

Journal Pre-proof

“Real world assessment of asthma control and severity in children, adolescents, and adults with asthma: Relationships to care settings and co-morbidities”

Sharmilee M. Nyenhuis, MD FAAAAI, Esra Akkoyun, MD, Li Liu, PhD, Michael Schatz, MD FAAAAI, Thomas B. Casale, MD FAAAAI



PII: S2213-2198(19)30923-7

DOI: <https://doi.org/10.1016/j.jaip.2019.10.032>

Reference: JAIP 2527

To appear in: *The Journal of Allergy and Clinical Immunology: In Practice*

Received Date: 13 June 2019

Revised Date: 17 October 2019

Accepted Date: 18 October 2019

Please cite this article as: Nyenhuis SM, Akkoyun E, Liu L, Schatz M, Casale TB, “Real world assessment of asthma control and severity in children, adolescents, and adults with asthma: Relationships to care settings and co-morbidities”, *The Journal of Allergy and Clinical Immunology: In Practice* (2019), doi: <https://doi.org/10.1016/j.jaip.2019.10.032>.

This is a PDF file of an article that has undergone enhancements after acceptance, such as the addition of a cover page and metadata, and formatting for readability, but it is not yet the definitive version of record. This version will undergo additional copyediting, typesetting and review before it is published in its final form, but we are providing this version to give early visibility of the article. Please note that, during the production process, errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

© 2019 Published by Elsevier Inc. on behalf of the American Academy of Allergy, Asthma & Immunology

Title: “Real world assessment of asthma control and severity in children, adolescents, and adults with asthma: Relationships to care settings and co-morbidities”

Sharmilee M. Nyenhuis MD FAAAAI^{1,2}, Esra Akkoyun MD¹, Li Liu PhD³, Michael Schatz MD FAAAAI⁴, Thomas B. Casale MD FAAAAI⁵

Affiliations:

¹Division of Pulmonary, Critical Care, Sleep and Allergy, Department of Medicine, University of Illinois at Chicago, Chicago, IL, USA

²Center for Dissemination and Implementation Science, Department of Medicine, University of Illinois at Chicago, Chicago, IL, USA

³Division of Epidemiology and Biostatistics, School of Public Health, University of Illinois at Chicago, Chicago, IL, USA

⁴Kaiser Permanente, San Diego, CA

⁵University of South Florida, Tampa, FL

Corresponding Author: Sharmilee M. Nyenhuis, MD FAAAAI
Associate Professor of Medicine and Director of Allergy/Asthma/Immunology Program
Division of Pulmonary, Critical Care, Sleep and Allergy
Center for Dissemination and Implementation Science
University of Illinois at Chicago
840 S. Wood St. MC 719
Chicago, IL 60612
snyenhui@uic.edu
312-413-1655

Word Count: 3435

Key words: Asthma, Comorbidity, Practice Guideline, Medical Decision Making, Computer-Assisted

Funding: Asthma IQ was funded in part from a grant awarded to American Academy of Allergy, Asthma and Immunology (AAAAI) by Novartis, Inc. and Genentech. We would also like to acknowledge support from University of Illinois at Chicago (UIC) Center for Clinical and Translational Science (CCTS), Award Number KL2RR029878 from the National Center for Research Resources and NHLBI K01HL133370 (awarded to SN). The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Center for Research Resources or the National Institutes of Health.

Conflict of Interest Statement: The authors have no conflicts related to the content of this manuscript.

Abstract:

Background: Little is known about how patient-level factors and care settings relate to asthma outcomes in real-world settings.

Objective: We therefore examined the rates and relative contributions of co-morbidities and care settings in terms of asthma severity and control among pediatric and adolescent/adult patients in a large national sample.

Methods: We examined de-identified patient data from 28,508 unique encounters documented in the Asthma IQ database, obtaining patient level factors (demographics, asthma characteristics, co-morbidities), care setting (primary care physician [PCP] versus specialist physician [Allergist or Pulmonologist]), and guideline-defined levels of asthma control/severity. Rates of co-morbidities were identified by asthma severity and control and by care setting. We calculated odds ratios (ORs) for asthma control and severity based on each co-morbidity.

Results: Baseline demographic data indicated that patients seen by specialists versus PCPs, were older, and had more severe and poorly controlled asthma ($p<0.05$). Patients cared for by specialists also had more comorbid conditions, including gastroesophageal reflux disease (GERD; $p<0.01$), rhinosinusitis ($p<0.01$) and obstructive sleep apnea (OSA; Adolescents/Adults only: $p<0.01$). GERD, smoke exposure, depression (adolescents/adults), rhinosinusitis (children) and African American race, were associated with uncontrolled asthma. Smoke exposure (children), rhinosinsitis, and African American race, were associated with severe disease.

Conclusions: We identified several demographics and co-morbidities that are independently associated with the specialist care setting, persistent asthma and poor asthma control. Awareness of these relationships may be helpful for clinicians caring for asthma patients.

69

70 **Highlights Box:**

- 71 • What is already known about this topic? Patient-level factors and care settings
72 impact asthma outcomes but evidence is lacking in a real world setting.
- 73 • What does this article add to our knowledge? We have confirmed the association of
74 specific demographic and co-morbid conditions associated with uncontrolled asthma
75 and greater asthma severity in a real world population.
- 76 • How does this study impact current management guidelines? An understanding of
77 these associations in a real world population will help clinicians manage their patients
78 with asthma and aid in the development of interventions that target the co-morbidities
79 associated with greater asthma severity and poor asthma control.

Abbreviations**ACT:** Asthma Control Test**ANOVA:** Analysis of Variance models**Asthma IQ:** Asthma Specialist Tool to Help Manage Asthma and Improve Quality**BMI:** Body Mass Index**CI:** Confidence Interval**FVC:** Forced Vital Capacity**FEV₁:** Forced Expiratory Volume in 1 second**FeNO:** Fractional exhaled nitric oxide**GERD:** Gastroesophageal Reflux Disease**OR:** Odds ratio**OSA:** Obstructive Sleep Apnea**PCP:** primary care physicians

Background

Asthma is a common chronic disease that affects approximately 26.5 million Americans.¹ The disease has a significant impact on the quality of life (QOL) of those afflicted and on their caregivers.² In the United States, an estimated 12.6 million Americans had at least one asthma exacerbation in 2016; children with asthma missed over 13 million school days in 2013.¹ The yearly cost of asthma in the United States is estimated at over \$50 billion.¹ Much of the morbidity associated with asthma is due to inadequate asthma control and severe disease.

Asthma is managed by both primary care physicians (PCPs) and specialty physicians (Allergists, Pulmonologists), although most patients with asthma are seen in primary care settings. There is evidence to suggest that patients treated by specialty physicians report greater improvements in asthma control and a reduction in asthma exacerbations.³⁻⁴ Practice differences between PCPs and asthma specialists that may relate to outcomes of care have been identified. This includes specialty physicians' additional training and self-reported expertise in treating asthma have been found to contribute to better patient-reported care and outcomes.⁵ Further, adherence to the national asthma guidelines may also be a factor; a recent study by Cloutier and colleagues found greater adherence to the national asthma guidelines by specialty physicians compared to PCPs.⁶ It is important to investigate the knowledge, attitudes, and practices of PCPs with regard to asthma care.⁷ Referral to specialists or modifying the approach to asthma care by PCPs may improve the degree to which the care of patients with asthma is consistent with the national guidelines.⁸ No study to date has examined the patient-level factors that might contribute to the outcomes differences found among primary care and specialist physicians in a real-world setting and using guideline-defined tools.

To better understand the differences in patients cared for by PCPs and by specialists in a real-world setting, we utilized the Asthma IQ (Asthma Specialist Tool to Help Manage

Asthma and Improve Quality). Asthma IQ is a web-based tool (www.asthmaiq.org) to help primary care providers and asthma specialists track and manage patients with asthma. It not only collects and stores de-identified patient data such as the Asthma Control Test, spirometry values, medications, and other medical conditions, but provides a guideline-derived assessment of the patient's asthma severity and control level in a real-world setting. We examined individual patient records from the Asthma IQ database and compared demographic information, rates of common co-morbidities associated with worse asthma, and asthma severity and control, among pediatric and adolescent/adult patients of specialists versus patients of primary care physicians. Additionally, we evaluated the relationships between co-morbidities and uncontrolled and more severe asthma in these patients.

Methods

Asthma IQ was developed by the American Academy of Allergy, Asthma and Immunology (AAAAI) as a unique, comprehensive and easy-to-use tool for clinicians who treat asthma patients. The Web-based Asthma IQ helps clinicians to: 1. Use evidence-based medicine to make treatment decisions; 2. Graph and report patients' asthma status over time; 3. Analyze statistics for the asthma patients in their practice; and 4. Report quality improvement measures for Pay for Performance and Maintenance of Certification (MOC). Ultimately, the goal of the Asthma IQ program is to provide quality care for asthma patients by helping clinicians learn and apply the key components of the NAEPP Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma (EPR-3) (1) with patients in everyday practice to improve the quality of asthma care. The AAAAI also developed a primary care version of the Asthma IQ program in conjunction with the American Academy of Family Physicians and the AAFP National Research Network. The Asthma IQ database is not publicly available and the researchers obtained access to the data by written request to

the AAAAI. This study was deemed not to require informed consent or formal IRB approval by an Institutional Review Board as all data accessed and analyzed was de-identified.

The Asthma IQ database contained 43,537 encounters from 28,508 unique patients from March 2008 to March 2017 (See Online Repository Figure E1). Only data from the first encounter was used analysis. Pediatric patients included those <12 years old and adolescent/adult patients included those ≥ 12 years old. Data entered by providers included current asthma status (asthma control test–ACT, current exacerbation, taking long-term controller medication), asthma history (history of medication use, medication side effects, past exacerbations, tobacco smoke exposure, family history of allergic diseases), vital signs, asthma tests (spirometry: Forced Vital Capacity–FVC; Forced Expiratory Volume in 1 second–FEV₁, peak flow; immunoglobulin E, and fractional exhaled nitric oxide–FeNO) and co-morbidities evaluated (rhinosinusitis [RS], obesity, obstructive sleep apnea [OSA], gastroesophageal reflux disease [GERD, and depression]). Operationalized definitions of guideline-derived asthma control and severity in the Asthma IQ database were taken directly from the EPR-3 guidelines for every age group. As suggested by the guidelines, severity was assessed in patients not currently on controller medication, and control was assessed for patients on controllers. The Asthma Control Test, a five question validated tool with scores ranging from 5-25, with higher scores indicating better control, was included in the assessment.⁹ Continuous variables are presented as mean $\pm$ standard deviation, whereas categorical variables are presented as frequency and percent.

Guideline asthma control was separated into three categories: very poorly controlled, not well controlled. and well controlled. Guideline asthma severity was categorized into intermittent, and persistent (mild, moderate, severe).

In bivariate analyses, Chi-square tests were performed to examine associations between ordinal outcomes (guideline-derived control or severity), and categorical predictors such as co-morbidities, race, and healthcare provider. T-tests (for dichotomized outcomes) and

Analysis of Variance models (ANOVA), were employed to examine the association between the ordinal outcome variables and continuous predictors.

The rates of co-morbidities were compared across categories of guideline asthma control or guideline asthma severity by multivariate logistic regression models for ordinal outcomes, controlling for demographic variables. Backward elimination method of model selection was used. Proportional odds assumption was evaluated for all multivariate logistic ordinal models. No evidence of model assumption violation was found. All statistical tests were 2-sided tests controlling for Type I error probability of 0.05. SAS® 9.4 (SAS Inc., Cary, NC) was used for all analyses; $p < 0.05$ was used to indicate statistical significance.

Results

Patient Characteristics

Pediatric patients

We analyzed 13,479 pediatric patients entered into the Asthma IQ database by primary care physicians (PCPs) ($n = 7505$) and asthma specialists ($n = 5974$) (Table 1). Children seen by asthma specialists were older compared to those seen by PCPs (7.0 ± 2.7 vs. 6.1 ± 2.9 , $p < 0.01$). PCPs cared for a larger proportion of Hispanic/Latino patients than asthma specialists ($p < 0.01$). We found no difference in FEV₁% predicted and ACT in children cared for by PCPs vs. asthma specialists (Table 1). Differences were found in smoking status, with higher rates of passive smoke exposure in those cared for by PCPs (14.97% vs. 10.01%, $p < 0.01$).

Data were available for asthma severity in 2661 children (PCP group: $n=1387$, Specialist group: $n=1274$), and asthma control in 5477 children (PCP group: $n=2037$, Specialist group: $n=3440$). Children cared for by asthma specialists were more likely to have severe persistent asthma, and poorly controlled asthma, compared to those seen by PCPs (10.5% vs 3.8%; 10.0% vs. 7.3%, $p < 0.01$; Table 1). Asthma Control Test score was positively associated with

the level of guideline-derived asthma control in all children regardless of the provider type (p<0.001; Figure 1). Differences in the prevalence of co-morbid conditions were also found based on care setting. Children seen by specialists had a greater prevalence of GERD (4.7% vs. 2.4%, p<0.01) and rhinosinusitis (46.5% vs. 19.3%, p<0.01; Table 1).

Adolescent and adult patients

We analyzed 15,029 adolescent and adult patients entered into the Asthma IQ database. Of these adolescents and adults, 3530 were seen by PCPs, and 11,499 were seen by specialists (Table 2). Adolescent and adult patients who were seen by PCPs were on average 15 years younger than patients seen by specialists (24.3±18 vs. 39.1±19.9, p<0.01). The majority of adolescents and adults were white, but PCPs saw a more racially and ethnically diverse patient population with greater number of Hispanic/Latino and African American patients compared to asthma specialists (Hispanic/Latino: 19.5% vs. 8.8%, African American: 17.2% vs. 11.7%, p<0.01). Patients in both groups were overweight and had similar FEV₁% predicted and ACT scores.

Data were available for 1) asthma severity, in 3088 adolescents and adults (PCP group: n=878, Specialist group: n=2210), and 2) asthma control, in 7740 adolescents and adults (PCP group: n=1290, Specialist group: n=6450). Compared to PCPs, asthma specialists cared for a greater percentage of patients with severe persistent asthma (17.0% vs. 6.0%, p<0.01) and poorly controlled asthma (12.3% vs. 10.3%, p<0.01) (Table 2). PCPs overwhelmingly cared for patients with intermittent asthma, while asthma specialists cared for an equal mix of intermittent and persistent asthma patients (p<0.01). Specialists cared for twice as many patients with moderate and severe persistent asthma than PCPs (Moderate: 21.0% vs. 10.6%, Severe: 17.0% vs. 6.0%, p<0.01). Similar to the pediatric population, the ACT score was positively associated with the level of asthma control in adolescents and adults (p<0.01; Figure 2). Differences were found in tobacco smoke exposure between patients seen by PCPs and asthma specialists, with over twice the rate of passive smoke

exposure in those cared for by PCPs (9.11% vs. 4.08%, $p<0.01$). Adolescents and adults cared for by specialists had higher rates of co-morbid conditions including GERD (14.8% vs. 4.8%, $p<0.01$), rhinosinusitis (44.8% vs. 22.0% $p<0.01$) and OSA (2.5% vs. 1.3% $p<0.01$; Table 2).

Characteristics and co-morbidities associated with asthma control and severity

Pediatric patients (Table 3)

African American race (OR=1.41 95% CI 1.19-1.67, $p<0.01$), GERD (OR=1.36 95% CI 1.02-1.81, $p=0.04$), OSA (OR=2.23 95% CI 1.23-4.03, $p=0.01$), rhinosinusitis OR=1.15 95% CI 1.01-1.31, $p=0.04$), tobacco smoke exposure (OR=1.37 95% CI 1.12-1.68, $p<0.01$) and seen by a specialist (OR=1.28 95% CI 1.11-1.48, $p<0.01$) were associated with uncontrolled asthma. African American race (OR=1.50 95% CI 1.17-1.93, $p<0.01$), rhinosinusitis (OR=1.28 95% CI 1.07-1.53, $p<0.01$), tobacco smoke exposure (OR=1.62 95% CI 1.23-2.13, $p<0.01$) and seen by a specialist (OR=3.03 95% CI 2.51-3.65, $p<0.01$) were associated with greater guideline-derived asthma severity.

Adolescent and Adult patients (Table 4)

Adolescent and adult patients who were African American (OR=2.22 95% CI 1.85-2.65, $p<0.01$), older (OR=1.01 95% CI 1.01-1.02, $p<0.01$), had a high BMI (OR=1.02 95% CI 1.01-1.03, $p<0.01$), GERD (OR=1.20 95% CI 1.02-1.40, $p<0.05$), depression (OR=1.48 95% CI 1.07-2.05, $p=0.02$), or were current smokers (OR=1.81 95% CI 1.29-2.56, $p=0.05$), were associated with uncontrolled asthma. When compared to white patients, African American patients (OR=1.65 95% CI 1.28-2.14, $p<0.001$) patients were more likely to have guideline-derived severe asthma. Hispanic patients (OR=0.80 95% CI 0.59-1.08) were less likely to have guideline-derived severe asthma compared to their white counterparts but the finding was not statistically significant. Seeing a specialist provider and having rhinosinusitis were also with greater guideline-derived asthma severity in our model (OR=2.16 95% CI 1.73-2.70, $p<0.01$; OR=1.31 95% CI 1.09-1.58, $p=0.004$).

Discussion

This is the first cross-sectional study to date that examined patient characteristics that may contribute to outcomes differences found among primary care and specialist physicians (Allergists and Pulmonologists) in a real-world setting. We found that patients seen by specialists were different in several important ways. One of the main differences was that asthma patients cared for by asthma specialists had more severe disease and uncontrolled asthma; they were also more likely to have co-morbid conditions such as rhinosinusitis, GERD, and OSA, as compared to patients cared for by PCPs. Common co-morbidities (GERD, smoke exposure, depression, rhinosinusitis), and African American race were associated with uncontrolled asthma, while smoke exposure, BMI, rhinosinusitis and African American race were associated with severe disease. Taken as a whole, these findings indicate that primary care and specialist physicians care for different segments of the asthma population. These differences should be taken into consideration to understand variations in practice patterns and outcomes.

Our results add to a growing body of literature examining differences in asthma care among PCPs and specialists. In this study, we examined differences in characteristics of patients cared for by these two groups of physicians. We used data collected from a unique database (Asthma IQ database) of both primary care and specialist providers, from across the United States (Online Respository Figure E2). Previous work in this area has looked at differences only within a specific healthcare organization or geographic location.¹⁰⁻¹²

We found an increase in asthma severity and poorer asthma control in patients cared for by asthma specialists, which is likely due to several factors. One important factor is that national asthma guidelines recommend referral of patients with more severe disease to specialists.¹³ A recent study conducted by Price and colleagues assessed national and international asthma guidelines for specialist referral recommendations. Four common themes emerged

in all the guidelines regarding when to consider specialist referral: 1) diagnostic uncertainty, 2) asthma severity and high-risk patients, 3) use of corticosteroid treatment (high doses, long-term use and side effects), and 4) the use of add-on specialist therapy (biologics).¹⁴

Asthma severity and high-risk patients as indications for referral to a specialist are in line with our findings. Other studies examining patients seen by asthma specialists have found similar findings of greater disease severity.^{15,16} One could also speculate from our findings that care provided by specialists is inferior to that provided by PCPs, resulting in more uncontrolled asthma. Unfortunately, we were not able to determine if patients entered by physicians into the Asthma IQ database were established or new patients and therefore cannot evaluate the quality of care provided by specialists. In our patients, we saw some demographic differences between patients that were seen by specialists. In both age groups, the patients were older, which is consistent with previous studies of patients with more severe disease.¹⁵ Patients seen by specialists in both the child and adolescent/adult populations, were more likely to be white. This is similar to previous studies that specialty care was lower among minorities.¹⁷⁻¹⁸

While other studies have characterized patients seen by specialists, none used a guideline-derived tool as was done in this study.¹⁶ Previous studies used physician report to determine asthma control and severity.¹⁹ This may be due to the low adoption of asthma assessment tools in the clinical setting by both primary care and asthma specialist physicians.⁶ As physicians were required to use our Asthma IQ tool as a part of their MOC and used the asthma guidelines to determine patient asthma control and severity, our results may provide a better estimate of the characteristics of asthma patients as seen in the real world. Previous studies show that an integrated and structured diagnostic and therapeutic management protocol consistent with the recommendations of GINA international guidelines and supported by new technologies significantly reduces the impact of asthma and improves QOL.⁵ As longitudinal data were not assessed in this study, it is difficult to know if the

guidelines-derived assessment of asthma control and severity in the Asthma IQ program impacts asthma outcomes.

In our study, we found the control level to be strongly associated with the Asthma Control Test (ACT), which is a validated questionnaire used to assess asthma control.²⁰ In a clinical setting, the ACT is a useful tool to help physicians identify patients with uncontrolled asthma and facilitate their ability to follow patients' progress with treatment.²¹ A recent study of over 1500 primary care and asthma specialists found that more than half utilized these tools either sometimes or never.⁶ While we found use of this tool to be closely associated with asthma control, studies that focus on the implementation of the regular use of these tools by physicians are needed.

One major component of the NAEPP asthma guidelines is a focus on identifying and treating co-morbid conditions known to affect asthma control, such as OSA, obesity, depression, tobacco exposure, GERD, and rhinitis.¹³ In our pediatric population, we found GERD, OSA, rhinosinusitis and tobacco smoke exposure were associated with uncontrolled asthma. Similarly, in adolescents and adults, GERD and current tobacco use were associated with uncontrolled asthma, along with older age, high BMI, and depression. Fewer data were available on the presence of depression in our pediatric cohort, which may account for the lack of association of depression on asthma control. Our findings confirm previous studies that have shown uncontrolled asthma is negatively associated with GERD, OSA, BMI, rhinosinusitis, tobacco exposure, and depression. Obesity is a major risk factor for the development of GERD and OSA²². We also examined if this held true in our real-world dataset and found a close association between BMI with GERD and OSA in adolescents and adults (data not shown).

Many of the co-morbid conditions associated with asthma control were also associated with asthma severity, including tobacco smoke exposure (children only) and rhinosinusitis

(children only). Our findings of increased asthma severity in those children exposed to tobacco smoke are consistent with the findings of several studies examining this association.²³ In our study, rhinosinusitis was more prevalent in patients seeing a specialist and was associated with increased asthma severity and uncontrolled asthma. Several studies have demonstrated the association of rhinosinusitis with greater asthma severity and poor asthma control.²⁴⁻²⁵ Effective interventions that target reduction of tobacco smoke exposure and identify and treat rhinosinusitis in children should be supported and implemented.²⁶ It is not clear why some of the co-morbid conditions (GERD, OSA, depression) associated with poor asthma control were not associated with asthma severity. The components of asthma control are mostly symptom based, and the co-morbid conditions of GERD, OSA, BMI and depression may be more closely associated with asthma symptoms but not asthma severity (exacerbations, lung function). Further, we utilized a guideline-based severity tool which may be more sensitive in determining asthma severity. Additional studies are needed to identify the reasons for this lack of association with asthma severity.

African American race in both children and adolescents/adults was associated with greater asthma severity, confirming previous reports.²⁷ The reasons for the greater severity in African Americans are varied and occur at levels ranging from individuals, institutions, communities, and a broader sociopolitical context.²⁸ Interestingly, Hispanic/Latino ethnicity was not associated with greater asthma severity in children and was associated with lower asthma severity in adolescents and adults. Hispanics/Latinos are frequently studied as one group, when in fact they are a heterogeneous population. Rates and severity of asthma are very different among the Hispanic/Latino population, with lower rates and less severe asthma found in Mexicans and Argentinians and some of the highest rates and greater asthma severity found in Puerto Ricans and Cubans.²⁹ Our study did not account for these variations within the Hispanic/Latino population, and this may account for the less severe asthma we found in adolescents and adults and the lack of association of asthma severity in

Hispanic/Latino children.

There are some potential limitations of our findings. The information for this database was entered by individual physicians and therefore information about the patient's asthma and co-morbidities may be inconsistently reported. While physicians were able to use the patient's chart to enter the required information, it is not known if they used their recall memory or relied on the findings in the chart. In the tool, the encounter type was not listed. It was not known if the patient entered into the system was a new patient versus an established patient. This should not have impacted the assessment of control or severity. However, if the patient was new or newly established, the physician may not have had access to the patient's complete records which may document the presence of co-morbid conditions. Finally, only 20% of our study sample had data available on guideline asthma control and severity. This low rate of available data may be due to poor adoption of asthma assessment tools in the clinical setting by both primary care and asthma specialist physicians.⁶ Identification of barriers and facilitators to the use of these tools in different care settings is needed.

Conclusion

Our findings describe the characteristics of asthma patients seen by primary care providers and specialists (allergist and pulmonologists) using a guideline-derived assessment tool. This is the first time that patient data collected from Part IV of Maintenance of Certification has been utilized to help understand the characteristics of patients in different care settings. This provides a real-world confirmation of the relationships of co-morbidities to asthma severity and control in adolescents/adults and children and identifies the differences found in patients cared for by primary care and specialty providers. This information will be useful to healthcare providers managing asthma, especially if a structured approach that addresses the co-morbid conditions (e.g., BMI, rhinosinusitis, tobacco exposure) is used. Differences in

398 asthma management between specialists and PCPs identify gaps in care that can be targets
399 for futures studies that aim to improve asthma guideline implementation.

400

401

402 **Acknowledgements:** We would like to thank Lauri Sweetman for her administrative support
403 on this project.

404

Journal Pre-proof

References

- 1- Centers for Disease Control and Prevention. Asthma Surveillance Data; Last updated May 2018. Available at: https://www.cdc.gov/asthma/most_recent_data_states.htm
Accessed August 8,2018.
- 2- Sullivan PW, Smith KL, Ghushchyan VH, Globe DR, Lin SL, Globe G. Asthma in USA: its impact on health-related quality of life. J Asthma 2013; 50(8):891-899.
- 3- Harmsen L, Nolte H, Backer V. The effect of generalist and specialist care on quality of life in asthma patients with and without allergic rhinitis. Int Arch Allergy Immunol. 2010;152(3):288-94.
- 4- Kanter LJ, Siegel CJ, Snyder CF, Pelletier EM, Buchner DA, and Goss TF. Impact of respiratory symptoms on health-related quality of life and medical resource utilization of patients treated by allergy specialists and primary care providers. Ann Allergy, Asthma & Immunol 2002; 89(2): 139-147.
- 5- Wu AW, Young Y, Skinner EA, Diette GB, Huber M, Peres A et al. Quality of care and outcomes of adults with asthma treated by specialists and generalists in managed care. Arch Int Med 2001; 161(21): 2554-2560.
- 6- Cloutier MM, Salo PM, Akinbami LJ, Cohn RD, Wilkerson JC, Diette GB, et al. Clinician Agreement, Self efficacy, and Adherence with the Guidelines for the Diagnosis and Management of Asthma. J Allergy Clin Immunol. In Practice 2018; 6(3):886-894.
- 7- Tsuyuki RT, Sin DD, Sharpe HM, Cowie RL, Nilsson C, Man SFP, Alberta Strategy to Help Manage Asthma (ASTHMA) Investigators. Management of asthma among community-based primary care physicians. J Asthma 2005; 42(3): 163-167.
- 8- Diette GB, Skinner EA, Nguyen TH, Markson L, Clark BD, Wu AW. Comparison of quality of care by specialist and generalist physicians as usual source of asthma care for children. Pediatrics 2001; 108(2): 432-437.

- 9- Schatz M, Kosinski M, Yarlas AS, Hanlon J, Watson ME, Jhingran P. The minimally important difference of the Asthma Control Test. *J Allergy Clin Immunol.* 2009;124(4): 719-723.
- 10- Zeiger RS, Heller S, Mellon MH, Wald J, Falkoff R, Schatz M. Facilitated referral to asthma specialist reduces relapses in asthma emergency room visits. *J Allergy Clin Immunol.* 1991;87(6):1160–1168.
- 11- Vollmer WM, O'Hollaren M, Ettinger KM, Stibolt T, Wilkins J, Buist AS, et al. Specialty differences in the management of asthma. A cross-sectional assessment of allergists' patients and generalists' patients in a large HMO. *Arch Intern Med.* 1997;157(11):1201–1208.
- 12- Schatz M, Zeiger RS, Mosen D, Apter AJ, Vollmer WM, Stibolt, TB, et al. Improved asthma outcomes from allergy specialist care: a population-based cross-sectional analysis. *J Allergy Clin Immunol.* 2005;116(6):1307–1313.
- 13- Urbano, FL. Review of the NAEPP 2007 Expert Panel Report (EPR-3) on asthma diagnosis and treatment guidelines. *J Managed Care Pharmacy* 2008; 14(1): 41-49.
- 14- Price D, Bjermer L, Bergin DA, Martinez R. Asthma referrals: a key component of asthma management that needs to be addressed. *J Asthma Allergy* 2017; 10: 209-223.
- 15- Chen H, Johnson CA, Haselkorn T, Lee JH, Israel E. Subspecialty differences in asthma characteristics and management. *Mayo Clin Proc.* 2008; 83 (7): 786-793.
- 16- Braido, Fulvio. "Failure in asthma control: reasons and consequences." *Scientifica* 2013 (2013).
- 17- Flores G, Snowden-Bridon C, Torres S, Perez R, Walter T, Brotanek J, et al. Urban minority children with asthma: substantial morbidity, compromised quality and access to specialists, and the importance of poverty and specialty care. *J Asthma* 2009; 46(4): 392-398.
- 18- Kuhlthau K, Nyman RM, Ferris TG, Beal AC, Perrin JM. Correlates of use of specialty care. *Pediatrics* 2004; 113(3 Pt 1): e249-255.

- 19- Colice GL. Categorizing asthma severity: an overview of national guidelines. Clin Med Res 2004; 2(3): 155-163.
- 20- Bateman ED, Hurd SS, Barnes PJ, Bousquet J, Drazen JM, FitzGerald J, et al. Global strategy for asthma management and prevention: GINA executive summary. ERJ 2008; 31(1): 143-178.
- 21- Lai L, Hopp RJ, and Lusk RP. Pediatric chronic sinusitis and asthma: a review. J Asthma 2006; 43 (10): 719-725.
- 22- Dixon AE, Clerisme-Beaty EM, Sugar EA, Cohen RI, Lang JE et al. Effects of Obstructive Sleep Apnea and Gastroesophageal Reflux Disease on Asthma Control in Obesity. J Asthma 2011; 48 (7): 707-713.
- 23- Boulet LP and Boulay ME. Asthma-related comorbidities. Expert Rev Resp Med 2001; 5 (3): 377-393.
- 24- Pawankar R and Zernotti ME. Rhinosinusitis in children and asthma severity. Curr Opin Allergy Clin Immunol. 2009; 9 (2): 151-153.
- 25- Lin DC, Chandra RK, Tan BK, Zirkle W, Conley DB, Grammer LC et al. Association between severity of asthma and degree of chronic rhinosinusitis. Am J Rhinol Allergy 2011; 25 (4): 205-208.
- 26- Daly JB, Mackenzie LJ, Freund M, Wolfenden L, Roseby R, Wiggers JH. Interventions by health care professionals who provide routine child health care to reduce tobacco smoke exposure in children: a review and meta-analysis. JAMA Ped 2016; 170 (2): 138-147.
- 27- 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 (3): 547-553.
- 28- Ford JG and McCaffrey L. Understanding disparities in asthma outcomes among African Americans. Clin Chest Med 2006; 27 (3): 423-430.
- 29- Rosser FJ, Forno E, Cooper PJ, Celedón JC. Asthma in Hispanics. An 8-year update. Am J Resp Crit Care Med 2014; 189 (11): 1316-1327.

Journal Pre-proof

488 Figure Legends:

489 Figure 1. c-ACT score based on guideline control level in children

490 Figure 2. ACT score based on guideline control level in adults

491

Table 1. Pediatric Patient Characteristics (n=13479)			
	Primary Care (n=7505)	Specialist (n=5974)	p-value
Age at visit (mean $\pm$SD)	6.1 $\pm$ 2.9	7.0 $\pm$ 2.7	<0.01
Race/ethnicity			
White	41.2	53.6	<0.01
African American	17.0	18.2	
Hispanic/Latino	21.6	14.0	
Other	20.3	14.23	
FEV₁% predicted	90.1 $\pm$ 18.8 (n=641)	91.4 $\pm$ 16.5 (n=3146)	0.12
FEV₁/FVC	84.7 $\pm$ 12.3 (n=643)	85.0 $\pm$ 11.2 (n=2991)	0.64
Asthma Control Test	22.0 (n=1394)	22.2 (n=2318)	0.33
Smoking History (%)	(n=4882)	(n=4235)	<0.01
Never	84.99	89.82	
Former	0	0.02	
Current	0.04	0.14	
Passive/second hand exposure	14.97	10.01	
Co-morbid conditions (%)	(n=7505)	(n=5974)	0.43
Depression	0.23	0.15	
GERD	2.4	4.7	
OSA	0.6	0.7	
Rhinosinusitis	19.3	46.5	<0.01
Guideline Control (%)	(n=2037)	(n=3440)	<0.01
Poorly Controlled	7.3	10.0	
Not well controlled	24.3	27.0	
Well controlled	68.4	63.0	
Guideline Severity (%)	(n=1383)	(n=1269)	<0.01
Intermittent	68.8	44.6	
Mild Persistent	18.3	23.1	
Moderate Persistent	9.2	21.8	
Severe Persistent	3.8	10.5	

GERD=Gastroesophageal Reflux Disease; OSA=Obstructive Sleep Apnea

Table 2. Adolescent and Adult Patient Characteristics			
	Primary Care (n=3530)	Specialist (n=11499)	p-value
Age at visit (mean $\pm$SD)	24.3 $\pm$ 18	39.1 $\pm$ 19.9	<0.01
Race/ethnicity			
White	49.2	68.9	<0.01
African American	17.2	11.7	
Hispanic/Latino	19.5	8.8	
Other	14.1	10.7	
Body Mass Index (BMI) kg/m²	26.1 $\pm$ 7.8 (n=2275)	27.9 $\pm$ 9.4 (n=8034)	<0.01
FEV₁ % predicted	85.2 $\pm$ 19.9 (n=678)	85.2 $\pm$ 17.9 (n=7347)	0.19
Asthma Control Test	21.1 $\pm$ 3.7 (n=1139)	21.1 $\pm$ 3.8 (n=5411)	0.83
Smoking History (%)	(n=2492)	(n=8662)	<0.01
Never	77.01	80.82	
Former	8.11	10.90	
Current	5.78	4.20	
Passive/second hand exposure	9.11	4.08	
Co-morbid conditions (%)	(n=3530)	(n=11499)	0.85 <0.01 <0.01 <0.01
Depression	2.5	2.4	
GERD	4.8	14.8	
OSA	1.3	2.5	
Rhinosinusitis	22.0	44.8	
Guideline Control (%)	(n=1290)	(n=6450)	<0.01
Poorly Controlled	10.3	12.3	
Not well controlled	24.3	27.5	
Well controlled	65.4	60.3	
Guideline Severity (%)	(n=878)	(n=2210)	<0.01
Intermittent	66.4	50.7	
Mild Persistent	16.9	11.3	
Moderate Persistent	10.6	21.0	
Severe Persistent	6.0	17.0	

GERD=Gastroesophageal Reflux Disease; OSA=Obstructive Sleep Apnea

Table 3. Co-morbidities associated with Guideline-Derived Control and Severity in Children with Asthma (Odds ratio, 95% Confidence Interval)

	Guideline Control (n=2939)	Guideline Severity (n=1433)
Age	N/A	N/A
Race		
African American vs. Caucasian	1.41 (1.19-1.67)**	1.50 (1.17-1.93)**
Hispanic/Latino vs. Caucasian	1.21 (1.01-1.46)	0.98 (0.76-1.27)
Other vs. Caucasian	1.04 (0.84-1.29)	1.14 (0.90-1.44)
GERD	1.36 (1.02-1.81)*	N/A
OSA	2.23 (1.23-4.03)**	N/A
Depression	N/A	N/A
Rhinosinusitis	1.15 (1.01-1.31)*	1.28 (1.07-1.53)**
Tobacco Smoke Exposure	1.37 (1.12-1.68)**	1.62 (1.23-2.13)**
Specialist Provider vs. Primary Care	1.28 (1.11-1.48)**	3.03 (2.51-3.65)**

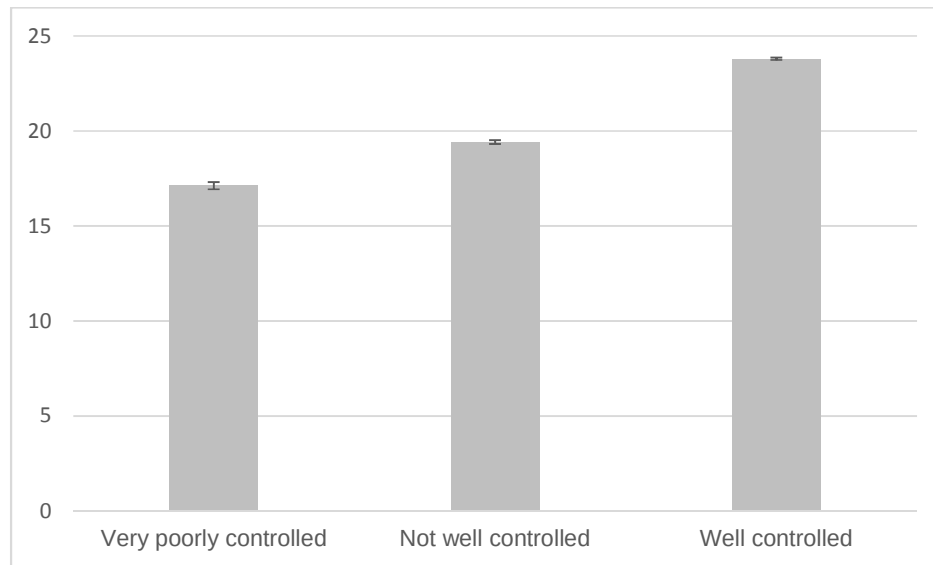
GERD= Gastroesophageal Reflux Disease; OSA= Obstructive Sleep Apnea; N/A: Not applicable as removed by backward elimination method of model selection; *p<0.05; **p<0.01

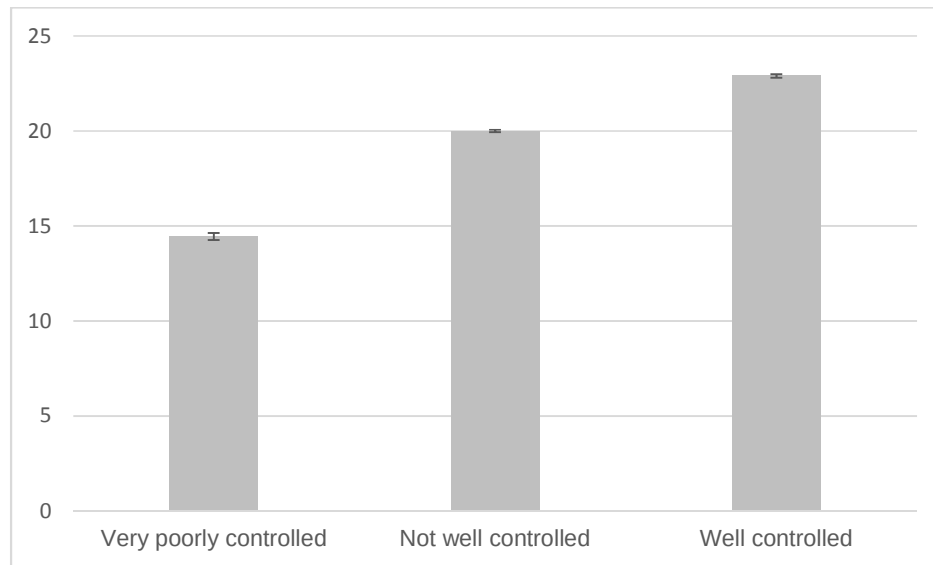
Table 4. Co-morbidities associated with Guideline-Derived Control and Severity in Adolescents and Adults with Asthma (Odds ratio, 95% Confidence Interval)

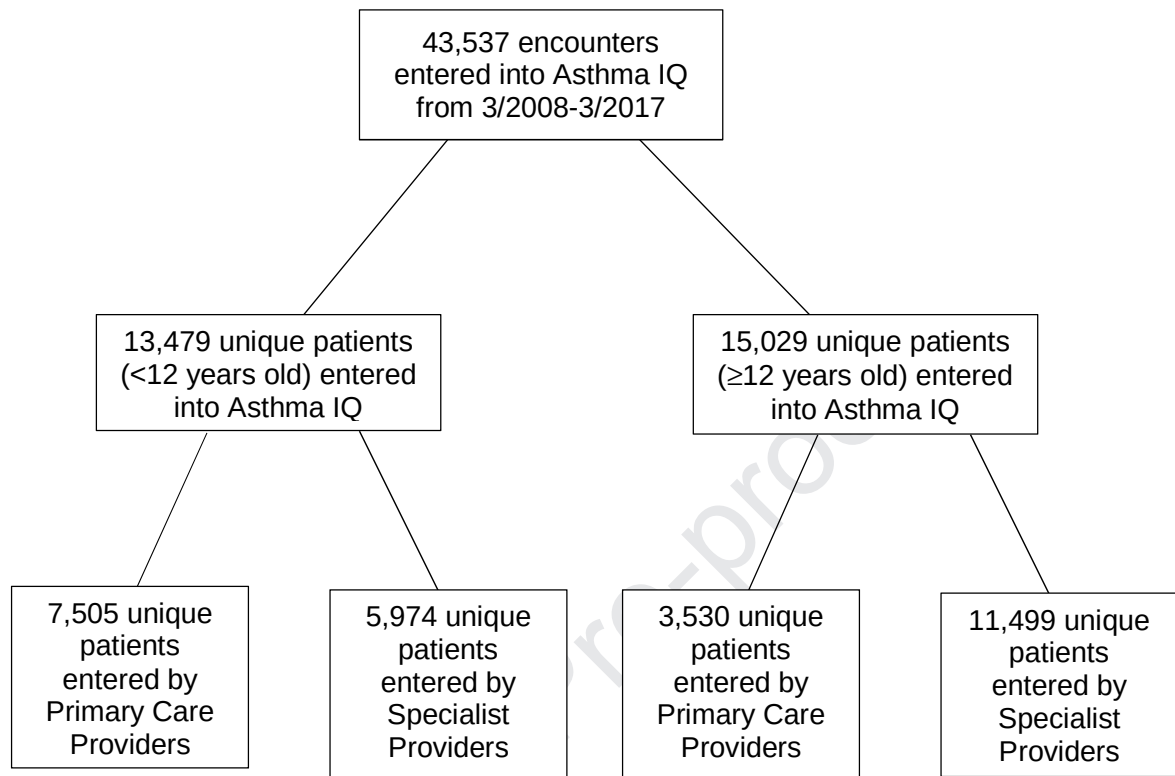
	Guideline Control (n=4337)	Guideline Severity (n=1906)
Age	1.01 (1.01-1.02)***	N/A
BMI	1.02 (1.01-1.03)***	N/A
Race		
African American vs. Caucasian	2.22 (1.85-2.65)***	1.65 (1.28-2.14)**
Hispanic/Latino vs. Caucasian	1.34 (1.09-1.65)	0.80 (0.59-1.08)
Other vs. Caucasian	1.59 (1.30-1.96)	1.31 (0.99-1.72)
GERD	1.20 (1.02-1.40)**	N/A
OSA	N/A	N/A
Depression	1.48 (1.07-2.05)**	N/A
Rhinosinusitis	N/A	1.31 (1.09-1.58)**
Tobacco smoke exposure		
Former smoker vs. never smoker	1.62 (1.29-2.03)	1.52 (1.1-2.1)
Current smoker vs. never smoker	1.81 (1.29-2.56)*	1.28 (0.86-1.9)
Passive/secondhand smoke vs. never smoker	1.30 (0.99-1.71)	1.5 (1.03-2.22)
Specialist Provider vs. Primary Care	N/A	2.16 (1.73-2.70)**

BMI= Body mass index; GERD= Gastroesophageal Reflux Disease; OSA= Obstructive Sleep Apnea; N/A: Not applicable as removed by backward elimination method of model selection;

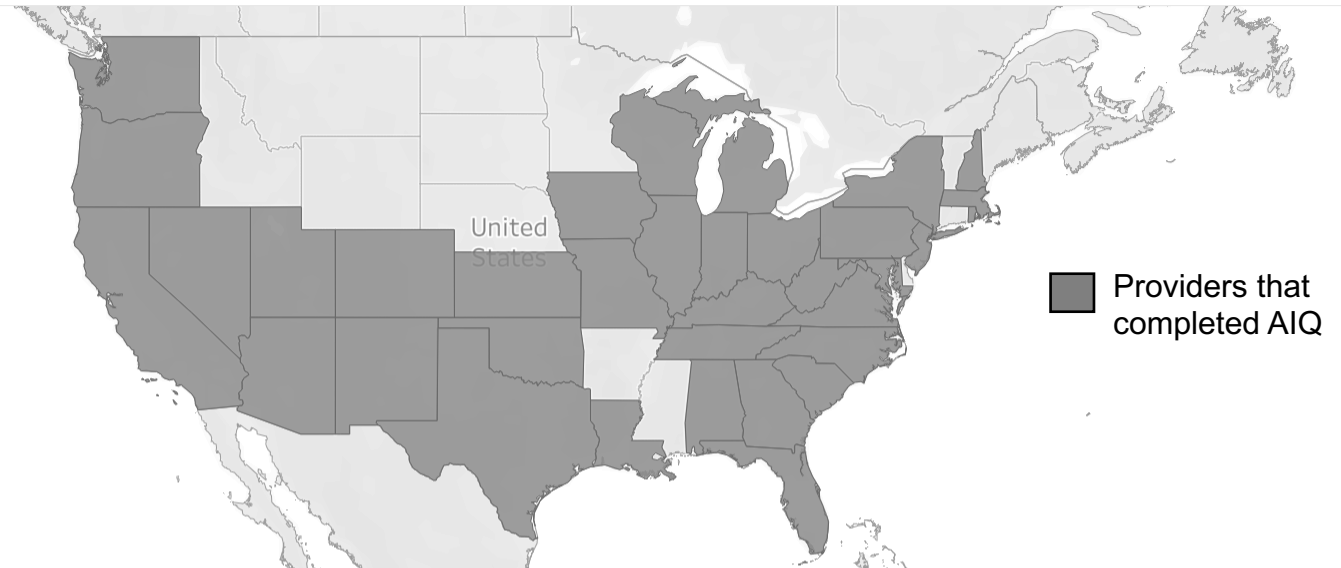
*p=0.05; **p<0.05; ***p<0.01







Primary Care Providers



Specialist Providers

