthma medication use before hospitalization. The exposure data may be underestimated by the LAR, especially for SHS where there is known underreporting in the inpatient setting.[24] This was minimized by using a 4-question panel that provides a comprehensive account of SHS.[11] Lastly, the current OPAR infrastructure does not take full advantage of technology and the electronic medical record due to the high cost and a lack of availability of clinical data in electronic form at all sites, but we continue to develop methodologies to work toward automated data collection.

FUTURE DIRECTIONS

OPAR continues to recruit and as of September 23, 2014, includes 2608 unique children ranging from 176 to 795 individuals at each site. Current ongoing and future analyses will compare ED, inpatient, and discharge practices, along with patient demographics, exposures, and asthma severity with respect to LOS, reutilization, and readmission rates to determine the practices that lead to the best clinical outcomes across all hospitals. Efforts will also be made to determine if personalized or phenotype directed practices improve outcomes. In the future, OPAR will enable the best practices identified from our CER studies to be implemented and tested in intervention trials across the sites. The collection of biologic samples including hair, serum, urine, saliva, and nasal epithelial cells has begun at CCHMC and are planned at the other sites. These samples will be quantified for environmental exposures, stress measures, immune profiles, and genomic variation and analyzed with respect to site heterogeneity, LOS, and admission patterns and rates.

CONCLUSIONS

OPAR is a valuable and unprecedented resource in which to conduct observational, comparative effectiveness, and intervention studies for pediatric asthma. Data collected thus far reveal significant variability in the patient demographic served and in hospital practices for the treatment and management of pediatric asthma. These data will better define asthma phenotypes, identify best care practices while avoiding unnecessary variation in care practices, as well as inform personalized care plans to reduce reutilization and readmission for asthma.

ACKNOWLEDGMENTS

We thank the staff at each of the participating sites who helped recruit the patients for this study, as well as the participants and their families.

Dr McCoy contributed to the conception and design of the study, oversaw subject recruitment at the Columbus site, and reviewed and revised the manuscript; Dr Forbis contributed to the conception and design of the study, oversaw subject recruitment at the Dayton site, and reviewed and revised the manuscript; Dr McBride contributed to the conception and design of the study, oversaw subject recruitment at the Akron site, and reviewed and revised the manuscript; Dr Ross contributed to the conception and design of the study, oversaw subject recruitment at the Cleveland site, and reviewed and revised the manuscript; Dr Vauthy contributed to the conception and design of the study, oversaw subject recruitment at the Toledo site, and reviewed and revised the manuscript; Dr Khurana Hershey conceived the study, oversaw its design, implementation, and acquisition of data at all 6 sites, oversaw data analyses and interpreted the analyses, and reviewed and revised the manuscript; and all authors approved the final manuscript as submitted.

www.pediatrics.org/cgi/doi/10.1542/peds.2014-2230

DOI: 10.1542/peds.2014-2230

Accepted for publication Nov 13, 2014

Address correspondence to Gurjit K. Khurana Hershey, MD, PhD, Division of Asthma Research, Cincinnati Children's Hospital Medical Center, 3333 Burnet Ave, Cincinnati, OH 45229. E-mail: gurjit.hershey@cchmc.org

Downloaded from pediatrics.aappublications.org at University of Liverpool Library on February 20, 2015

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

Copyright © 2015 by the American Academy of Pediatrics

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: Supported by The Ohio Department of Job and Family Services grant number G-1 213-07-0561.

POTENTIAL CONFLICT OF INTEREST: Dr Kercsmar reports personal fees from GSK, outside the submitted work; Dr Guilbert reports grants and personal fees from Teva, personal fees from GSK and Regeneron Pharmaceuticals, grants from Abbott Laboratories, Array BioPharma, Mylan, Forest Research Institute, F. Hoffmann-La Roche, Medimmune, KaloBios Pharmaceuticals, Vertex Pharmaceuticals, Roxane Laboratories and CompleWare Corporation, CF Foundation Therapeutics, and Roche/Genentech, outside the submitted work; the other authors have indicated they have no potential conflicts of interest to disclose.

REFERENCES

1. Centers for Disease Control and Prevention. Vital signs. Asthma in the US: growing every year. May 2011. Available at: http://www.cdc.gov/VitalSigns/Asthma/. Accessed November 25, 2014
2. Akinbami L; Centers for Disease Control and Prevention National Center for Health Statistics. The state of childhood asthma, United States, 1980–2005. *Adv Data*. 2006;(381):1–24
3. American Lung Association. Asthma & Children Fact Sheet. Chicago, IL: American Lung Association; October 2012
4. Ohio Department of Health Asthma Program; Ohio Surveillance System for Asthma. *Burden of Asthma in Ohio, 2012*. Columbus, OH: Ohio Department of Health Asthma Program; 2012
5. Sly RM. Changing prevalence of allergic rhinitis and asthma. *Ann Allergy Asthma Immunol*. 1999;82(3):233–248, quiz 248–252
6. Martinez FD, Wright AL, Taussig LM, Holberg CJ, Halonen M, Morgan WJ; The Group Health Medical Associates. Asthma and wheezing in the first six years of life. *N Engl J Med*. 1995;332(3):133–138
7. Drazen JM, Silverman EK, Lee TH. Heterogeneity of therapeutic responses in asthma. *Br Med Bull*. 2000;56(4):1054–1070
8. Fassl BA, Nkoy FL, Stone BL, et al. The Joint Commission Children's Asthma Care quality measures and asthma readmissions. *Pediatrics*. 2012;130(3):482–491
9. Reddel H, Ware S, Marks G, Salome C, Jenkins C, Woolcock A. Differences between asthma exacerbations and poor asthma control. *Lancet*. 1999;353(9150):364–369
10. Butsch Kovacic M, Biagini Myers JM, Lindsey M, et al. The Greater Cincinnati Pediatric Clinic Repository: A Novel Framework for Childhood Asthma and Allergy Research. *Pediatr Allergy Immunol Pulmonol*. 2012;25(2):104–113
11. Biagini Myers JM, Khurana Hershey GK, Deka R, et al. Asking the right questions to ascertain early childhood secondhand smoke exposures. *J Pediatr*. 2012;160(6):1050–1051
12. National Asthma Education and Prevention Program; National Heart, Lung, and Blood Institute. *Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma. NIH Publication No. 07-4051*. Bethesda, MD: National Institutes of Health, National Heart, Lung, and Blood Institute; 2007
13. Cohen ME, Dimick JB, Bilimoria KY, Ko CY, Richards K, Hall BL. Risk adjustment in the American College of Surgeons National Surgical Quality Improvement Program: a comparison of logistic versus hierarchical modeling. *J Am Coll Surg*. 2009;209(6):687–693
14. Bishaw A. Areas with concentrated poverty: 2006–2010. US Department of Commerce. Economics and Statistics Administration. 2011. Available at: www.census.gov/prod/2011pubs/acsbr10-17.pdf. Accessed November 25, 2014
15. Kinsman L, Rotter T, James E, Snow P, Willis J. What is a clinical pathway? Development of a definition to inform the debate. *BMC Med*. 2010;8:31
16. Sylvester AM, George M. Effect of a Clinical Pathway on Length of Stay and Cost of Pediatric Inpatient Asthma Admissions: An Integrative Review. *Clin Nurs Res*. 2013;23(4):384–401
17. Banasiak NC, Meadows-Oliver M. Inpatient asthma clinical pathways for the pediatric patient: an integrative review of the literature. *Pediatr Nurs*. 2004;30(6):447–450
18. McCarthy D, Cohen A, Bihrle Johnson M. *Gaining Ground: Care Management Programs to Reduce Hospital Admissions and Readmissions Among Chronically Ill and Vulnerable Patients*. New York, NY: The Commonwealth Fund; January 2013
19. Bhogal S, Bourbeau J, McGillivray D, Benedetti A, Bartlett S, Ducharme F. Adherence to pediatric asthma guidelines in the emergency department: a survey of knowledge, attitudes and behaviour among health care professionals. *Can Respir J*. 2010;17(4):175–182
20. Public Law No. 111-148: H.R. 3590. The Patient Protection and Affordable Care Act. March 23, 2010
21. Manchikanti L, Caraway DL, Parr AT, Fellows B, Hirsch JA. Patient Protection and Affordable Care Act of 2010: reforming the health care reform for the new decade. *Pain Physician*. 2011;14(1):E35–E67
22. Krishnan JA, Schatz M, Apter AJ. A call for action: Comparative effectiveness research in asthma. *J Allergy Clin Immunol*. 2011;127(1):123–127
23. Hernán MA, Robins JM. Estimating causal effects from epidemiological data. *J Epidemiol Community Health*. 2006;60(7):578–586
24. Howrylak JA, Spanier AJ, Huang B, et al. Cotinine in children admitted for asthma and readmission. *Pediatrics*. 2014;133(2). Available at: www.pediatrics.org/cgi/content/full/133/2/e355

Downloaded from pediatrics.aappublications.org at University of Liverpool Library on February 20, 2015

Heterogeneity in Asthma Care in a Statewide Collaborative: the Ohio Pediatric Asthma Repository

Jocelyn M. Biagini Myers, Jeffrey M. Simmons, Carolyn M. Kercsmar, Lisa J. Martin, Valentina V. Pilipenko, Stephen R. Austin, Mark A. Lindsey, Katharine M. Amalfitano, Theresa W. Guilbert, Karen S. McCoy, Shalini G. Forbis, John T. McBride, Kristie R. Ross, Pierre A. Vauthy and Gurjit K. Khurana Hershey

Pediatrics 2015;135;271; originally published online January 19, 2015;
DOI: 10.1542/peds.2014-2230

Updated Information & Services	including high resolution figures, can be found at: http://pediatrics.aappublications.org/content/135/2/271.full.html
Supplementary Material	Supplementary material can be found at: http://pediatrics.aappublications.org/content/suppl/2015/01/13/peds.2014-2230.DCSupplemental.html
References	This article cites 17 articles, 4 of which can be accessed free at: http://pediatrics.aappublications.org/content/135/2/271.full.html#ref-list-1
Subspecialty Collections	This article, along with others on similar topics, appears in the following collection(s): **Health Briefs** http://pediatrics.aappublications.org/cgi/collection/health_briefs
Permissions & Licensing	Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at: http://pediatrics.aappublications.org/site/misc/Permissions.xhtml
Reprints	Information about ordering reprints can be found online: http://pediatrics.aappublications.org/site/misc/reprints.xhtml

PEDIATRICS is the official journal of the American Academy of Pediatrics. A monthly publication, it has been published continuously since 1948. PEDIATRICS is owned, published, and trademarked by the American Academy of Pediatrics, 141 Northwest Point Boulevard, Elk Grove Village, Illinois, 60007. Copyright © 2015 by the American Academy of Pediatrics. All rights reserved. Print ISSN: 0031-4005. Online ISSN: 1098-4275.

American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN™

Downloaded from pediatrics.aappublications.org at University of Liverpool Library on February 20, 2015

PEDIATRICS®
OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Heterogeneity in Asthma Care in a Statewide Collaborative: the Ohio Pediatric Asthma Repository

Jocelyn M. Biagini Myers, Jeffrey M. Simmons, Carolyn M. Kercsmar, Lisa J. Martin, Valentina V. Pilipenko, Stephen R. Austin, Mark A. Lindsey, Katharine M. Amalfitano, Theresa W. Guilbert, Karen S. McCoy, Shalini G. Forbis, John T. McBride, Kristie R. Ross, Pierre A. Vauthy and Gurjit K. Khurana Hershey

Pediatrics 2015;135;271; originally published online January 19, 2015;
DOI: 10.1542/peds.2014-2230

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://pediatrics.aappublications.org/content/135/2/271.full.html

PEDIATRICS is the official journal of the American Academy of Pediatrics. A monthly publication, it has been published continuously since 1948. PEDIATRICS is owned, published, and trademarked by the American Academy of Pediatrics, 141 Northwest Point Boulevard, Elk Grove Village, Illinois, 60007. Copyright © 2015 by the American Academy of Pediatrics. All rights reserved. Print ISSN: 0031-4005. Online ISSN: 1098-4275.

American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN™

Downloaded from pediatrics.aappublications.org at University of Liverpool Library on February 20, 2015

Supplemental Information

QUESTIONNAIRE DATA COLLECTION

The questionnaires collect demographic information, asthma symptom history, severity, triggers, activity limitations and night awakenings, health care utilization for wheeze/asthma, medication adherence, environmental and food allergies, skin symptoms, family allergic disease history, and environmental exposures. Questions regarding asthma and allergy symptoms were adapted from the International Study of Allergies and Asthma in Children Questionnaire.[11] Components for the classification of asthma severity were adapted from the EPR-3 (see statistical analyses section below).[12] To compare neighborhood demographics, the participant's primary address was geo-coded by using ArcGIS software (Esri, Redlands, CA) and census tract-level estimates were obtained from the 2007–2011 American Community Survey 3-Year Estimates (www.census.gov).

DATA VALIDATION AND FLOW

For collection and management of data collected as part of OPAR, we deployed a custom-built Web application, which stores study data in a secure MySQL database. Study staff uses this application to track enrollment, assign study IDs, enter study data, and print and upload study documents. Questionnaires completed by participants are processed at the CCHMC coordinating center by using TeleForm (Cardiff Software, Inc, Vista, CA), using a 2-stage verification process. Data from OPAR encounter reports are securely entered into the OPAR database by using the enrollment tracking Web application. Upon entry, data are validated and any errors or discrepant data are clarified by the coordinating center or the participating sites. After clarification, the cleaned data are then used for reporting, statistical analysis, and data sharing as outlined in Fig 1.

DATA REPORTING AND SHARING PROCESS

OPAR has implemented multiple custom-built Web-based dynamic reporting and data sharing tools to visualize and query the data. These tools allow authorized users to fluidly navigate a collection of dichotomized charts and heat maps dynamically generated from cleaned data. To allow participating sites to perform complex queries on their own data, the CCHMC Division of Biomedical Informatics deployed an instance of i2b2. The Web-based i2b2 workbench allows sites to build queries against their site's data by selecting terms from a graphical ontology, providing functionality for cohort identification to each site.