Original Article

Association Between Rhinitis and Depression in United States Adults

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What is already known about this topic? Increasing evidence suggests a link between allergic disorders and depression, but little is known about the relationship between rhinitis and depression on a population level.

What does this article add to our knowledge? This cross-sectional study demonstrates that United States adults with nonallergic rhinitis are twice as likely to have depression as those without rhinitis, whereas there was no association with allergic rhinitis.

How does this study impact current management guidelines? This population-based study demonstrates that United States adults with nonallergic rhinitis are twice as likely to suffer from depression as those without rhinitis, suggesting that providers should consider depression while evaluating patients for rhinitis.

BACKGROUND: Growing evidence suggests a link between allergic disorders and depression, but literature assessing the association between rhinitis and depression is conflicting, and large population-based studies are lacking.
OBJECTIVE: To assess the association between depression and rhinitis in a representative sample of United States adults.
METHODS: We performed a cross-sectional analysis of 4320 participants in the 2005-2006 National Health and Nutrition Examination Survey. Rhinitis was defined as self-reported hay fever and/or nasal symptoms in the past 12 months. Rhinitis was further stratified as allergic rhinitis (AR) if participants had a positive serum IgE or nonallergic rhinitis (NAR) if participants did not have a positive serum IgE to any aeroallergen. The outcome variable was depression, defined as a score ≥10 on the Patient Health Questionnaire-9.
RESULTS: The odds of depression were 42% higher in subjects with rhinitis compared with those without rhinitis (odds ratio [OR]: 1.42, confidence interval [CI]: 1.03-1.95, $P = .04$) and 2 times higher in subjects with NAR compared with those without rhinitis (OR: 1.99, CI: 1.34-2.96, $P = .002$). Subjects with NAR had 64% higher odds of mild depression (OR: 1.64, CI: 1.32-2.02, $P < .001$) and 2.4 times higher odds of moderate depression (OR: 2.43, CI: 1.39-4.26, $P = .004$) compared with subjects with no rhinitis.
CONCLUSIONS: Rhinitis is significantly associated with depression, and patients with NAR may be at higher risk of depression than those with AR. Although further studies are required to elucidate the relationship between rhinitis and depression, these findings reinforce the need to consider depression in patients undergoing evaluation for rhinitis. **© 2019 American Academy of Allergy, Asthma & Immunology** **(J Allergy Clin Immunol Pract 2019;7:2013-20)**

Key words: *Allergic rhinitis; Nonallergic rhinitis; Rhinitis; Depression; National Health and Nutrition Examination Survey*

Major depression is a worldwide public health problem that affects approximately 4% of the global population.[1] This psychiatric disorder represents a major cause of impairment, disability, economic burden, and mortality.[2-5] Allergic rhinitis (AR) and nonallergic rhinitis (NAR) are 2 of the most common diseases globally. Prevalence estimates for AR range from 10% to 40% worldwide depending on geographic location, and AR affects approximately 60 million people in the United States.[6-9] NAR affects at least 200 million people worldwide, and approximately 20 million people in the United States.[10,11] AR and NAR affect approximately 60 and 20 million people in the United States, respectively.[9,11] These disorders also have a profound impact on patient quality of life and productivity and have been shown to have a significant economic burden as well.[12]

There is increasing evidence in the literature to suggest an association between allergic disorders and depression.[13] A small cohort study suggested a correlation between seasonal aeroallergen counts and depression scores,[14] and a large population study from Denmark reporting a spring peak in suicide rates that

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Abbreviations used
AR- Allergic rhinitis
BMI- Body mass index
NAR- Nonallergic rhinitis
NHANES- National Health and Nutrition Examination Survey
PHQ-9- Patient Health Questionnaire-9

may coincide with peaks in aeroallergen levels, particularly pollen.[15] However, this association needs further exploration, and previous large-scale population-based studies in the United States have largely analyzed asthma and atopic dermatitis rather than AR,[16-20] with 1 previous study revealing an association between hay fever, lower back pain, and depression in 20- to 39-year-old US adults.[21] A recent large systematic review of 51 studies revealed a significant association between AR and depression,[22] but previous population-based analyses in Australia and Asia showed inconsistent results regarding the relationship between AR and depression.[23-26]

To our knowledge, there are no US population-based studies assessing the association between AR, NAR, and depression. The National Health and Nutrition Examination Survey (NHANES) is an ongoing population-based survey conducted by the US Centers for Disease Control and Prevention, with the purpose of estimating disease prevalence.[27] The purpose of this study was to investigate the relationship between rhinitis and depression in a representative sample of US adults.

METHODS

Data source

The NHANES uses a complex stratified multistage sampling design to select a nationally representative sample of noninstitutionalized US civilians to participate in a series of comprehensive health-related interviews and examinations every 2 years. Recruitment and testing are performed across the United States, with 15 different counties visited yearly. The NHANES purposefully oversamples larger numbers of certain subgroups of particular public health interest including Mexican Americans, African Americans, and persons 60 years of age or older, to increase the reliability and precision of the health-related information gathered about these demographic groups. The NHANES protocols were approved by the National Center for Health Statistics research ethics review board and informed consent was obtained from all participants.

Demographics

Data regarding participants' age, gender, and race were collected in a demographic questionnaire. NHANES investigators categorized race and ethnicity into 5 categories: Mexican American, other Hispanic, non-Hispanic black, non-Hispanic white, and non-Hispanic other or multiracial. For this analysis, race was classified as white, black, Hispanic, and other. Participants' body mass indices (BMI) were obtained from the body measurements examination, and obesity was defined as BMI $\geq$ 30 kg/m^2.

Allergy questionnaire

The NHANES allergy component was administered in the 2005-2006 cycle and consisted of 3 parts: (1) collecting self-reported allergic disease information through household interview questionnaires, (2) analyzing allergen and endotoxin from the dust extract, and (3) measuring total and allergen-specific IgE from a blood sample drawn at the NHANES mobile examination site. The laboratory analysis of sensitization to specific serum IgE antigens was performed using the Pharmacia Diagnostics ImmunoCAP 1000 System (Kalamazoo, Mich) and included perennial aeroallergens (*Dermatophagoides farinae*, Dermatophagoides pteronyssinus, cat, dog, mouse, rat, cockroach, *Alternaria*, and *Aspergillus*), seasonal aeroallergens (ragweed, rye grass, Bermuda grass, oak, birch, and thistle), and food allergens (peanut, egg, milk, and shrimp). For each allergen, a positive result was defined as a serum level at or above the detection limit, and a negative result was defined as a serum level below the lower detection limit. The lower limit of detection was the same for the each of the allergen-specific IgE antibody tests, and equal to 0.35 kU/L.

This study included analyses of questionnaire data and serum IgE data, but did not include analyses of endotoxin from dust extracts. The questionnaire included questions about common allergic diseases such as hay fever, allergies and eczema, as well as symptoms associated with these conditions. For this analysis, rhinitis was defined as an answer of "yes" to either of these 2 questions: "during the past 12 months, have you had an episode of hay fever?" and/or "during the past 12 months, have you had a problem with sneezing, or a runny, or blocked nose when you did not have a cold or the flu?"

Rhinitis was subsequently subclassified into AR and NAR groups using serum allergen-specific IgE data. Participants were classified as having AR if they answered "yes" to either of 2 rhinitis questions and also had a history of positive serum IgE. Participants were classified as having NAR if they answered "yes" to either of 2 rhinitis questions and did not have a history of positive serum IgE. Patients with missing serum IgE data were classified as having an unknown type of rhinitis and were excluded from analyses comparing AR versus NAR. Patients with AR were also stratified into perennial AR if they had a positive serum IgE to any of the perennial aeroallergens and seasonal AR if they had a positive serum IgE to any of the seasonal aeroallergens. This study was focused on the relationship of inhalant AR and NAR to depression, and therefore food allergens were not included in any data analysis.

Depression screener questionnaire

Participants 18 years or older in the 2005-2006 NHANES were offered the mental health − depression screener, which consisted of questions from the Patient Health Questionnaire-9 (PHQ-9). This questionnaire is a validated, self-reported version of the depression module of the Primary Care Evaluation of Mental Disorders questionnaire. It is designed to assess each of 9 diagnostic criteria of major depression as outlined by the Diagnostic and Statistical Manual of Mental Disorders, fourth edition, with respect to how much each symptom has bothered the participant in the previous 2 weeks. Scores of 0 (not at all) to 3 (every day) are tabulated with an overall score ranging from 0 to 27. A score of $\geq$10 was previously reported to be 88% sensitive and 88% specific for major depression.[28] Further stratification of depression severity was performed based on PHQ-9 scores of 5, 10, 15, and 20 corresponding to mild, moderate, moderately-severe, and severe depression.[28]

Covariates

Potential confounders in this analysis included demographic factors including age, gender, race, obesity; comorbid medical conditions including self-reported history of asthma, coronary artery disease, heart attack, stroke, thyroid disease, emphysema, chronic bronchitis, and trouble seeing; and self-rated general health condition (excellent, very

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TABLE I. Characteristics of the study population

	Study population
	N = 4320
	Mean or % (CI)
Age, y	46.5
Age, y	
20-29	18.7% (16.9% to 20.7%)
39-30	19.0% (15.6% to 21.6%)
40-49	21.5% (19.0% to 24.3%)
50-59	18.0% (16.1% to 20.1%)
60-69	11.2% (9.6% to 13.0%)
70-79	7.7% (6.1% to 9.8%)
80 and above	3.8% (3.0% to 4.9%)
Sex	
Male	48.4% (46.9% to 50.0%)
Female	51.6% (50.1% to 53.1%)
Race	
White	73.3% (67.2% to 78.7%)
Black	10.9% (7.5% to 15.5%)
Hispanic	11.0% (8.4% to 14.3%)
Other	4.8% (3.8% to 6.2%)
Obesity	34.5% (31.3% to 37.9%)
Smoking	
Never	50.7% (47.7% to 53.7%)
Current	24.0% (21.4% to 26.7%)
Former	25.3% (23.0% to 27.8%)
Comorbidities	
Asthma	14.0% (12.6% to 15.6%)
Emphysema	1.8% (1.3% to 2.4%)
Chronic bronchitis	6.6% (5.8% to 7.7%)
Coronary artery disease	3.3% (2.6% to 4.2%)
Heart attack	3.4% (2.6% to 4.5%)
Stroke	2.8% (2.2% to 3.5%)
Thyroid disease	10.1% (8.7% to 11.7%)
Trouble seeing	18.4% (16.6% to 20.4%)
General health	
Excellent	10.9% (9.4% to 12.6%)
Very good	35.8% (32.6% to 39.1%)
Good	37.2% (34.5% to 39.9%)
Fair	14.0% (12.6% to 15.6%)
Poor	2.1% (1.8% to 2.6%)
Depression	
PHQ score ≤ 9	94.6% (93.3% to 95.6%)
PHQ score ≥ 10	5.5% (4.4% to 6.7%)
Depression	
None	80.1% (77.6% to 83.4%)
Mild	14.5% (12.9% to 16.1%)
Moderate	3.7% (3.0% to 4.5%)
Moderate-severe	1.4% (1.0% to 2.0%)
Severe	0.4% (0.3% to 0.6%)

NHANES, National Health and Nutrition Examination Survey; *PHQ*, Patient Health Questionnaire.

Means, proportions (%), and confidence intervals (CI) are weighted estimates of US population characteristics taking into account NHANES' complex sampling design. Depression severity none (PHQ score 0-4), mild (PHQ score 5-9), moderate (PHQ score 10-14), moderate-severe (PHQ score 15-19), and severe (PHQ score 20-27).

good, good, fair, poor). The prevalence of each of the medical comorbidities was compared among subjects with and without rhinitis, and those that differed across the 2 groups were included as a covariate in the multivariable logistic regression.

Study population

The study population for this analysis included 4320 subjects from the 2005-2006 NHANES cycle aged 20 years and older at the time of NHANES participation who participated in the allergy and depression screener questionnaires. There was 1 subject aged 20 years and older with missing data from the allergy questionnaire, so his rhinitis status could not be ascertained, and this subject was excluded from further analysis. Although the depression screener was offered to subjects aged 18 years and older, most of the questions about self-reported medical comorbidities were only asked to subjects aged 20 years and older, so there were insufficient covariate data to include 18- and 19-year-old subjects in the multivariable logistic regression analysis. There were 452 subjects aged 20 years and older with missing data from the depression questionnaire, so their depression status could not be ascertained, and these subjects were excluded from further analysis.

Data analysis

US population-weighted baseline demographic and medical characteristics and PHQ-9 scores were calculated for the study population and compared across subjects with and without rhinitis and across subjects with AR and NAR using the design-adjusted Rao-Scott Pearson-type χ^2 and Wald tests for categorical and continuous variables, respectively. Multivariable logistic regression analyses was performed to investigate whether or not rhinitis was an independent predictor for depression screener score ≥ 10, with adjustment for age, gender, race, and the medical comorbidities that differed between subjects with and without rhinitis. An additional series of multivariable logistic regression analyses were performed with the depression outcome variable stratified into groups by severity (mild, moderate, moderately-severe, and severe depression, as determined by PHQ-9 cutoffs described above).

To most accurately calculate confidence intervals around estimates for the US population, all data analysis was performed using 2-year population-weighted data, calculating standard errors of population estimates using Taylor linearization methods. Analyses were performed using Stata (version 12.0; Stata Statistical Software, College Station, Tex). Forest plots were created using R Studio (Version 1.1.447—© 2009-2018 RStudio).

RESULTS

The 2005-2006 NHANES yielded 4320 subjects aged 20 years and older who completed the allergy and depression questionnaires. There were 452 subjects who did not complete the depression questionnaire and were excluded from further analysis. Subjects who did not complete the depression questionnaire were less likely to be white (55.9% vs 73.3%, $P < .01$) compared with those who did complete the depression questionnaire, but there were no differences in age or gender between these 2 groups.

Among the study population, the number of subjects without rhinitis was 2873 and the number of subjects with rhinitis was 1447 (699 with AR, 692 with NAR, and 52 with unknown type of rhinitis). The population-weighted mean age was 46.5 years,

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TABLE II. Characteristics of subjects with and without rhinitis

	No rhinitis N = 2873	All rhinitis N = 1447	
	Mean or % (CI)	Mean or % (CI)	*P* value
Age, y	46.2	47.0	.20
Age, y			.21
20-29	19.6% (17.5% to 21.9%)	17.2% (14.8% to 19.8%)	
39-30	19.4% (16.6% to 22.6%)	18.2% (14.8% to 22.1%)	
40-49	20.2% (17.3% to 23.6%)	23.7% (21.3% to 26.4%)	
50-59	18.1% (15.7% to 20.7%)	18.0% (15.7% to 20.6%)	
60-69	11.3% (9.7% to 13.1%)	11.1% (9.2% to 13.2%)	
70-79	7.4% (6.0% to 9.1%)	8.3% (5.8% to 11.8%)	
80 and above	4.0% (3.2% to 5.0%)	3.6% (2.6% to 4.9%)	
Sex			.01
Male	50.4% (47.9% to 52.8%)	45.2% (42.8% to 47.5%)	
Female	49.7% (47.2% to 52.1%)	54.8% (52.5% to 57.2%)	
Race			<.001
White	69.5% (62.4% to 75.8%)	79.8% (74.9% to 83.9%)	
Black	12.2% (8.4% to 17.4%)	8.6% (5.8% to 12.3%)	
Hispanic	13.1% (9.8% to 17.2%)	7.5% (5.7% to 9.8%)	
Other	5.2% (3.9% to 7.0%)	4.2% (3.2% to 5.5%)	
Obesity	33.8% (30.4% to 37.3%)	35.8% (31.8% to 40.0%)	.24
Smoking			.53
Never	51.5% (49.3% to 53.8%)	49.3% (44.0% to 54.7%)	
Current	23.2% (20.6% to 26.1%)	25.3% (20.8% to 30.3%)	
Former	25.2% (22.6% to 28.1%)	25.4% (22.2% to 28.9%)	
Comorbidities			
Asthma	9.5% (8.4% to 10.7%)	21.8% (19.2% to 24.6%)	<.001
Emphysema	0.9% (0.5% to 1.6%)	3.2% (2.5% to 4.3%)	<.001
Chronic bronchitis	4.8% (3.7% to 6.1%)	9.9% (8.6% to 11.3%)	<.001
Coronary artery disease	3.1% (2.3% to 4.1%)	3.8% (2.8% to 5.0%)	.14
Heart attack	3.0% (2.2% to 4.1%)	4.1% (3.0% to 5.7%)	.02
Stroke	2.5% (1.9% to 3.4%)	3.2% (2.0% to 4.9%)	.37
Thyroid disease	9.0% (7.5% to 10.7%)	12.0% (9.3% to 15.4%)	.052
Trouble seeing	16.0% (14.0% to 18.2%)	22.7% (20.0% to 25.6%)	<.001
General health			.26
Excellent	12.0% (10.4% to 13.7%)	9.1% (6.8% to 12.2%)	
Very good	35.9% (32.2% to 39.8%)	35.5% (29.8% to 41.8%)	
Good	36.9% (34.2% to 39.7%)	37.7% (32.9% to 42.7%)	
Fair	13.1% (11.6% to 14.8%)	15.6% (13.4% to 18.2%)	
Poor	2.2% (1.8% to 2.7%)	2.1% (1.4% to 3.1%)	
Depression			.01
PHQ score ≤ 9	95.4% (94.2% to 96.4%)	93.0% (90.8% to 94.8%)	
PHQ score ≥ 10	4.6% (3.6% to 5.8%)	7.0% (5.2% to 9.2%)	
Depression			<.001
None	83.0% (80.4% to 85.3%)	75.2% (71.2% to 78.8%)	
Mild	12.5% (10.7% to 14.5%)	17.9% (15.8% to 20.1%)	
Moderate	3.0% (2.3% to 3.8%)	4.9% (3.6% to 6.7%)	
Moderate-severe	1.1% (0.7% to 1.8%)	1.8% (1.1% to 3.2%)	
Severe	0.5% (0.3% to 0.9%)	0.2% (0.1% to 0.5%)	

NHANES, National Health and Nutrition Examination Survey; *PHQ*, Patient Health Questionnaire.
Means, proportions (%), and confidence intervals (CI) are weighted estimates of US population characteristics taking into account NHANES' complex sampling design. Depression severity none (PHQ score 0-4), mild (PHQ score 5-9), moderate (PHQ score 10-14), moderate-severe (PHQ score 15-19), severe (PHQ score 20-27).

51.6% of the population was female, and the distribution by race was 73.3% white, 10.9% black, 11.0% Hispanic, and 4.8% other. The prevalence of obesity, smoking, medical comorbidities, general health status, and depression is shown in Table I.

Compared with subjects without rhinitis, subjects with rhinitis were more likely to be female (54.8% vs 49.7%, $P = .01$), white (79.8% vs 69.5%, $P < .001$) and have asthma (21.8% vs 9.5%, $P < .001$), emphysema (3.2% vs 0.9%, $P < .001$), chronic

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TABLE III. Characteristics of subjects with allergic rhinitis and nonallergic rhinitis

	Allergic rhinitis N = 699	Nonallergic rhinitis N = 692	
	Mean or % (CI)	Mean or % (CI)	*P* value
Age, y	43.8	50.7	<.001
Age, y			<.001
20-29	20.3% (17.5% to 23.6%)	12.6% (10.1% to 15.6%)	
39-30	22.3% (17.5% to 28.0%)	14.4% (10.8% to 19.0%)	
40-49	25.6% (21.7% to 29.9%)	21.9% (17.8% to 26.7%)	
50-59	15.1% (10.9% to 20.7%)	21.4% (18.0% to 25.2%)	
60-69	10.3% (7.6% to 13.6%)	11.7% (8.5% to 15.8%)	
70-79	4.3% (2.7% to 6.9%)	12.8% (9.1% to 17.7%)	
80 and above	2.0% (1.3% to 3.0%)	5.2% (3.7% to 7.4%)	
Sex			<.001
Male	51.8% (47.4% to 56.2%)	38.3% (34.5% to 42.3%)	
Female	48.2% (43.8% to 52.6%)	61.7% (57.7% to 65.5%)	
Race			<.001
White	75.2% (69.3% to 80.3%)	84.3% (80.1% to 87.7%)	
Black	10.8% (7.2% to 15.9%)	6.0% (4.0% to 8.8%)	
Hispanic	9.3% (6.9% to 12.5%)	6.0% (4.2% to 8.5%)	
Other	4.6% (3.3% to 6.5%)	3.8% (2.6% to 5.3%)	
Obesity	34.5% (30.6% to 38.6%)	37.1% (31.3% to 43.4%)	.41
Smoking			<.001
Never	57.2% (50.3% to 63.8%)	41.6% (36.7% to 46.6%)	
Current	19.8% (14.9% to 25.8%)	31.1% (25.4% to 37.5%)	
Former	23.0% (19.7% to 26.8%)	27.3% (22.7% to 32.4%)	
Comorbidities			
Asthma	29.1% (23.7% to 35.1%)	15.4% (13.6% to 17.4%)	<.001
Emphysema	1.9% (1.0% to 3.5%)	4.5% (3.3% to 6.1%)	.02
Chronic bronchitis	9.0% (7.1% to 11.2%)	11.0% (8.8% to 13.8%)	.26
Coronary artery disease	2.9% (2.2% to 3.8%)	4.9% (3.4% to 7.0%)	.03
Heart attack	2.8% (1.7% to 4.5%)	5.5% (3.9% to 7.8%)	.01
Stroke	2.0% (1.1% to 3.9%)	4.4% (2.7% to 7.2%)	.04
Thyroid disease	11.0% (8.6% to 14.1%)	13.9% (10.0% to 19.1%)	.14
Trouble seeing	17.7% (13.9% to 22.3%)	28.6% (25.0% to 32.6%)	.002
General health			.001
Excellent	11.6% (8.3% to 16.0%)	7.3% (5.1% to 10.5%)	
Very good	37.0% (30.0% to 44.5%)	34.3% (28.9% to 40.1%)	
Good	38.6% (31.9% to 45.8%)	36.5% (31.8% to 41.5%)	
Fair	11.8% (9.0% to 15.4%)	18.7% (15.6% to 22.2%)	
Poor	1.0% (0.5% to 2.2%)	3.2% (2.0% to 5.3%)	
Depression			<.001
PHQ score ≤ 9	95.5% (94.1% to 96.6%)	90.4% (86.8% to 93.1%)	
PHQ score ≥ 10	4.5% (3.4% to 5.9%)	9.6% (6.9% to 13.2%)	
Depression			<.001
None	79.5% (74.8% to 83.5%)	70.9% (66.3% to 75.1%)	
Mild	16.0% (12.7% to 20.0%)	19.5% (16.9% to 22.4%)	
Moderate	3.1% (2.4% to 4.0%)	7.0% (4.8% to 10.1%)	
Moderate-severe	1.2% (0.6% to 2.3%)	2.5% (1.2% to 4.9%)	
Severe	0.3% (0.1% to 0.6%)	0.2% (0.03% to 1.0%)	

NHANES, National Health and Nutrition Examination Survey; *PHQ*, Patient Health Questionnaire.
Means, proportions (%), and confidence intervals (CI) are weighted estimates of US population characteristics taking into account NHANES' complex sampling design. Depression severity none (PHQ score 0-4), mild (PHQ score 5-9), moderate (PHQ score 10-14), moderate-severe (PHQ score 15-19), severe (PHQ score 20-27).

bronchitis (9.9% vs 4.8%, $P < .001$), heart attack (4.1% vs 3.0%, $P = .02$), trouble seeing (22.7% vs 16.0%, $P < .001$), and depression screener score $\geq$10 (7.0% vs 4.6%, $P = .01$) (Table II).

Compared with subjects with AR, subjects with NAR were more likely to be older (50.7 years vs 43.8 years, $P < .001$), female (61.7% vs 48.2%, $P < .001$), white (84.3% vs 75.2%, $P < .001$), and have

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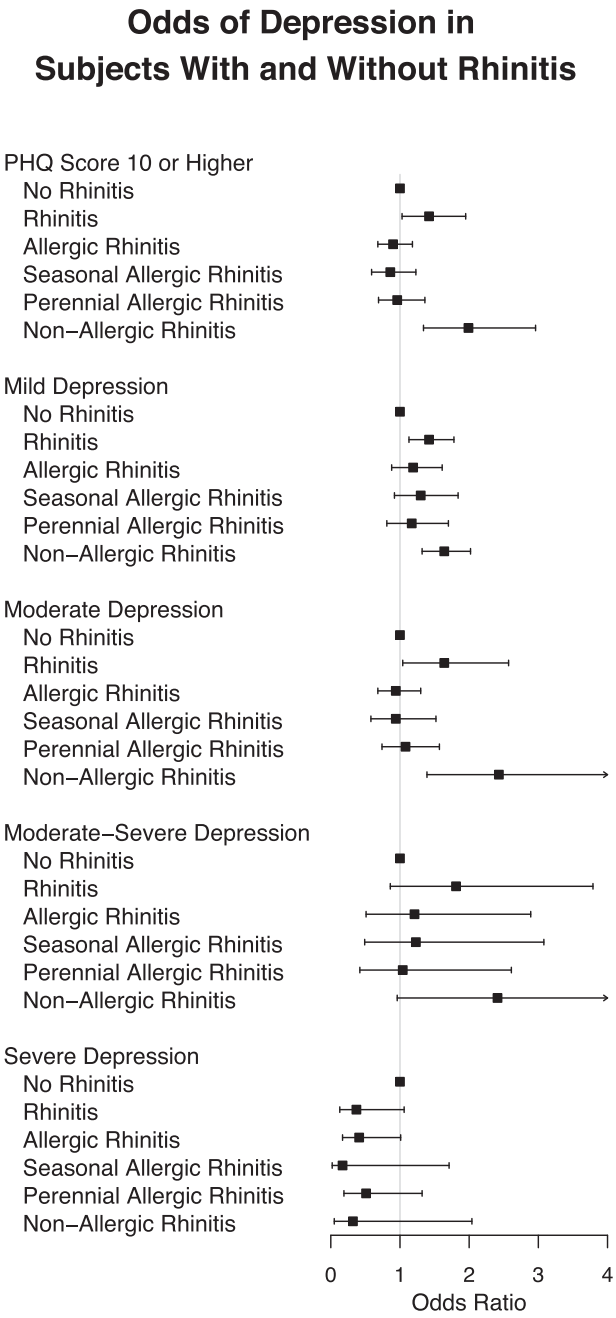

FIGURE 1. Multivariable logistic regression investigating the independent association between rhinitis and depression, stratified by the type of rhinitis and severity of depression. *PHQ*, Patient Health Questionnaire.

emphysema (4.5% vs 1.9%, $P < .02$), coronary artery disease (4.9% vs 2.9%, $P = .03$), heart attack (5.5% vs 2.8%, $P = .01$), stroke (4.4% vs 2.0%, $P = .04$), trouble seeing (28.6% vs 17.7%, $P = .0020$), general health that is fair (18.7% vs 11.8%) or poor (3.2% vs 1.0%) ($P = .001$ for the distribution of general health status), and depression screener score ≥ 10 (9.6% vs 4.5%, $P < .001$) (Table III).

On multivariable logistic regression adjusting for age, gender, race, asthma, emphysema, chronic bronchitis, heart attack, and trouble seeing, subjects with rhinitis had 42% higher odds of depression screener score ≥ 10 compared with subjects without rhinitis (odds ratio [OR]: 1.42, confidence interval [CI]: 1.03-1.95, $P = .04$). When stratifying by type of rhinitis, subjects with NAR had 2 times higher odds of depression screener score ≥ 10 compared with subjects without rhinitis (OR: 1.99, CI: 1.34-2.96, $P = .002$), but there was no association between AR and depression screener score ≥ 10 (Figure 1 and Table IV).

When depression was examined further based on severity, subjects with rhinitis had 42% higher odds of mild depression (OR: 1.42, CI: 1.13-1.78, $P = .006$) and 64% higher odds of moderate depression (OR: 1.63, CI: 1.04-2.57, $P = .03$) compared with subjects without rhinitis. On further stratification by type of rhinitis, subjects with NAR had 64% higher odds of mild depression (OR: 1.64, CI: 1.32-2.02, $P < .001$) and 2.4 times higher odds of moderate depression (OR: 2.43, CI: 1.39-4.26, $P = .004$) compared with subjects without rhinitis, but there was no association between AR and any depression severity (Figure 1 and Table IV).

DISCUSSION

This study uses NHANES data to assess the relationship between both AR and NAR and depression in US adults on a population level. These data suggest that patients with NAR are more likely to experience depression. More specifically, these patients have a higher prevalence of mild and moderate depression compared with those without rhinitis. Although there was an association between NAR and depression, interestingly there was no association between AR and depression. Compared with the AR group, the NAR group had an older mean age, higher prevalence of white race, female sex, comorbid conditions, and worse general health condition, but the association between NAR and depression remained significant even when controlling for these potential confounders.

There is a paucity of literature assessing the relationship between rhinitis, and in particular NAR and depression. To our knowledge, this is the first study to uncover an association between depression and NAR, while at the same time revealing no association with AR. Although one may hypothesize that the patients with NAR in this cross-sectional cohort were more likely to experience depression due to their generally poorer health status and increased prevalence of comorbid conditions, the association between depression and NAR did not appear to be mediated by these factors. One factor that may mediate the increased rate of depression in the NAR group is the chronicity of the disease. For instance, patients with AR may present with either perennial or seasonal symptoms, whereas those with NAR typically have symptoms year round. This hypothesis was tested by assessing whether those patients with AR and a positive serum IgE to any perennial allergen were at higher risk for depression than normal controls, and this analysis did not reveal any significant association with depression in this group.

Another factor that may mediate the relationship between NAR and depression is the difference in presenting symptoms in this group compared with those with AR. Although patients with AR are more likely to note sneezing, itching, and watery eyes, patients with NAR are more likely to note nasal obstruction and rhinorrhea.[11] It could be that patients find this constellation of symptoms especially bothersome, or they may be less responsive to therapy and therefore more problematic for the patient. As a

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TABLE IV. Multivariable logistic regression investigating rhinitis as an independent predictor for depression

	Odds ratio	95% confidence interval	*P* value
PHQ score $\geq$ 10			
No rhinitis	Reference	Reference	Reference
Rhinitis	1.42	1.03-1.95	.04
Allergic rhinitis	0.90	0.68-1.18	.40
Seasonal allergic rhinitis	0.86	0.59-1.23	.38
Perennial allergic rhinitis	0.96	0.69-1.36	.83
Nonallergic rhinitis	1.99	1.34-2.96	.002
Mild depression			
No rhinitis	Reference	Reference	Reference
Rhinitis	1.42	1.13-1.78	.006
Allergic rhinitis	1.19	0.88-1.61	.25
Seasonal allergic rhinitis	1.30	0.92-1.84	.13
Perennial allergic rhinitis	1.17	0.81-1.70	.38
Nonallergic rhinitis	1.64	1.32-2.02	<.001
Moderate depression			
No rhinitis	Reference	Reference	Reference
Rhinitis	1.64	1.04-2.57	.03
Allergic rhinitis	0.94	0.68-1.30	.70
Seasonal allergic rhinitis	0.94	0.58-1.52	.78
Perennial allergic rhinitis	1.08	0.74-1.57	.68
Nonallergic rhinitis	2.43	1.39-4.26	.004
Moderate-severe depression			
No rhinitis	Reference	Reference	Reference
Rhinitis	1.81	0.86-3.79	.11
Allergic rhinitis	1.21	0.51-2.89	.64
Seasonal allergic rhinitis	1.23	0.49-3.08	.64
Perennial allergic rhinitis	1.04	0.42-2.61	.92
Nonallergic rhinitis	2.41	0.96-6.00	.058
Severe depression			
No rhinitis	Reference	Reference	Reference
Rhinitis	0.37	0.13-1.06	.06
Allergic rhinitis	0.41	0.17-1.01	.052
Seasonal allergic rhinitis	0.17	0.02-1.71	.12
Perennial allergic rhinitis	0.51	0.19-1.32	.15
Nonallergic rhinitis	0.32	0.05-2.04	.21

PHQ, Patient Health Questionnaire.
Multivariable logistic regressions including the predictor (rhinitis), outcome (depression), age, gender, race, asthma, emphysema, chronic bronchitis, heart attack, and trouble seeing. Depression severity none (PHQ score 0-4), mild (PHQ score 5-9), moderate (PHQ score 10-14), moderate-severe (PHQ score 15-19), severe (PHQ score 20-27).

result, this specific symptomatology may lead to an increase in depression in the NAR group. Unfortunately, to date there is little evidence assessing specific rhinitis symptoms and their impact on depression. One small cohort study assessed nasal obstruction and found an association with depression,[29] but there is little evidence assessing rhinorrhea specifically and therefore no definitive conclusions can be drawn.

There are several limitations to the current study. The NHANES is a cross-sectional database without longitudinal follow-up, so it is not possible to draw conclusions about the direction of causation or the mechanism of the hypothesized association between rhinitis and depression. Although rhinitis was stratified into allergic and nonallergic groups by the presence of a positive serum IgE, it is possible that some patients with AR may have been misclassified as having NAR. Moreover, nasal endoscopy was not performed and therefore there was no ability to distinguish those patients with more severe nasal inflammation or chronic rhinosinusitis, which has previously been reported to be associated with depression.[30,31] Furthermore, there was no ability to distinguish between rhinitis symptoms, and therefore no analysis could be performed to assess if specific rhinitis symptoms were more likely to be associated with depression than others. In addition, the NHANES allergy questionnaire does not specifically ask about the severity of rhinitis symptoms, and it was therefore not possible to determine whether more severe rhinitis symptoms may be associated with higher odds of depression. Future prospective studies are needed to elucidate whether a psychologically meaningful minimum cutoff can be identified regarding the duration or severity of rhinitis symptoms. Lastly, although the NHANES does oversample racial groups such as blacks and Hispanics, these results may not be generalizable to individuals belonging to smaller ethnic groups such as Asians and other minorities that were not oversampled in NHANES.

Despite these limitations, these population-level data show a strong association between NAR and depression, even with adjustment for age, gender, race, obesity, and medical comorbidities. These associations provide a basis for future large-scale and prospective studies further assessing differences between the NAR and AR subpopulations, with particular interest in addressing the potential impact of differences in presenting symptoms, disease course, and management options on depression symptoms.

In conclusion, this is the first study to analyze the association between self-reported rhinitis and depression in a representative sample of US adults. These results suggest that rhinitis is associated with a greater risk of depression, and in particular mild-to-moderate depression. When further stratifying by type of rhinitis, patients with nonallergic rhinitis had the highest odds of depression when adjusting for demographic factors and comorbid conditions. Although future studies are required to increase our understanding of the link between allergic and nonallergic rhinitis and depression, these findings reinforce the need to consider depression in patients being evaluated for rhinitis.

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