

Racial Disparities in Asthma-Related Health Outcomes in Children with Severe/Difficult-to-Treat Asthma



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What is already known about this topic? The burden of asthma is disproportionately higher among minorities, particularly black children.

What does this article add to our knowledge? In a real-world cohort, the present study extends the finding of an increase in asthma burden in black compared with white children to a phenotype with severe or difficult-to-treat asthma. This increased burden could not be explained by confounding factors.

How does this study impact current management guidelines? These results comprehensively describe the asthma burden in black children and those factors that may explain their increased burden, highlighting the high unmet need in this population and the importance of improving their outcomes.

BACKGROUND: There are limited data that examine differences in asthma etiology between black and white children with severe or difficult-to-treat asthma.

OBJECTIVE: To describe demographic, clinical, and asthma-related outcomes in black and white children and examine whether differences in outcomes are explained by confounding factors in sequential multivariable models.

METHODS: Black (n = 86) and white (n = 262) children aged 6-11 years from The Epidemiology and Natural History of Asthma: Outcomes and Treatment Regimens 3-year observational study were analyzed. Baseline demographics and clinical

characteristics were described for both cohorts, and outcomes at month 12 were analyzed using statistical models, sequentially adjusting for potential confounders.

RESULTS: Black children were more likely to be male (79.1% vs 66.4%; $P < .05$), obese (12.8% vs 1.5%; $P < .001$), and from a lower income stratum (USD43,400 vs 55,770; $P < .001$) than white children. Black children had higher geometric mean IgE levels (434.8 vs 136.8 IU/mL; $P < .001$), were more likely to have very poorly controlled asthma (72.1% vs 53.4%), use long-term systemic corticosteroids (30.2% vs 9.2%; $P < .001$), have poorer quality of life (5.5 vs 6.1; $P < .001$), and have an emergency

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Abbreviations used

ATAQ- Asthma Therapy Assessment Questionnaire
BMI- Body mass index
CI- Confidence interval
ED- Emergency department
FEV₁- Forced expiratory volume in 1 second
ICS- Inhaled corticosteroids
NHLBI- National Heart, Lung, and Blood Institute
PAQLQ- Pediatric Asthma Quality of Life Questionnaire
QoL- Quality of life
SES- Socioeconomic status
TENOR- The Epidemiology and Natural History of Asthma:
Outcomes and Treatment Regimens
WPAI- Work Productivity and Activity Impairment

department visit (27.4% vs 7.7%, $P < .001$) in the 3 months before month 12. Differences in asthma control and the severity of exacerbations persisted even after accounting for all confounding factors.

CONCLUSIONS: Among children with severe or difficult-to-treat asthma, asthma burden is greater in black than white children particularly related to several clinical and patient-reported outcome measures that are not explained by differences in background or clinical characteristics. © 2018 Published by Elsevier Inc. on behalf of the American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2019;7:568-77)

Key words: Asthma-related quality of life; Difficult-to-treat asthma; Pediatric asthma; Severe asthma; Exacerbations; Racial disparities; Patient-reported outcomes

Asthma imposes a significant public health burden in the United States, with a prevalence of 18.4 million adults (7.6%) and 6.2 million children (8.4%) in 2015.¹ Nearly half of children and adults with asthma report ever having one or more asthma attacks,¹ and asthma accounted for 11.0 million physician office visits in 2014,² 2.0 million emergency department (ED) visits in 2014,³ and 1.3 million hospital outpatient department visits in 2010.⁴

Of those children affected by asthma, 13.4% are of black (non-Hispanic) race, 8.0% of Hispanic race, and 7.4% are of white (non-Hispanic) race.¹ In addition, asthma burden is disproportionately higher among minorities. In general population asthma cohorts, black children have greater asthma morbidity, higher rates of severe asthma, and worse outcomes than white children.⁵ Many factors, including asthma severity, differences in access to health care, and environmental exposures, have been offered to explain these racial disparities in asthma burden. In addition, genetics and pharmacogenetics, including reduced responsiveness to some asthma therapies, such as inhaled corticosteroids (ICSs) compared with white patients, have been linked to racial differences.⁶

Previous studies assessing racial disparities in pediatric asthma have been primarily descriptive in nature, limited in the assessments utilized, or focused primarily on asthma in the general population.⁷⁻⁹ The Severe Asthma Research Program has studied black children with severe asthma within the context of assessing asthma phenotypes.¹⁰⁻¹³ To date, an in-depth assessment of

black children with severe or difficult-to-treat asthma using a broad array of both clinical and patient-reported outcomes has not been performed, including multivariable analyses to examine whether the poorer outcomes in black versus white children can be explained by modifiable and unmodifiable confounding factors.

Using real-world data from the 3-year, prospective, observational study, The Epidemiology and Natural History of Asthma: Outcomes and Treatment Regimens (TENOR), our primary objective was to describe demographic, clinical, and asthma-related health outcomes in black and white children with severe or difficult-to-treat asthma. We hypothesized that among a severe or difficult-to-treat asthma phenotype, black children would evidence greater asthma burden, independent of potential confounding factors.

METHODS

TENOR study design

TENOR was a 3-year (2001-2004), multicenter, prospective, observational study conducted at 283 sites in the United States. The details of the study design and methodology, as well as baseline cohort characteristics, have been previously published.^{14,15} Briefly, TENOR enrollment included patients 6 years of age and older from diverse geographic areas with severe or difficult-to-treat asthma receiving care from an allergist or pulmonologist. Patients were selected for TENOR if they: (1) had received care from their asthma specialist (allergist or pulmonologist) for ≥ 1 year; (2) had high health care use (≥ 2 unscheduled asthma care visits or ≥ 2 oral corticosteroid courses) or high medication use (requiring ≥ 3 asthma controller medications, long-term daily high doses of ICSs, or use of ≥ 5 mg/day oral prednisone) in the past 12 months; and (3) were able to read and understand English. Patients were recruited from typical patient care settings, including managed care organizations, community physicians/practices, and academic centers. Because TENOR was an observational study, no experimental intervention was implemented; patients continued to receive treatment as recommended by their allergist or pulmonologist. Each patient's legally authorized representative provided informed consent before participating in the study. TENOR was approved by a central institutional review board and, when necessary, by the institutional review board at each site.

Data collection

Demographic and clinical data were collected by study coordinator interview and evaluated at baseline and every 6 months. The present analyses included patients 6-11 years of age, and the child's parent or guardian was present to help answer interview questions and complete the questionnaires.

Asthma control

To evaluate asthma control, patients completed the Asthma Therapy Assessment Questionnaire (ATAQ). The ATAQ control index ranges from 0 to 4 problems and has been validated in adult populations.¹⁶

The impairment domain of the National Heart, Lung, and Blood Institute (NHLBI) asthma guidelines was also used to classify children's asthma as very poorly controlled, not well controlled, or well controlled.¹⁷ Assessment categories included symptoms, nighttime awakenings, interference with normal activity, short-acting β_2 -agonist use for symptom control, and lung function via the

measurement of forced expiratory volume in 1 second (FEV₁) or peak flow.¹⁸

Asthma exacerbations

Asthma exacerbations were based on self-reported health care utilization at baseline and semiannually, and were defined as overnight hospitalizations, ED visits, or oral corticosteroid courses due to asthma in the 3 months before each study visit. Asthma exacerbation severity was defined in descending order of severity: hospitalization, ED visit, steroid course, and no exacerbation. A value of 3 was assigned for hospitalization, a value of 2 was assigned for an ED visit, a value of 1 was assigned for steroid course, and a value of 0 was assigned for no exacerbation. For each patient, an asthma exacerbation was defined as the highest value in the hierarchy from both the month 6 and 12 visits.

Spirometry

Pre- and postbronchodilator FEV₁ was measured at baseline and annually conforming to recommendations from ATS guidelines (ATS 1995) and interpreted using Global Lung Initiative reference standards.¹⁹ Patients were instructed not to use a bronchodilator for at least 4 hours before prebronchodilator testing.

Medication compliance

Medication compliance was assessed using 2 questions from the ATAQ: "Do you believe you are able to take your asthma medicine(s) as directed?" and "What best describes how you take this medicine now?"

Quality of life

Asthma-related quality of life (QoL) was measured using the Pediatric Asthma Quality of Life questionnaire (PAQLQ), a validated tool that measures functional problems in children with asthma.²⁰⁻²² The questions are scored on a 7-point Likert scale (1 = extremely bothered to 7 = not bothered at all) with the mean of all responses comprising the overall PAQLQ score. Lower scores indicate poorer QoL.

Work productivity and activity impairment (WPAI)-asthma

The school impairment and activity impairment domains of the WPAI-asthma were examined.²³ Parents or caregivers were asked to score the impact of their child's asthma on their ability to attend classes and perform regular daily activity during the past 7 days. Values for each domain range from 0% to 100%, with higher scores indicating greater impairment.

Statistical analyses

Black and white children aged 6-11 years were included in the analyses. The primary analysis was the comparison of baseline demographics, clinical characteristics, and patient-reported outcomes between black and white children. *P* values and 95% confidence intervals (CIs) for comparing between-group differences were computed using the Mantel-Haenszel χ^2 test for categorical variables and the 2-sample *t* test for continuous variables. Fisher's exact test was used for categorical data when cell sizes were small. For the secondary analysis, multivariable linear models were used to evaluate least-squares mean differences in continuous outcomes at month 12 (mean PAQLQ overall score and ATAQ control index), adjusting for potential confounders using a sequential approach. *P* values were based on the *t* test for the associated least-squares mean differences. Logistic regression models were used to estimate odds ratios and 95% CIs for black versus white children for categorical outcomes at

month 12 (asthma exacerbation hierarchy), adjusting for potential confounders using a sequential approach. The series of sequential models were: (1) unadjusted, (2) baseline age and sex adjusted, (3) socioeconomic status (SES) adjusted (adds urban/rural, region, income, education, and insurance to the age/sex model), (4) medication compliance and treatment setting adjusted (adds medication compliance and whether treated by a pulmonologist or allergist), (5) comorbidity adjusted (adds weight and body mass index [BMI] percentile), (6) allergy adjusted (adds history of allergic rhinitis, history of atopic dermatitis, log of IgE, and skin test result), and (7) number of asthma controllers adjusted (adds number of controller medications used <3 vs ≥ 3) (Figure 1). In addition, each set of models was adjusted separately for NHLBI asthma control classification, as a measure of asthma severity.

RESULTS

Univariable analyses

A total of 86 black children and 262 white children aged 6-11 years were included in the analyses. Mean age at baseline was similar between black and white children: 9.2 ± 1.6 vs 9.0 ± 1.7 , respectively (Table I). Black children were more likely than white children to be male (79.1% vs 66.4%; *P* = .03), to reside in urban core areas (80.2% vs 61.8%; *P* = .006 for overall comparison of residential area), to be in a lower family income stratum (USD43,400 vs 55,770; *P* < .001), and to have Medicaid coverage (44.2% vs 11.5%; *P* < .001 for overall comparison of insurance type), respectively. There were no differences in geographic region, with the majority of children in both groups residing in the South.

Mean BMI percentile in black children was higher than in white children (74.8 ± 27.6 kg/m² vs 66.9 ± 27.8 kg/m², respectively; *P* = .02), and a greater proportion of black children were considered obese compared with white children (12.8% vs 1.5%, respectively; *P* < .001) (Table II). Black children were more likely to have a history of atopic dermatitis than white children (30.2% vs 16.4%, *P* = .02 for overall comparison of atopic dermatitis categories), but a history of allergic rhinitis was similar and high in both groups. Total geometric mean IgE levels were higher in black children than in white children (434.8 IU/mL vs 136.8 IU/mL; *P* < .001), but skin test sensitization was similar and high in both groups. Black children were more likely to be under the care of a pulmonologist than white children (69.8% vs 58.0%, respectively; *P* = .053). Medication compliance was similar between the 2 groups. The proportion of black children with very poorly controlled asthma was higher than in white children (72.1% vs 53.4%; *P* < .004 for overall comparison of NHLBI asthma control categories) (Figure 2). Across all spirometry measures, black children had poorer Global Lung Function Initiative-adjusted lung function compared with white children (Figure 3).

Medication use

Medication use was generally similar between black and white children, with the exception of systemic corticosteroid use, which was more common in black children (30.2% vs 9.2%; *P* < .001) (Table III). In addition, black children who were categorized as having very poorly controlled asthma were more likely to be treated with 3 or more long-term controller medications compared with white children (Table IV). Interestingly, black children who were classified as having well-controlled or not well-controlled asthma were also more likely to be treated with 3

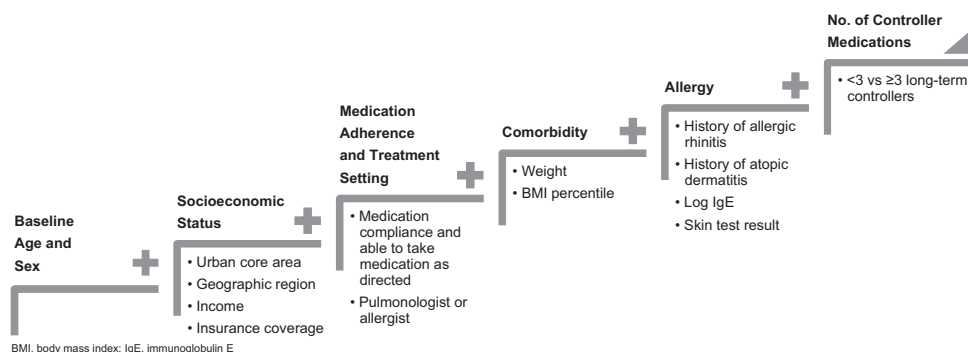


FIGURE 1. Sequential adjustments in multivariable models.

TABLE I. Demographics in black and white children enrolled in TENOR

Characteristic	Black n = 86	White n = 262	95% CI for difference	P value
Age at baseline (y), mean ± SD	9.2 ± 1.6	9.0 ± 1.7	−0.6, 0.2	NS
Males, n (%)	68 (79.1)	174 (66.4)	−23.0, −2.3	.03
Insurance type, n (%)				<.001
Commercial/PPO	23 (26.7)	157 (59.9)	22.1, 44.3	
HMO	19 (22.1)	65 (24.8)	−7.5, 12.9	
Medicaid	38 (44.2)	30 (11.5)	−43.9, −21.6	
Other*	6 (7.0)	10 (3.8)	−9.0, 2.7	
Income estimate (USD), mean ± SD†	43,400 ± 14,124	55,770 ± 20,402	7712.1, 17,026.1	<.001
Geographic region, n (%)				NS
Northeast	6 (7.0)	23 (8.8)	−4.6, 8.2	
Midwest	27 (31.4)	86 (32.8)	−9.9, 12.8	
South	42 (48.8)	107 (40.8)	−20.1, 4.1	
West	11 (12.8)	46 (17.6)	−3.7, 13.2	
Residential area, n (%)				.006
Urban core area	69 (80.2)	162 (61.8)	−28.7, −8.1	
Suburban area	8 (9.3)	45 (17.2)	0.2, 15.5	
Large town area	6 (7.0)	20 (7.6)	−5.6, 6.9	
Small town and isolated rural area	3 (3.5)	35 (13.4)	4.2, 15.5	

CI, Confidence interval; HMO, health maintenance organization; NS, not significant; PPO, preferred provider organization; SD, standard deviation; TENOR, The Epidemiology and Natural History of Asthma: Outcomes and Treatment Regimens.

*Other category includes Medicare, military/veteran, and self-pay.

†Median family income calculated from 2000 US census for reported zip code.

or more long-term controller medications compared with white children.

Asthma-related health outcomes

Overall activity and school impairment, as measured by the WPAI-asthma at month 12, was higher in black children than in white children (27.4 ± 31.1 vs 16.7 ± 23.1 ; $P = .004$) and (29.9 ± 51.3 vs 15.8 ± 26.2 ; $P = .01$), respectively. Mean overall pediatric asthma-related QoL score at month 12 was significantly lower in black children than in white children (5.5 vs 6.1 ; $P < .001$), indicating poorer asthma-related QoL (Figure 4, A, unadjusted). Black children had higher mean ATAQ control domain scores at month 12, indicating more asthma control problems, compared with white children (1.9 vs 1.3 ; $P = .006$) (Figure 4, B, unadjusted). Exacerbation severity at month 12, as measured by the exacerbation hierarchy score, was

worse in black children than in white children (1.2 vs 0.6 ; $P < .001$) (Figure 4, C, unadjusted).

Multivariable analysis

In multivariable analyses, the difference in asthma-related QoL scores decreased but remained significantly different after adjusting for age at baseline and sex ($P < .001$); age at baseline, sex, and SES ($P < .05$); and age at baseline, sex, SES, medication compliance, and treatment setting ($P < .05$). Once comorbidity measures (weight and BMI percentile) were added into the sequential model (model 5), the difference was no longer statistically significant (Figure 4, A). Separate sequential modeling was also performed with the inclusion of NHLBI asthma control classification as a covariate. Estimated differences in mean PAQLQ scores between black and white children were slightly smaller than without adjustment, but were again no longer

TABLE II. Clinical characteristics at baseline in black and white children in TENOR

Characteristic	Black n = 86	White n = 262	95% CI for difference	P value
Weight (kg), mean $\pm$ SD	42.1 $\pm$ 14.9	35.1 $\pm$ 11.1	−10.0, −4.1	<.001
Height (cm), mean $\pm$ SD	138.8 $\pm$ 10.6	134.9 $\pm$ 12.3	−6.8, −0.9	.01
BMI percentile, mean $\pm$ SD	74.8 $\pm$ 27.6	66.9 $\pm$ 27.8	−14.7, −1.1	.02
Obese, n (%)	11 (12.8)	4 (1.5)	−18.5, −4.1	<.001
History of atopic dermatitis, n (%)	26 (30.2)	43 (16.4)	−24.5, −3.1	.02
History of allergic rhinitis, n (%)	50 (58.1)	172 (65.6)	−4.4, 19.4	NS
Total IgE (IU/mL), geometric mean (95% CI)	434.8 (320.5-589.7)	136.8 (110.6-169.3)	—	<.001
Skin test result, n (%)				NS
No	22 (25.6)	78 (29.8)	−6.6, 15.0	
Yes, negative	5 (5.8)	24 (9.2)	−2.7, 9.4	
Yes, positive	59 (68.6)	160 (61.1)	−19.0, 3.9	
Treatment setting, n (%)				.053
Pulmonologist	60 (69.8)	152 (58.0)	−23.2, −0.4	
Allergist	26 (30.2)	110 (42.0)	0.4, 23.2	
Medication compliance				
Able to take medication as directed, n (%)				NS
Yes	69 (80.2)	191 (72.9)	−17.3, 2.7	
No	1 (1.2)	4 (1.5)	−2.3, 3.1	
Missing	16 (18.6)	67 (25.6)	−2.8, 16.7	
Compliance, n (%)				NS
I take it every day	54 (62.8)	162 (61.8)	−12.8, 10.8	
Some days I take it, but other days I don't	7 (8.1)	19 (7.3)	−7.5, 5.7	
I used to take it, but now I don't	1 (1.2)	5 (1.9)	−2.1, 3.6	
I only take it when I have symptoms	1 (1.2)	5 (1.9)	−2.1, 3.6	
Missing	23 (26.7)	71 (27.1)	−10.4, 11.2	

BMI, Body mass index; CI, confidence interval; NS, not significant; SD, standard deviation; TENOR, The Epidemiology and Natural History of Asthma: Outcomes and Treatment Regimens.

P value based on Fisher's exact test.

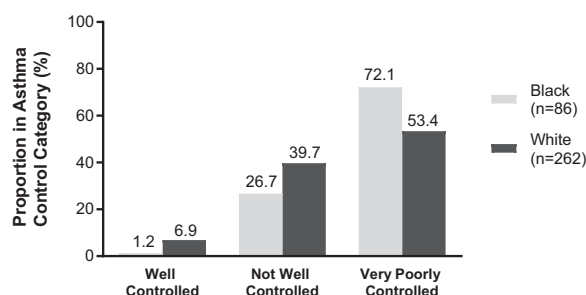


FIGURE 2. Classification of asthma control in black and white children in TENOR based on NHLBI asthma guidelines. $P = .004$ for overall comparison of NHLBI asthma control categories based on Fisher's exact test. NHLBI, National Heart, Lung, and Blood Institute; TENOR, The Epidemiology and Natural History of Asthma: Outcomes and Treatment Regimens.

statistically significant after adjusting for comorbidities (model 5) (data not shown). Differences in mean ATAQ control domain scores remained statistically significant after adjusting for all sets of sequential models, including the fully adjusted model (model 7) (Figure 4, B). For exacerbation severity scores at month 12, the difference in black and white children tended to decrease with adjustment for each set of sequential models; however, the difference persisted even in the fully adjusted model (model 7)

(Figure 4, C). Additional adjustment for NHLBI asthma control classification did not affect the differences in black and white exacerbation hierarchy scores in the sequential modeling.

DISCUSSION

This report from the TENOR observational study provides the most comprehensive assessment of the black/white differences in pediatric asthma by attempting to explain the poorer asthma-related health outcomes in black patients using a rigorous statistical approach of sequential adjustment for confounding variables. In addition, this study examined a wide breadth of variables, including demographic, clinical, and patient-reported outcomes in a real-world setting, some of which have not been previously reported. Although black children were more likely to be treated with systemic corticosteroids and a greater number of long-term controllers, even when classified as having very poorly controlled asthma, they fared worse than their white counterparts on several clinical and patient-reported outcome measures including BMI, IgE, and allergy measures, lung function, asthma control, risk of severe asthma exacerbation, asthma-related QoL, and activity and school impairment. Differences in asthma control and the severity of exacerbations persisted even after accounting for confounding factors, including demographics, SES, medication compliance, treatment setting, comorbidity, allergy status, and controller use.

These results extend the findings in severe and difficult-to-treat asthma in black and white adults aged 18 years and older

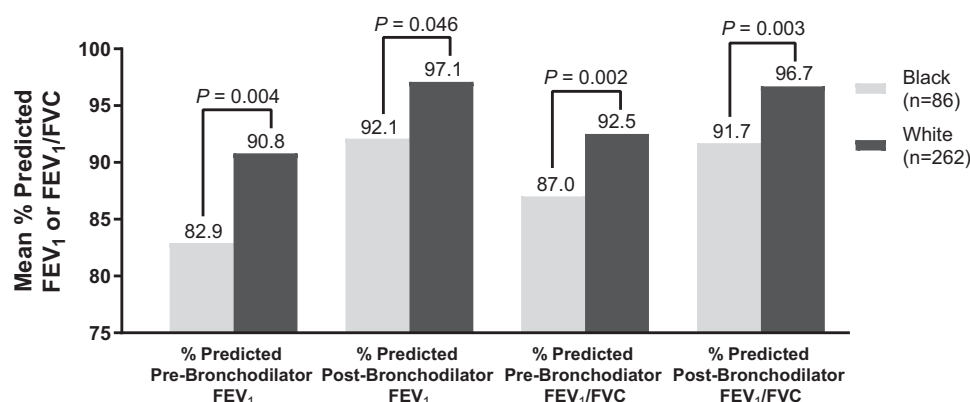


FIGURE 3. Lung function at month 12 in black and white children in TENOR. Global Lung Function Initiative-Adjusted. *FEV₁*, Forced expiratory volume in 1 second; *FVC*, forced vital capacity; *TENOR*, The Epidemiology and Natural History of Asthma: Outcomes and Treatment Regimens.

TABLE III. Medication use at baseline in black and white children in TENOR

Medication	Black n = 86	White n = 262	95% CI for difference	P value
Inhaled corticosteroids, n (%)	82 (95.3)	246 (93.9)	−6.8, 3.9	NS
Long-acting β_2 -agonist, n (%)	65 (75.6)	170 (64.9)	−21.5, 0.1	NS
Leukotriene modifiers, n (%)	63 (73.3)	193 (73.7)	−10.4, 11.2	NS
Short-acting β_2 -agonist, n (%)	83 (96.5)	251 (95.8)	−5.3, 3.9	NS
Anticholinergics, n (%)	4 (4.7)	21 (8.0)	−2.2, 8.9	NS
Systemic corticosteroids, n (%)	26 (30.2)	24 (9.2)	−31.4, −10.8	<.001

CI, Confidence interval; NS, not significant; *TENOR*, The Epidemiology and Natural History of Asthma: Outcomes and Treatment Regimens.

TABLE IV. Use of long-term controllers at baseline by NHLBI asthma control classification in black and white children in TENOR

	Black			White			P value*
	0-1 controller	2 controllers	≥3 controllers	0-1 controller	2 controllers	≥3 controllers	
NHLBI asthma control category, n (%)							
WC/NWC	1 (5.0)	5 (25.0)	14 (70.0)	19 (17.9)	44 (41.5)	43 (40.6)	.046
VPC	5 (9.4)	6 (11.3)	42 (79.3)	13 (10.2)	38 (29.9)	76 (59.8)	.02

NHLBI, National Heart, Lung, and Blood Institute; NWC, not well controlled; *TENOR*, The Epidemiology and Natural History of Asthma: Outcomes and Treatment Regimens; VPC, very poorly controlled; WC, well controlled.

*Differences in long-term controller use tested across race in each asthma control category; P values based on the χ^2 test.

to black and white children aged 6 to 11 years.²⁴ Among adults, after adjusting for demographics, SES, medication compliance, treatment setting, comorbidities, and allergy measures, statistically significant differences remained between black and white adults for asthma-related QoL (as measured by the MiniAQLQ) and for asthma control (as measured by ATAQ control domain scores) at month 12.²⁴ In the younger population reported here, significant differences in the PAQLQ persisted after accounting for demographics, SES, medication compliance, and treatment setting (model 4); however, once comorbidity measures (weight and BMI percentile) were added into the sequential model (model 5), the difference in pediatric asthma-related QoL was no longer statistically significant. This highlights the substantial impact of body weight on asthma-related QoL in children. Findings were consistent in the ATAQ outcome between the

adult and pediatric analyses, with statistically significant differences persisting after accounting for all factors in the sequential models.

In the current analysis, exacerbation hierarchy was significantly greater in black than in white children, indicating more severe exacerbations in black children. This significant difference persisted even after adjusting for potential confounders. In the adult analysis, ED visits in the 3 months before month 12 were used to measure severe exacerbations. The difference in risk tended to decrease with adjustment for each set of sequential models; however, black adults were still more than twice as likely to report an ED visit in the fully adjusted model. The results support a study that found that African American children were 2 times as likely as white children to be readmitted for asthma or wheezing,²⁵ and another that concluded that black children were

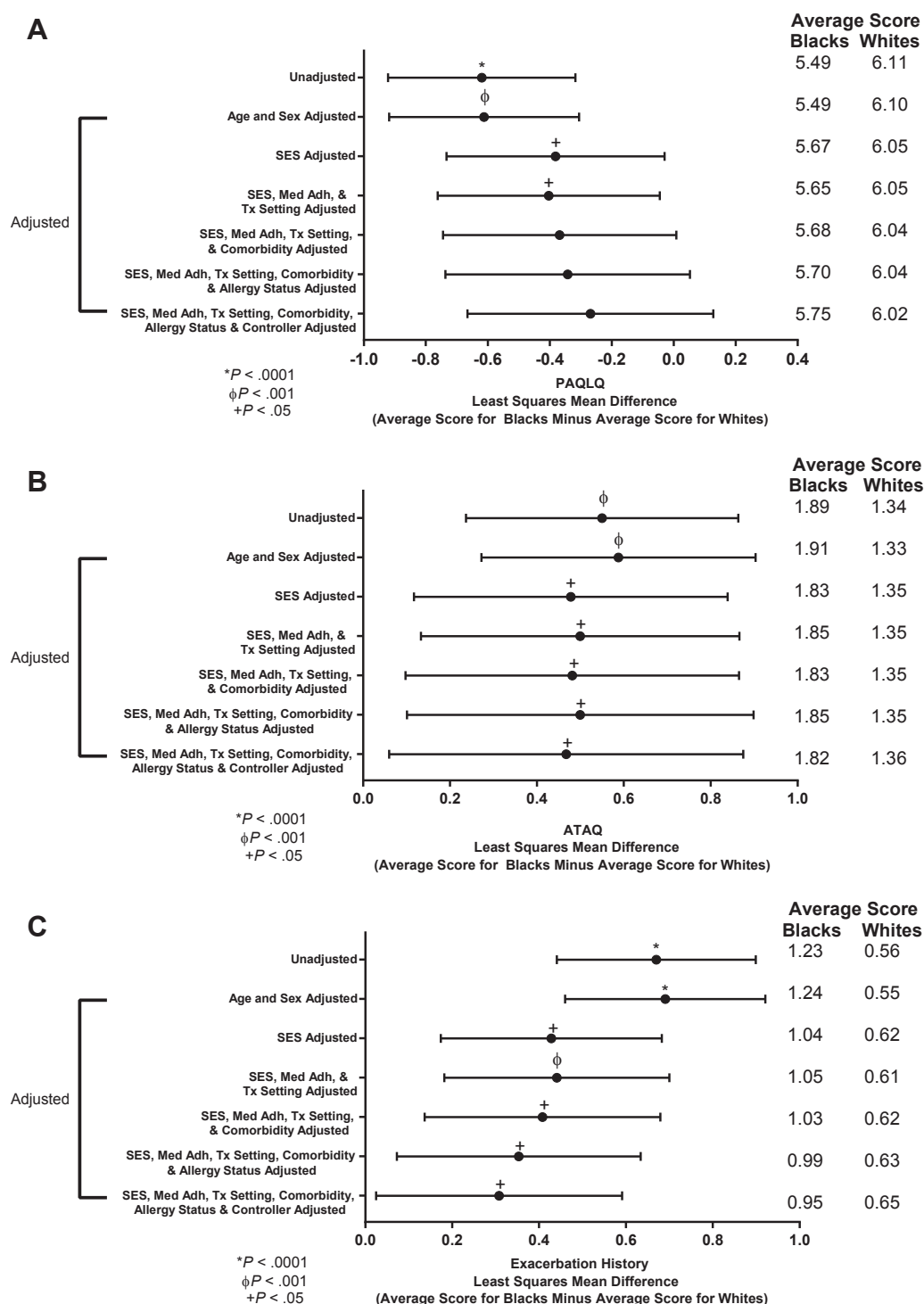


FIGURE 4. Multivariable regression comparing Pediatric Asthma Quality of Life Questionnaire (PAQLQ) overall scores (**A**), Asthma Therapy Assessment Questionnaire (ATAQ) control domain scores (**B**), and exacerbation hierarchy (**C**) at month 12 in black versus white children in TENOR. SES, Socioeconomic status; TENOR, The Epidemiology and Natural History of Asthma: Outcomes and Treatment Regimens.

2 times more likely than white children to be hospitalized for asthma.²⁶ It has been suggested that asthma in those with African descent is more severe than in those with European descent.²⁷ In addition, children with severe asthma have higher health care

utilization and medication use compared with children with mild-to-moderate asthma.¹³

Black children were more likely to reside in urban core areas. It has been shown that children who grow up in crowded urban

neighborhoods have higher rates of asthma and experience greater morbidity due to asthma.^{5,27-29} According to the Environmental Protection Agency, indoor and outdoor triggers such as cockroaches, pets, air pollution, or high levels of ozone can warrant asthma attacks.²⁷ In the current analysis, we found that black children evidenced a higher level of T-2 features than their white counterparts, as documented by higher geometric mean IgE levels and a greater frequency of atopic dermatitis; it has been reported that African American children are more likely to have higher IgE levels, at least one positive skin prick test, and atopic dermatitis in comparison with white children, and differences between racial groups do not change after adjusting for SES, environmental, or racially differing characteristics.³⁰ Recent research has shown that accounting for individual risk factors and neighborhood qualities, as well as race, somewhat reduced but did not fully diminish the higher odds of asthma diagnosis among black versus white children.³¹ Recent research has also concluded that African American children suffer disproportionately from asthma in every type of neighborhood, including poor or wealthy ones.³² Thus, it appears that residing in urban areas, and the resulting increased exposure to environmental allergens, does not fully account for the increased prevalence or severity of asthma in black children versus white children.

In this TENOR analysis, black children had significantly lower lung function in comparison with their white counterparts. The results are consistent with other studies that have shown that African American children have significantly smaller forced vital capacity and FEV₁ values than white children,³³⁻³⁵ which is not accounted for by gender, age, education, and paternal or maternal smoking during pregnancy.³³ In a study of 1018 participants from the Asthma Clinical Research Network and AsthmaNet,³⁴ African American subjects were found to have a lower percent predicted FEV₁, higher total IgE levels, and a greater proportion with uncontrolled asthma compared with white subjects. Poorer lung function in African American versus white patients with asthma was attributed to the increased prevalence of eosinophilic versus noneosinophilic airway inflammatory phenotypes in African American patients.³⁴ An inverse relationship between IgE and lung function has also been suggested, with higher IgE levels demonstrated in blacks in TENOR, as well as in other studies.^{26,33,34,36}

The inability to explain the differences in asthma-related health outcomes in black and white children despite accounting for the major demographic and clinical characteristics between the 2 groups lends support to the growing body of evidence for the role of other factors, such as genetics and pharmacogenetics, in mediating the response to certain medications. Black subjects with asthma have been shown to require greater concentrations of glucocorticoid to suppress activation of T-lymphocytes, suggesting that black subjects have a racial predisposition to reduced glucocorticoid response.⁶ Notably, elevated BMI, which is associated with an increased risk in exacerbations and poor asthma control,³⁷ may itself be associated with reduced response to glucocorticoids, leading to lower clinical efficiency of glucocorticoid therapy in overweight or obese patients with asthma.³⁸ The clinical implications of steroid resistance include impaired bronchodilator reversibility, potentially contributing to chronic airway remodeling in patients with steroid-resistant asthma.³⁹ Genetic differences alone may account for low corticosteroid response,⁴⁰ suggesting the need for biomarkers to identify children who may respond differentially to treatment.

Other factors unaccounted for or measured in the TENOR study may also help explain the increased disease burden of asthma in black children, such as the impact of obesity on comorbidities, access to care, and social or environmental factors. Black children, for instance, are more likely than their white counterparts to experience significant life stressors arising from gun violence,⁴¹ economic hardship, and living in single-parent homes⁴² and substandard housing.⁴³ Neighborhood property crime, violent crime, and drug abuse crime are associated with an increase in the odds of developing asthma and asthma severity scores.⁴⁴ The ability of stressors to induce asthma may relate to chronic alterations in the hypothalamic pituitary axis,⁴⁵ which stimulates inflammation through the production of proinflammatory cytokines IL-6, IL-10, and TNF-alpha.⁴⁶

Limitations should be considered when interpreting the study results. We compared the 348 children with nonmissing covariates who were included in the analysis with the 189 patients with missing covariates who were excluded. We found that those children included were more likely to be in a higher family income stratum, to have commercial/preferred provider organization insurance coverage, to have well-controlled or not well-controlled asthma versus very poorly controlled asthma, to have better asthma-related QoL, and were less likely to have an unscheduled office visit in the prior 3 months compared with the children who were excluded from the analyses. To explore this further, we stratified those children included versus those excluded by race/ethnicity and found that this same pattern emerged, that is, in both the black subgroup of children and the white subgroup of children, those included in the analyses were less severe than those who were excluded. Although this selection bias was present in the analysis, the bias was nondifferential, affecting both the black and white subgroups of children similarly, and thus, would not be expected to affect the findings.

Other limitations include the collection of some data through self-report, including comorbidities and health care utilization. Although the child's parent or guardian was present to help answer interview questions and complete the questionnaires, self-reported data are subject to variability based on the patient or caregiver's ability to recall information and may introduce recall bias. In addition, 6-month gaps in data collection prevented full assessment of exacerbations over the previous year. However, limiting recall to 3 months was deemed necessary to maximize the quality of the patient-reported data. There may also be residual confounding due to unidentified factors not measured in the TENOR study. For example, there is no measure of genetic polymorphisms or environmental exposures. In addition, we were unable to assess the presence of eosinophilic airway inflammation, as it was not collected in TENOR, which has been linked to a higher asthma burden and has been shown to be more prevalent in African Americans.³⁴ Income data were not directly collected and instead alternative measures were used based on patient zip code. Finally, the study included only children with severe or difficult-to-treat asthma treated by allergists or pulmonologists who were able to speak English. These results may, therefore, not be generalizable to other children with asthma of different severity, those primarily treated by general pediatricians or those who do not speak English. Indeed, a recent analysis indicated that children with persistent asthma symptoms are not likely to receive guideline-recommended preventive actions for asthma during primary care office visits.⁴⁷

This analysis highlights the differences in asthma-related health outcomes between black and white children with severe or difficult-to-treat asthma and demonstrates that differences in asthma control and severity of asthma exacerbations were not explained by demographics, SES, medication compliance, treatment setting, comorbidities, allergy status, and long-term controller use. These results emphasize the high unmet need for this population and shed light on the importance of improving outcomes for black patients with pediatric asthma. Furthermore, findings suggest that other factors may account for these disparities and warrant further exploration. This information supports the paradigm of personalized medicine to help improve response to asthma treatments, leading to more successful asthma-related health outcomes.

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