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## Mental Health Diagnoses among Children and Adolescents with Chronic Medical Conditions in a Large Urban Cohort

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## Abstract

We analyzed data for 6,458 children with chronic conditions. The most prevalent diagnoses were mood disorders (8.6%), attention deficit hyperactivity disorder (ADHD; 7.4%), conduct disorders (6.1%), and anxiety disorders (4.8%). Adjusted odds of having a mental health diagnosis increased with age for mood disorders and anxiety disorders and decreased with age for ADHD and conduct disorders. When compared with females, males had lower odds of being diagnosed with mood and anxiety disorders and higher odds of being diagnosed with ADHD and conduct disorders. Blacks had lower odds of being diagnosed with anxiety, mood disorders, and ADHD than children in the other racial category. Hispanics had lower odds of being diagnosed with ADHD than children in the other racial category. Racial/ethnic minorities were less likely to have a mental health diagnosis than children in the other race/ethnicity category, which suggests under identification of mental health needs particularly in minority children.

## Keywords

mental health diagnosis in children; children with chronic medical conditions; behavioral health disparities; race and mental health diagnosis

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## Introduction

Mental health disorders among children are a serious public health concern in the United States (U.S.) [1]. According to surveillance estimates from the Centers for Disease Control and Prevention Morbidity and Mortality Weekly Report (MMWR), from 2005–2011the annual prevalence rate of mental health disorders was between 13%–20% in children (persons aged <18 years) in the U.S. [2]. The annual prevalence of mental health disorders in children is steadily rising in the U.S. with an annual estimated cost of \$247 billion [3]. Mental health disorders in children can have a profound and serious impact on peer and family relationships, educational attainment, and behavior [2]. Half of all mental health disorders increase the risk of adult chronic medical conditions, continuing mental health problems, and decreased productivity and employment [4]. Mental health disorders, along with a combination of other factors such as substance use and access to lethal means, are also associated with suicide, which is the second leading cause of death among children and young adults aged 10 to 34 years [5].

Children with mental health disorders are more likely to suffer from chronic medical conditions, such as asthma, diabetes, and epilepsy, compared with children without mental health disorders [6–9]. However, surveillance of mental health disorders among children with chronic medical conditions is limited, and the literature has substantial methodological limitations [2]. For example, many studies have relied on secondary data analyses of national surveys (e.g., National Survey of Children with Special Health Care Needs), of caregiver reports of mental health symptoms and problems (e.g., feels anxious or depressed, and other similar caregiver indicators of mental health problems) rather than clinical assessment using diagnostic criteria [2]. Reports of mental health symptoms in children vary based on the individual who is reporting and the measure used in the evaluation [2,9]. Evidence suggests that parents are more likely to report externalizing mental health symptoms (e.g., hyperactivity or aggression) than to report internalizing mental health symptoms (e.g., feelings of sadness, worry, hopelessness), which might introduce bias in estimates of mental health symptoms [9,10]. Documenting the prevalence of mental health disorders among children with chronic medical conditions is critical for providers so that they can identify children at higher risk for mental health disorders, provide screening, diagnosis, and subsequent treatment. In addition, early identification can prevent further problems in this at-risk group of children, including poor health, mental health, and social outcomes. Prevalence estimates also inform the development of mental health policies and resource allocation [9,11].

We analyzed data from the Coordinated Health Care for Complex Kids (CHECK) program in Chicago to examine the prevalence of mental health diagnoses among publicly insured children with chronic medical conditions. The current study had two goals: 1) to describe the distribution of the most common mental health diagnoses among children with chronic medical conditions who are enrolled in CHECK, and 2) to examine how the presence of mental health diagnoses may differ by age, race/ethnicity, and type of chronic medical condition (asthma, diabetes, sickle cell disease, epilepsy, and other chronic medical conditions). This study adds to the literature by examining children with mental

health disorders that were diagnosed by clinicians using the International Classification of Diseases, 9th and 10th Revisions, Clinical Modification (ICD).

## Methods

#### Study Sample

Data for this study were from CHECK, a \$19.8 million demonstration project funded by the Centers for Medicare and Medicaid Innovation Center [12]. The CHECK program provided comprehensive services (care coordination, oral health, provider support, technology systems, legal services, and behavioral health) to address the social determinants of health of publicly insured children with chronic medical conditions. The CHECK intervention model is described in detail elsewhere [12–17],.

The data for this study were collected from December 1, 2014 through September 1, 2017. Children were identified for CHECK program eligibility based on Medicaid claims data that included their medical diagnosis, age, and Medicaid eligibility. The CHECK program is located at the University of Illinois at Chicago, which has a primary service area that covers approximately 2 million people including the poorest communities in Chicago, IL [18]. Our analytic sample included children between age 5–18 who were enrolled in Medicaid and had a diagnosis of asthma, diabetes mellitus, sickle cell disease, and/or epilepsy (target diagnoses). The CHECK program targeted these chronic conditions because of the high prevalence of asthma and the high medical needs and costs associated with the other conditions. Many of the CHECK participants had more than one of the chronic conditions and may also have had other conditions such as obesity, food allergies, and hypertension. For the purposes of this study, we analyzed the chronic conditions targeted by the CHECK program. The CHECK program did not target children with mental health diagnoses for enrollment. The University of Illinois at Chicago Institutional Review Board approved this study (protocol #2017–0604).

#### Measures

Mental health diagnoses were extracted using ICD codes from Medicaid claims data. We developed a list of codes a priori and then screened for identification of these codes. We limited our analyses to the four most prevalent mental health diagnostic categories among the sample; (1) mood disorders [F30-F39], (2) attention deficit hyperactivity disorder (ADHD) [F90], (3) anxiety disorders [F40-F48], and (4) conduct disorders [F91]). Conduct disorders included oppositional defiant disorder (F91.3). Mental health diagnoses were not mutually exclusive, children with any combination of the four most prevalent mental health diagnostic categories were included. The covariates, age, sex, and chronic medical condition, were extracted from medical claims data. Age was categorized as 5–8, 9–13, and 14–18. Sex was dichotomized female or male. Chronic medical condition was categorized as Black, Hispanic, or other. Because a large proportion of children's race/ethnicity variable was missing (10.9%), race/ethnicity was imputed using the multiple imputation method. Missing race/ethnicity was predicted from the distribution of observed data iteratively [19] with improved degrees of freedom for multivariate significance tests obtained from multiple

imputed datasets [20,21]. The variable was estimated 40 times, which allows a reasonable level of power falloff, less than 5%, that is acceptable considering the fact that our dataset has a relatively large sample size [22]. Census tract level sociodemographic variables were used for the multiple imputation including: % Black, % White, % Hispanics, % of females with less than high school education, and % of children with asthma and diabetes. A total of 705 cases were imputed.

#### Data analysis

Data were analyzed using Stata<sup>®</sup> 15 (Stata Corporation LP, College Station, TX, USA). Univariate analyses were performed to describe the distribution within the sample. Bivariate analyses were conducted to identify variables that were significantly associated with mental health diagnoses. Logistic regression adjusting for age, sex, race/ethnicity, and chronic medical condition was used to examine predictors of a diagnosis of a mental health diagnosis. Adjusted predicted probabilities were calculated post estimation for age groups stratified by race/ethnicity. An alpha of 0.05 was used to determine significance for all statistical comparisons.

## Results

The sample included 6,458 children (Table 1) and contained more males (57.1%) than females (42.9%). There were fairly equal numbers of children within the three age categories, with 32.2% of children aged 5–8, 35.3% aged 9–13, and 32.5% aged 14–18. About 94% of the children were racial and ethnic minorities. The most common chronic medical condition was asthma (73.9%) followed by chronic conditions in the "other" category (16.7%), diabetes (4.8%), epilepsy (3.2%), and sickle cell disease (1.5%). Overall, 15.4% of children had one or more mental health diagnoses. The most prevalent diagnoses were mood disorders (8.6%), followed by ADHD (7.4%), conduct disorders (6.1%), and anxiety disorders (4.8%). Of the sample, 5.5% had only one reported mental health diagnosis, 6.1% had two, and 6.0% had three or more.

In the bivariate analyses (Table 2), mood disorders, ADHD and anxiety disorders were significantly associated with age, sex, and race/ethnicity. Conduct disorders were significantly associated with age and sex, but not with race/ethnicity categories (Table 2). Diabetes was associated with mood and anxiety disorders, sickle cell disease was associated with ADHD, anxiety disorder, and conduct disorders, and other chronic conditions was associated with conduct disorders. The multivariable analyses (Table 3) show that the adjusted odds of diagnoses increased with age for all four mental health diagnostic categories. Males had lower odds of being diagnosed with mood and anxiety disorders and higher odds of being diagnosed with ADHD and conduct disorders when compared with females. Blacks had lower odds of being diagnosed with anxiety and mood disorders and ADHD than children in the other race/ethnicity category. Hispanics had lower odds of being diagnosed with ADHD compared with children in the other race/ethnicity category. Children with asthma had higher odds of being diagnosed with mood, anxiety, conduct disorders and ADHD compared with children in the other chronic condition category. Children with epilepsy had significantly higher odds of being diagnosed with anxiety disorders, ADHD,

and conduct disorders. The predicted probability of diagnosis was significantly associated with child's age (Figure 1). Diagnosis of mood and anxiety disorders and conduct disorders increased with age. For ADHD, the probability of diagnosis increased from age category 5–8 to age category 9–13 and then decreased after age 14. The probability of receiving a diagnosis of an anxiety or mood disorder was lower for Blacks than for Hispanics and for children in the other race/ethnic category. The probability of being diagnosed with ADHD was significantly higher for children in the other race/ethnicity category than Blacks and Hispanics. However, the probability of being diagnosed with conduct disorders was similar for Blacks and children in the other race/ethnic category and lower in Hispanics.

## Discussion

Our study found higher rates of mental health diagnoses among children with chronic medical conditions when compared with national estimates of children without chronic medical conditions [2]. Also, compared with findings from the MMWR, we found that children in our cohort had higher rates of mood disorders (8.6% v. 2.1–6.7%), anxiety disorders (4.8% v. 0.7–3%), and conduct disorders (6.1% v. 2.1–3.5%), and similar rates of ADHD (7.4% v. 6.8–8.6%) [2]. One study found that after controlling for sociodemographic and healthcare variables, children with at least one chronic medical condition were 62% more likely to have a mental health diagnosis compared with children without chronic medical conditions [23]. Consistent with our findings, children with asthma, epilepsy, and diabetes have been found to have higher rates of mental health diagnoses than children without these conditions [8]. We also found that age and sex were significantly associated with all four the of the mental health diagnoses. Similar to national estimates, prevalence of mood, anxiety, and conduct disorders increased with age and children age 8 and younger and 15 and older were less likely to be diagnosed with ADHD compared with children age 9–14 [2]. Consistent with existing studies, males were less likely to be diagnosed with internalizing disorders (e.g., mood and anxiety disorders) and more likely to be diagnosed with externalizing disorders (e.g., ADHD and conduct disorders) compared with females [24].

The CHECK cohort is comprised of children with chronic medical conditions who are predominantly racial/ethnic minorities and enrolled in public health insurance. The cohort represents a particularly vulnerable and marginalized group of children, and we argue that the disparity in the higher mental health diagnostic rates between the cohort and the general population is due to the compounding effects of having a chronic medical condition, living in poverty, and the experiences of being a racial/ethnic minority. Children with chronic medical conditions and their families experience additional social, psychological, and financial stress that impact children's development, their social and academic outcomes, and their functioning [25]. Likewise, living in poverty can impede children's healthy development and lead to multiple adverse outcomes throughout the life course, including poor mental health [26, 27],. The intersection of poverty and racial/ethnic minority status is a complex interaction that produces disparities in financial and psychosocial resources, exposure to environmental risks, and differential access to health and behavioral health care [4]. Indeed, disparities in access to mental health care persists across time for racial/ethnic minorities [26,28].

The environment is an important predictor of the prevalence and course of mental health disorders [26]. Children in this cohort reside in highly disadvantaged areas of Chicago, IL with high rates of violence and disorganization [18]. These structural conditions shape children's lives and opportunities and have lasting social, physical, and mental health consequences [26]. Structural factors, including neighborhood living conditions, such as racial residential segregation, concentrated disadvantage, and violence play an important role in producing and maintaining health and behavioral health disparities [4]. Racial/ethnic minority children are disproportionately exposed and impacted by adverse factors such as trauma, stress, pollution, poor housing, violence, and bullying that produce harmful mental health outcomes [26,29]. In general, exposure to toxic stress and adverse childhood experiences are well-documented determinants of mental health problems and disorders [6,26],. Our findings warrant additional research to develop and test interventions that incorporate a multilevel approach to address the mental health of children with chronic medical conditions that mitigate the impact of neighborhood disadvantage.

We found that Blacks had lower odds of diagnosis of mood and anxiety disorders and ADHD than children in the other racial/ethnic category. Hispanics had lower odds of diagnosis of ADHD compared with children in the other racial/ethnic category. This difference in prevalence suggests a further disadvantage for racial/ethnic minority children if they have a mental health disorder but may not have been diagnosed with it. Previous studies also have found lower rates of diagnosis of ADHD in minority children compared with White children; moreover, confounding factors, such as poverty and limited access to care, have not explained the disparity in diagnosis and treatment, which seems to suggest that the disparity is related primarily to the children's status as a racial/ethnic minority [6,30]. The lower rate of mental health diagnoses among racial/ethnic minority children compared with children who are non-minority children may reflect the lack of access to mental health services in Chicago, particularly in the most disadvantaged areas where minorities reside [31]. State mental health funding has dramatically decreased in Illinois between 2011–2017 which are the years before and during enrollment in CHECK [31]. For example, between 2009 and 2012 Illinois made a \$187 million cut to mental health spending which was the fourth-largest decrease nationally [30] (Advocates, 2015). Then, at the city-level in 2012, the Chicago Department of Public Health consolidated 12 city mental health centers to six which may have further limited access to care [31].

Black children in the cohort were equally diagnosed with conduct disorders compared with children in the other racial/ethnic category. Children with conduct disorders display a pervasive pattern of behavior that is characterized by violating the rights of others, societal norms, and/or rules [32]. Often, children with conduct disorders engage in verbal and physical aggression towards others, bullying, cruelty towards animals, destruction of property, and severe rule violations across a variety of settings [32]. Among children aged 3–17 years, 8.1% of Blacks, 4.2% of Whites, and 3.9% of Hispanics report ever receiving a behavioral or conduct problem diagnosis and/or conduct problems have been reported by parents [2]. Available data of the lifetime prevalence of conduct disorders is 6.9% for Hispanics, 4.9% for Blacks, and 5.0% for Whites [33]. Multiple studies have documented that this diagnosis a strong predictor of later antisocial and criminal behavior and a multitude of other problematic issues such as co-occurring mental health diagnoses, substance abuse,

legal problems, academic, and occupational problems [34–37],. Some researchers have argued that diagnostic bias contributes to over diagnosis of conduct disorders in minority children who then often face poorer mental health and juvenile justice outcomes than their White counterparts [38,39].

Our study had several limitations. One of the limitations of our study was missing race/ ethnicity data. Medical claims data do not include race/ethnicity. The race/ethnicity data we used were collected by CHECK field-staff members who conducted assessments with families and entered the data into the medical record. We also received race/ethnicity data from schools. To address the missing race/ethnicity data, we imputed the data using the STATA multiple imputation method [40]. All other variables (i.e., age, sex, chronic medical condition) were obtained from the medical claims.

It is likely that mental health disorders were underestimated in our population. First, previous studies have found that many children are not screened for mental health disorders [1,26]. This is likely to be the case in our population. As a result, many of the children who were not identified and diagnosed in our sample could still have mental health disorders. Second, our study focused only on diagnosed mental health disorders. It is estimated that sub-threshold mental health disorders affect a large proportion of the population, [4]. Consequently, it is possible that our findings might have been different if we had the means to collect and include sub-threshold mental health disorders. Finally, medical claims data may include coding errors or missing documentation.

Another limitation is the potential for misdiagnosis, which occurs in the information gathering from the informant (e.g., child and parent) and/or influences on the clinician diagnosing the child [41]. Many clinicians have not received training in diagnosing mental health disorders, therefore it is possible that children may have been inaccurately diagnosed (e.g., misclassified). Moreover, clinicians rely on clusters of defined feelings, thoughts, and behaviors described in the ICD to diagnosis mental health disorders, which requires clinical judgement. Clinicians' judgement in diagnosing patients is affected by their training, heuristics, and biases [41]. Finally, evidence suggests that intentional over diagnosis of mental health disorders is a common practice because access to and reimbursement for treatment requires patients to have a documented mental health disorder. The study was limited to the data available about children and their families. All children were publically insured, however, most likely there was a range of socioeconomic factors and conditions that influence family's experiences and access to care. Finally, this study examined data from children in the CHECK program who have chronic medical conditions, are enrolled in Medicaid, and reside in Chicago. As such, the results may not be generalizable to other children without chronic medical conditions, who are not publicly insured, and/or reside outside of Chicago.

Our study advances knowledge about the prevalence of mental health diagnoses among children with chronic medical conditions, documents the magnitude of the needs of this cohort, and contributes to the growing literature documenting pediatric comorbidity of chronic medical conditions and mental health diagnoses. We analyzed data from a large cohort to ascertain prevalence estimates based on clinician diagnosed mental health

disorders. Understanding the prevalence of mental health diagnoses among children with chronic conditions is vital for planning and allocating resources for comprehensive health and mental health care delivery services, including pediatric universal mental health screening [42].

Our findings document the high prevalence of mental health diagnoses among children with chronic conditions and also raises awareness among clinicians and policymakers about the need for models of care delivery that integrate health and behavioral health care coordination and management. Although we report a higher prevalence of mental health diagnoses in our large cohort of children with chronic medical conditions compared with national estimates of children without chronic medical conditions, it is likely that the true prevalence of mental health diagnoses among this group of children may be even higher. Other studies have shown the children who were racial and ethnic minorities were less likely to have a mental health diagnosis when compared with White children, which suggests under identification of mental health needs particularly in minority children. Under identification of mental health disorders often results in a lack of treatment and resources to address the problem. For example, children with ADHD are eligible for additional school-related services such as specialized adaptations that support their educational success [26]. When children are identified as having ADHD, they are more likely to receive treatment to help them cope with their condition which can improve their psychosocial, behavioral, and educational outcomes. We believe that our findings support the proposition that universal mental health screening for children would remedy under-assessment, particularly for children with chronic medical conditions and racial/ethnic minorities [42]. Future research is needed to examine the complex intersection between having a chronic medical condition, living in poverty, and being a member of a racial/ethnic minority group.

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## Abbreviations:

ADHD	Attention Deficit Hyperactivity Disorder
CHECK	Coordinated Healthcare for Complex Kids
CI	Confidence Interval

ICD	International Classification of Diseases, 9th and 10th Revisions, Clinical Modification
MMWR	Centers for Disease Control and Prevention Morbidity and Mortality Weekly Report
U.S.	United States

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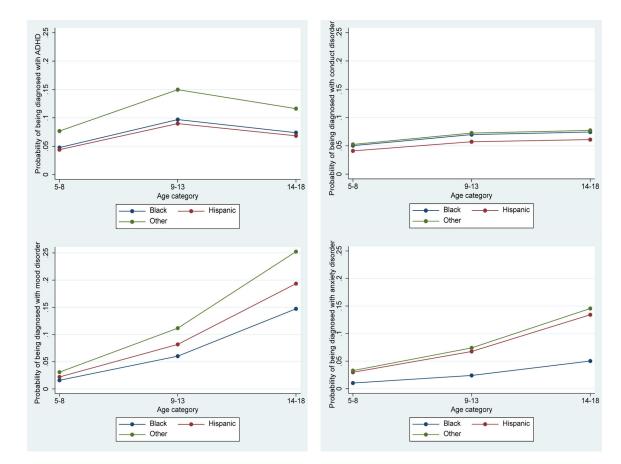
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### Figure 1.

Probability of children with chronic medical conditions enrolled in CHECK being diagnosed with mental health disorders by age and race, 2014-2017 (N = 6458): Chicago, IL.

Sample characteristics and prevalence of mental health disorders among children with chronic medical conditions enrolled in CHECK, 2014–2017.

	Total	No mental health diagnosis	Mental health diagnosis	s
	6458 (100.0%)	5463 (84.6%)	995 (15.4%)	<u>∽</u> I
Age				
5–8 years	2077 (32.2)	35.5	17.2	
9-13 years	2282 (35.3)	35.3	35.5	<.01
14–18 years	2099 (32.5)	29.2	47.3	
Sex				
Female	2772 (42.9)	43.2	41.8	
Male	3686 (57.1)	56.8	58.2	n.s.
Race/Ethnicity				
Black	3926 (60.8)	62.8	54.6	
Hispanic	2157 (33.4)	32.9	38.7	<.01
Other	375 (5.8)	4.3	6.7	
Chronic Condition				
Asthma	4772 (73.9)	3892 (73.6)	749 (75.3)	n.s.
Diabetes	309 (4.8)	235 (4.4)	67 (6.7)	<.01
Epilepsy	207 (3.2)	136 (2.6)	62 (6.2)	<.01
Sickle Cell Disease	96 (1.5)	82 (1.6)	12 (1.2)	n.s.
Other	1078 (16.7)	906 (17.1)	149 (14.8)	<.05
<b>Mental Health Disorders</b>				
Mood Disorders			558 (8.6)	
ADHD			479 (7.4)	
Anxiety Disorders			310 (4.8)	
Conduct Disorder			394 (6.1)	
Number of Mental Health Disorders				
0			5289 (81.9)	
1			358 (5.5)	
2			392 (6.1)	
3 or more			419(6.0)	

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	Total %	<b>Mood Disorders</b>	d	ADHD	d	<b>Anxiety Disorders</b>	d	<b>Conduct Disorders</b>	d
	N=6458	558 (8.6)		479 (7.4)		310 (4.8)		394 (6.1)	
Characteristics	Percent	Percent		Percent		Percent		Percent	
Age									
5-8 years	32.2	6.8		21.2		11.6		25.4	
9–13 years	35.3	28.3	<.01	47.5	<.01	30.3	<.01	38.6	<.05
14-18 years	32.5	64.9		31.3		58.1		36	
Sex									
Female	42.9	54.7	<.01	24.8	<.01	52.9	<.01	29.7	<.01
Male	57.1	45.3		75.2		47.1		70.3	
Race/Ethnicity									
Black	61.4	52.7		61		36		65	
Hispanic	33.9	39.6	<.01	31.5	<.05	55.5	<.01	29.7	n.s.
Other	4.7	7.7		7.5		8.5		5.3	
Chronic Condition									
Asthma	73.9	74.9	n.s.	76.9	n.s.	76.1	n.s.	76.9	n.s.
Diabetes	4.8	8.1	<.01	4.4	n.s.	7.7	<.05	4.6	n.s.
Epilepsy	3.2	3.6	n.s.	0.6	n.s.	1.6	n.s.	1.3	n.s.
Sickle Cell Disease	1.5	1.6	n.s.	8.2	<.01	7.1	<.01	7.6	<.01
Other	16.7	15.6	n.s.	14.1	n.s.	14.2	n.s.	13.5	<.05

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Adjusted odds ratios of children with chronic medical conditions enrolled in CHECK being diagnosed with a mental health disorder by demographic and health characteristics, 2014-2017 (N = 6458)

	Mood Disorders	ADHD	Anxiety Disorders	Conduct Disorders
Variables	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Age Category				
5-8 years	0.25 * (0.18, 0.36) *	$0.46^{*}(0.36, 0.59)^{*}$	$0.25 \ ^{*}(0.18, 0.36) \ ^{*}$ $0.46 \ ^{*}(0.36, 0.59) \ ^{*}$ $0.42 \ ^{*}(0.29, 0.62) \ ^{*}$ $0.31 \ ^{*}(0.21, 0.46) \ ^{*}$	$0.31$ $^{*}(0.21, 0.46)$ $^{*}$
9–13 years	Reference	Reference	Reference	Reference
14–18 years	2.71 *(2.22, 3.31) *	0.74 *(0.59, 0.92) *	2.16 <sup>*</sup> (1.66, 2.80) * 1.15 (0.93, 1.42)	1.15 (0.93, 1.42)
Sex				
Female	Reference	Reference	Reference	Reference
Male	$0.66^{*}(0.55, 0.78)^{*}$	2.41 *(1.94, 2.99) *	$0.71^{*}(0.56, 0.89)^{*}$ 1.83 <sup>*</sup> (1.47, 2.28) <sup>*</sup>	1.83 *(1.47, 2.28) *
Race/ethnicity				
Other	Reference	Reference	Reference	Reference
Black	$0.51$ $^{*}(0.35, 0.74)$ $^{*}$	0.64 (0.43, 0.94) *	$0.31^{*}(0.20, 0.54)^{*}$ 1.00 (0.64, 1.62)	1.00 (0.64, 1.62)
Hispanic	0.72 (0.49, 1.05)	0.59 (0.39, 0.89) *	0.96 (0.61, 1.51)	0.85 (0.51, 1.40)
Chronic Condition				
Other	Reference	Reference	Reference	Reference
Asthma	$1.32^{*}(1.05, 1.67)$	1.37 (1.07, 1.76) *	$1.68^{*}(1.23, 2.29)^{*}$	$1.68^{*}(1.23, 2.29)^{*}$ $1.54^{*}(1.18, 2.00)^{*}$
Diabetes	1.29 (0.89, 1.85)	1.11 (0.69, 1.81)	1.43 (0.89, 2.31)	1.20 (0.72, 2.01)
Epilepsy	1.22 (0.74, 2.01)	3.51*(2.38, 5.18) *	3.08 *(1.87, 5.06) *	3.16*(2.09, 4.78) *
Sickle cell disease	1.49 (0.71, 3.13)	$0.52\ (0.16,1.70)$	2.45 (0.94, 6.39)	1.29 (0.55, 3.06)

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\*\* p<.01, \* p<05