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journal homepage: www.elsevier.com/locate/psychiresAsthma and suicide behaviors: Results from the Third National Health and Nutrition Examination Survey (NHANES III)[☆]Renee D. Goodwin^{a,*}, Ryan T. Demmer^a, Sandro Galea^a, Adina R. Lemeshow^a, Alexander N. Ortega^b, Annette Beautrais^c^a Department of Epidemiology, Columbia University, 722 West 168th Street, New York, NY 10032, USA^b Department of Health Services, UCLA School of Public Health, Box 951772, Los Angeles, CA 90095-1772, USA^c University of Auckland, Faculty of Medical and Health Sciences, Department of Surgery, South Auckland Clinical School, Auckland, New Zealand

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ABSTRACT

Asthma and suicide attempts are leading causes of morbidity and mortality among adults in the United States. The objective of this study was to investigate the relationship between asthma and suicidal ideation and suicide attempt among adults in the United States, and to examine whether timing of asthma, mood disorders, poverty, allergies, cigarette smoking and sex differences confound these relationships. Data were drawn from the Third National Health and Nutrition Examination Survey (NHANES III), a representative sample of adults ($N = 6584$) in the United States. Logistic regression analyses were used to examine the relationships between current and former asthma and suicidal ideation and suicide attempt, adjusting for demographics, poverty, smoking, allergies and mood disorders. Current asthma is significantly associated with an increased likelihood of suicidal ideation (OR: 1.77, CI: 1.11, 2.84) and suicide attempt (OR: 3.26, CI: 1.97, 5.39), after adjusting for mood disorders, smoking, poverty and demographics. There does not appear to be a significant relationship between former asthma and suicidal ideation or suicide attempt. These findings confirm and extend previous evidence by showing that the link between asthma and suicide-related outcomes is evident among adults in a representative sample and that this relationship persists after adjusting for a range of variables. This study may provide an empiric foundation for including asthma in the clinical assessment of suicide risk.

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1. Introduction

Each year approximately 1,000,000 people die by suicide worldwide, accounting for nearly 3% of all deaths and 56% of all violent deaths in the world (Krug et al., 2002). Among 15–24 year olds, for every suicide death there are an estimated 100–200 attempts (Goldsmith et al., 2002), contributing to significant global morbidity, in addition to mortality. In the United States (US), suicide is the 11th leading cause of death overall and the 5th leading cause of death among US adults (Fields et al., 2001).

There is no single cause of suicidal behavior; suicide results from an interaction of multiple factors (Fields et al., 2001). The strongest and most common known risk factors for suicidal behavior are

untreated mental disorders, including mood disorders (Bruce et al., 2004), substance use disorders (Sher, 2005; Wilcox and Anthony, 2004), schizophrenia (Murphy, 2000), history of suicide attempts (Brown et al., 2000; Goldstein et al., 1991), physical disease (Goodwin et al., 2003a) and poor coping skills (Catanzaro, 2000). Suicide attempts are strongly linked to death by suicide and are a significant predictor of further suicidal behavior (Larkin et al., 2008).

Asthma is a common chronic condition affecting an enormous number of adults in the US. Estimates show that the condition affects approximately 17.5 million adults (2010) and accounts for 1.6 million visits to the Emergency Department each year (Schappert and Rechtsteiner, 2008). Evidence increasingly suggests a link between asthma morbidity and depression (Bartlett et al., 2004; Fritz et al., 1996; Shalowitz et al., 2001; Weil et al., 1999).

A number of studies have found statistically significant links between asthma and suicide ideation (Druss and Pincus, 2000; Goodwin and Marusic, 2004) and suicide attempts (SA). One longitudinal (Goodwin and Eaton, 2005) and two cross-sectional (Clarke et al., 2008; Goodwin and Marusic, 2004) studies have

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shown links between asthma and suicide attempt in community-based samples of youth and adults in the US. A number of studies (Goodwin et al., 2003c) have also shown that, relative to other common, chronic physical conditions, the association between asthma or other respiratory disease and suicide behavior is much stronger, for reasons that remain unclear (Goodwin et al., 2002).

Methodological shortcomings of previous studies have resulted in a limited understanding of the association between asthma and suicidal ideation and suicide attempts among adults, due in part to limited measurement of potential confounders of these relationships. Specifically, measurement of cigarette smoking, which is associated with both asthma and suicide behavior, has been measured with lifetime retrospective recall, which is vulnerable to self-report bias. Numerous studies have linked smoking with increased rates of adult asthma and asthma morbidity (McLeish and Zvolensky, 2010). Findings also suggest a strong relationship between smoking and risk of suicide behavior (Boden et al., 2008; Hughes, 2008; Riala et al., 2009; Schneider et al., 2005). Therefore, it is conceivable that the relationship between asthma and suicide behavior is due to confounding by cigarette smoking. In addition, previous studies have not examined the potential role of poverty in the link between asthma and suicide behavior. Asthma is disproportionately common among youth and adults living in poverty in the United States; depression and suicide behavior are also significantly more common among lower socioeconomic segments of the population. Therefore it is possible that lack of inclusion of poverty in previous studies has led to results that can be explained by confounding (Akinbami et al.; Ferretti and Coluccia, 2009; Nikiema et al.; Rojas and Stenberg).

Against this background, the proposed study aims to begin to fill these gaps. First, we will investigate the relationship between asthma and suicidal ideation among adults in the United States. Second, we will examine the relationship between asthma and suicide behaviors. Third, we will adjust for cigarette smoking, measured via blood cotinine level, and poverty, as well as other potential demographic confounders.

2. Methods

2.1. Sample

The Third National Health and Nutrition Examination Survey (NHANES) III used complex, multi-stage, stratified, clustered samples of civilian, noninstitutionalized populations to obtain a representative sample of the US population ages 2 months and older (1994). In addition, to ensure the representativeness of both ethnicity and age, African Americans, Mexican Americans, infants, children, and those over sixty years old were oversampled. The proposed study included data from adults ages 18 and older only. The NHANES III was originated with impetus from The National Health Survey Act of 1956. This legislation provided for the establishment of a continuing National Health Survey to obtain information about the health status of people living in the United States, including the services used related to health conditions. The National Center for Health Statistics (NCHS) was responsible for survey development and data collection. The NCHS is a research-oriented statistical organization housed within the Health Services and Mental Health Administration (HSMHA) of the Department of Health and Human Services.

NHANES III was conducted from October 1988 through October 1994 in two phases, each of which comprised a national probability sample. The first phase was conducted from October 18, 1988, through October 24, 1991, at 44 locations. The second phase was conducted from September 20, 1991, through October 15, 1994, at 45 different locations. A mobile examination center (MEC) was

used such that the survey could be conducted in the community and equipment needed for medical/physical evaluation could be transported—rather than asking participants to come into one centralized testing center. A home examination option was also used in order to obtain examination data for very young children and for elderly persons who were unable to visit the MEC. The home examination included only a subset of the components used in the full MEC examination since certain types of data are difficult to collect in a home setting.

2.2. Procedure

In the NHANES III, 39,695 persons were selected over six years. Of those, 33,994 (86%) were interviewed in their homes. NHANES data are derived primarily from two sources: a) direct interview; and b) direct clinical examination. All interviewed persons were invited to the MEC for a medical examination. Seventy-eight percent (30,818) of the selected persons were examined in the MEC, and an additional 493 persons were given a special, limited examination in their homes. At the MEC, an examination was performed, and five questionnaires or interviews were administered. The health examination component included a variety of tests and procedures. The respondent's age at the time of the interview and other factors determined which procedures were administered. A physician performed a limited standardized medical exam, and blood analyses were performed either in the MEC lab, or by contract laboratories. The home examination consisted of an abbreviated version of the tests and interviews performed in the MEC. Components included a questionnaire to inquire about selected health conditions such as asthma, tobacco use, and suicide thoughts and behaviors. After the study was described to each participant, written informed consent was obtained.

2.2.1. Mental health

The Diagnostic Interview Schedule (DIS) (Robbins, 1989), a standardized diagnostic instrument administered by trained lay interviewers, was used to diagnose mood disorders according to *The Diagnostic and Statistical Manual of Mental Disorders III* (1980), including major depression, dysthymia and mania. Diagnoses of mood disorders were generated by a computerized algorithm according to the standardized criteria established in the DIS, a valid method to obtain diagnoses for community-based studies (Robbins, 1989). As a part of the DIS, questions regarding suicide ideation and suicide attempt were asked as follows: All participants were asked, "Have you ever felt so low that you thought of committing suicide?" and "Have you ever attempted suicide?". Participants aged 17–39 were administered the adult DIS and we include those participants aged 20–39 in the current analysis.

2.2.2. Asthma

Participants were asked the following two questions about current asthma: a) "Has a doctor has ever told you that you have asthma?" b) "Do you still have asthma?" Former asthma was defined as affirmative response to ever having asthma and negative response to whether the respondent still has asthma.

2.2.3. Demographic variables

Demographic variables include age, gender, race/ethnicity (non-Hispanic White, non-Hispanic Black, Hispanic or Other), poverty income ratio (computed as a ratio of reported family income to poverty threshold, taking family size into account) and were provided by self-report in the questionnaire. Age, sex, ethnicity and poverty were controlled for in these analyses because they are associated with differences in asthma and/or suicide behaviors.

Cigarette smoking was defined both categorically (never, former, current) and based on serum cotinine levels. To assess serum cotinine levels, blood was drawn during the MEC examination and serum cotinine was measured using high performance liquid chromatography/atmospheric-pressure ionization tandem mass spectrometry (Bernert et al., 1997). Assessments were performed in a central laboratory to ensure consistency across time and region. Blind and bench serum pools are routinely included with analytic runs as a quality assurance method, and additional pools spiked with known amounts of cotinine perchlorate were analyzed periodically to confirm the validity and reliability of the method.

Allergies to animal dander, dust, pollen or occupational exposures were assessed via participant self-report.

2.3. Data analysis

SAS version 9.2 was used for all analyses. Multivariable logistic regression analyses were used to calculate odds ratios (with 95% confidence intervals) of the association between former and current asthma and either suicidal ideation or suicide attempts in separate analyses. Analyses were then adjusted for age, gender, race/ethnicity and poverty index; then additionally for smoking status, lifetime depression, recurrent depression, dysthymia, mania, and allergy. We ran additional analyses adjusting for rural vs. urban setting and these adjustments had little influence on the findings. For example, when adjusting for rural vs. urban, the ORs for former and current asthma and suicide attempt were 2.2 [0.96, 5.1] and 3.0 [1.9, 5.0]. In addition, living in a rural setting vs. urban was not associated with suicide attempt; OR = 1.04, $p = 0.85$. SAS survey procedures were used to account for the complex multi-stage probability sampling design of NHANES.

3. Results

3.1. General characteristics

The current report is based on 6584 participants who participated in the MEC examination, were administered the DIS and also had complete covariable data collection. Participants were mean age $\pm$ SD 29 ± 5 years and 55% were female. The prevalence of current or former asthma was 4% and 2% respectively, and 5% of participants reported an attempted suicide while 16% reported suicidal ideation. Only 1% of participants were determined to have had a non-severe or severe manic episode while a DSM-III lifetime diagnosis of major depression was prevalent in 8% of participants, and dysthymia was present in 7% of participants.

Being Black (non-Hispanic) or White (non-Hispanic), compared with Mexican American, current (vs. never) smoking and depression were associated with statistically significantly increased likelihood of asthma (see Table 1). Being male, former and current (vs. never) smoking and depression were associated with increased odds of suicide attempt.

3.2. Association between asthma and suicidal ideation

Current asthma was associated with a significantly increased likelihood of suicidal ideation, compared to those without lifetime asthma (see Table 2). The association was slightly attenuated after adjusting for differences in demographic characteristics, smoking and lifetime episode of depression, and was further reduced in strength after adjusting for current depression, dysthymia, mania and allergy but remained statistically significant. There was no statistically significant association between former asthma and suicidal ideation.

Table 1

Predictors of lifetime asthma and suicide attempt in the National Health and Nutrition Examination Survey III, 1988–1994, $n = 6584$.

	Asthma (vs. no asthma)	P-value	Suicide attempt (vs. no attempt)	P-value
Female vs. male	0.99 (0.77, 1.26)	0.92	0.5 (0.37, 0.68)	<0.0001
Age	1.01 (0.99, 1.03)	0.46	1.01 (0.97, 1.05)	0.73
Race/ethnicity				
Non-Hispanic Black vs. Mexican-American	1.79 (1.34, 2.39)	<0.0001	0.9 (0.6, 1.17)	0.32
Non-Hispanic White vs. Mexican-American	2.07 (1.66, 2.60)	<0.0001	1.1 (0.8, 1.4)	0.66
Other vs. Mexican-American	1.18 (0.63, 2.22)	0.60	1.1 (0.5, 2.9)	0.77
Smoking status				
Former vs. never	1.31 (0.85, 2.01)	0.22	1.8 (1.05, 3.02)	0.03
Current vs. never	1.53 (1.08, 2.18)	0.02	3.46 (2.46, 4.87)	<0.0001
Depression vs. none	1.60 (1.11, 2.31)	0.01	6.8 (4.8, 9.66)	<0.0001

3.3. Association between asthma and suicide attempt

Current asthma was associated with a statistically significant increased likelihood of suicide attempt, compared with those without asthma (see Table 3). The association was attenuated after adjusting for demographics, smoking, mood disorders and allergy, but remained statistically significant. After adjusting for the same covariates, there was no statistically significant association between former asthma and suicide attempt (although the small number ($n = 11$) who reported both made it statistically infeasible to consider these adjusted results). Table 2 results were consistent when adding adjustments for serum cotinine ($n = 5980$ participants had serum cotinine data available); after adjustment for serum cotinine in Table 2, model 3, ORs for suicide attempt among participants with former or current asthma (vs. no asthma) were 2.19 (0.96, 5.03) and 3.04 (1.85, 4.98), respectively.

4. Discussion

Our results add to extant knowledge in three ways. First, our results show that current asthma, but not former asthma, is associated with suicidal ideation and suicide attempt. This is relevant for several reasons. From a clinical perspective, these data suggest that adults with current asthma may be at increased risk for suicide behavior, independent of mood disorders. Because a substantial percentage of individuals “outgrow” childhood asthma in early

Table 2

Association between former and current asthma and suicide ideation among adults in the National Health and Nutrition Examination Survey III, 1988–1994, $n = 6584$.

	No asthma (reference) 979/5182 = 16%	Former asthma 30/123 = 20%	Current asthma 70/200 = 26%	P for trend
	OR (95% CI)	OR (95% CI)	OR (95% CI)	
Model 1	1.0	1.44 (0.84, 2.44)	2.07 (1.28, 3.34)	0.002
Model 2	1.0	1.43 (0.84, 2.44)	2.09 (1.30, 3.37)	0.001
Model 3	1.0	1.37 (0.79, 2.38)	2.06 (1.26, 3.35)	0.003
Model 4	1.0	1.40 (0.72, 2.70)	1.86 (1.09, 3.16)	0.02
Model 5	1.0	1.40 (0.74, 2.64)	1.73 (1.02, 2.93)	0.03
Model 6	1.0	1.44 (0.75, 2.77)	1.84 (1.07, 3.14)	0.05
Model 7	1.0	1.28 (0.74, 2.22)	1.77 (1.11, 2.84)	0.01

OR, odds ratios; CI, confidence intervals; model 1: crude; model 2: adjusted for age, gender, race/ethnicity and poverty index; model 3: model 2 + smoking status; model 4: model 3 + depression; model 5: model 3 + recurrent depression; model 6: model 4 + dysthymia and mania; model 7: model 3 + self-report allergies to animals, dust, pollen or occupational exposures.

Note, adjusting for poverty removed 544 observations and 72 cases.

Table 3

Association between former and current asthma and suicide attempt in the National Health and Nutrition Examination Survey III, 1988–1994, $n = 6584$.

	No asthma (reference) 314/5847 = 5%	Former asthma 11/142 = 7%	Current asthma 36/234 = 13%	P for trend
	OR (95% CI)	OR (95% CI)	OR (95% CI)	
Model 1	1.0	2.00 (0.90, 4.45)	3.83 (2.32, 6.34)	<0.0001
Model 2	1.0	2.24 (1.01, 4.96)	3.33 (2.11, 5.26)	<0.0001
Model 3	1.0	2.11 (0.92, 4.80)	3.29 (2.08, 5.19)	<0.0001
Model 4	1.0	2.21 (0.88, 5.57)	3.25 (1.78, 5.91)	<0.0001
Model 5	1.0	2.09 (0.83, 5.29)	3.11 (1.82, 5.31)	<0.0001
Model 6	1.0	1.87 (0.71, 4.90)	3.22 (1.58, 6.53)	<0.0001
Model 7	1.0	2.10 (0.92, 4.80)	3.26 (1.97, 5.39)	<0.0001

OR, odds ratio; CI, confidence interval; model 1: crude; model 2: adjusted for age, gender, race/ethnicity and poverty index; model 3: model 2 + smoking status; model 4: model 3 + depression; model 5: model 3 + recurrent depression; model 6: model 4 + dysthymia, mania; model 7: model 3 + self-report allergies to animals, dust, pollen or occupational exposures.

Note, adjusting for poverty removed 544 observations and 33 cases.

adulthood, this information is important from a clinical as well as a research perspective. We do not have information on disease severity, but we expect that current asthma reflects active disease – which is likely to contribute to these differences in results – while remitted asthma is inactive. Our findings suggest that this association is not likely to be applicable to the group of adults who have outgrown childhood/early onset asthma. Since suicidal ideation/attempt is the strongest risk factor of subsequent attempts and completion, this information is clinically relevant. Second, these analyses control more precisely for the possibly confounding influence of cigarette smoking by relying on a measure of blood cotinine, rather than self-report. Numerous studies have shown a link between smoking and suicide behavior (Boden et al., 2008; Hughes, 2008; Riala et al., 2009; Schneider et al., 2005) and between smoking and asthma (McLeish and Zvolensky, 2010). This study is the first to adjust for current cigarette smoking using cotinine levels, which eliminate self-report and recall bias. Third, these data adjust for poverty, which is consistently associated with both asthma and suicide behavior (Akinbami et al.; Ferretti and Coluccia, 2009; Nikiema et al.; Rojas and Stenberg). A body of evidence suggests that the relationship among mood disorders, smoking and nicotine dependence is, at least in part, attributable to shared genetic and environmental risk factors, although correlations amongst these factors are relatively modest (Edwards et al., 2011). However, our results do not support the hypotheses that the possible genetic or environmental confounders of smoking included in our study, mood disorders or poverty, explain the observed relationship between current asthma and suicidal ideation among adults.

The present study cannot identify the mechanisms of the association between asthma and suicidal ideation and suicide attempt. There are several possibilities. For instance, it is thought that the release of specific inflammatory markers and activation of the immune system may be related to the pathophysiology of depression potentially via the effects of cytokines on specific regions of the brain (Pace and Miller, 2009). Major depression is the strongest known risk factor for suicide behavior (Fawcett et al., 1987), and suicide ideation is so entwined with depression that it is part of the diagnostic criteria for major depression (APA, 1994). As such, it is reasonable to postulate that asthma may be related to suicide behavior through similar inflammatory pathways. However, we attempted to address this possibility by controlling for depression in our analyses. Alternatively, some have suggested a relationship between use of asthma medicines and increased risk of suicidal ideation and suicide behavior (Philip et al., 2009). One prior study found that asthma medicine did not explain the

relationship between asthma and suicide ideation, attempt or completion, but the measure of asthma medicine use was not specific (Goodwin and Eaton, 2005). Still, it is possible that other asthma medications could play a role. Future studies that can examine the potential role of asthma medicines and inflammation in the association between asthma and suicide behavior, are needed. Other possible mechanistic pathways may exist and need further study. Asthma is a very complex chronic inflammatory disease that involves many inflammatory mediators; only some of these may be involved in the observed association between asthma and suicide behavior. In addition, the relationship may reflect type and/or severity of asthma, or associations between severity and medication. Further research may require more detailed measures of asthma type, severity and treatment.

Limitations of this study should be considered when evaluating results. First, assessment of suicidal ideation and suicide attempt is lifetime, and therefore it is not possible to determine the sequence of events, although the distinction between current and remitted asthma is helpful in providing more information about the nature of this relationship beyond that available in previous reports. Specifically, we cannot determine whether suicidal ideation/attempt occurred contemporaneously with asthma, or whether a history of suicidal ideation/attempt preceded asthma. However, since a history of suicidal ideation/attempt is the strongest predictor of future behavior, this information can still be useful to clinicians in evaluating potential risk especially in the presence of other risk factors for suicide behavior. These results are not suggestive of the possibility that asthma causes the onset of suicidal ideation/behavior (in the absence of current disease) or results would have shown a link between remitted asthma and suicidal ideation/attempt. Second, no information is available on the severity of suicide attempt. A recent study showed a significant link between asthma and suicide completion among adolescents in China (Kuo et al., 2010), but it is not yet clear whether this relationship exists among adults (and/or in the US). Future studies that can clarify this relationship among adults are needed. Third, neither asthma nor allergy, were diagnosed by a physician. While self-report is subject to error, these are publicly available data that help to inform the question at hand in a fast and cost-effective manner. Future studies would be strengthened by use of physician evaluation of asthma and allergy. In addition, we lack information about the severity of asthma and asthma symptoms, and believe that future studies using physician diagnosis would provide better information regarding asthma severity. Fourth, the present study could not adjust for panic or other anxiety disorders, which are strongly associated with asthma (Cooper et al., 2007; Goodwin and Eaton, 2003; Goodwin et al., 2003b) and there is some evidence to suggest they are linked with suicide behavior (Cogle et al., 2009; Goodwin and Roy-Byrne, 2006; Katz et al., 2011; Nepon et al., 2011). Fifth, detailed information on use of asthma medicine was not available in the NHANES, so we were unable to examine the potential impact of this treatment on the observed relationship. Sixth, it is very possible that we did not find a statistically significant relationship between remitted asthma and suicide attempt due to the small number of individuals with remitted asthma who attempted suicide ($n = 11$). A study with a larger sample is needed to replicate these findings. Finally, the age range (20–39) of our study was quite limited and therefore it is possible that this association differs in youth or older adults. These results may not be generalizable to those populations.

In sum, these results add in several ways to the growing evidence that asthma is associated with increased suicidal ideation and suicide attempt among adults in the US, showing that current, not remitted, asthma is associated with increased risk and that neither mood disorders, smoking nor poverty appear to explain this

relationship. These findings would support further investigation into the disability and severity of asthma and other common chronic diseases and their links to suicidal ideation and behavior. In conjunction with previous evidence, this study may also provide an empiric foundation for including asthma in the clinical assessment of suicide risk, which ultimately may help identify individuals at high risk for suicide.

Contributors

Dr. Goodwin conceived of the study, planned original analyses and wrote the first draft of the manuscript; Drs Demmer, Galea, Lemeshow, Ortega, and Beautrais contributed to writing the manuscript and each made important contributions to the study design and interpretation of results; Dr. Demmer analyzed the data. Dr. Goodwin is the guarantor of the paper.

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Conflicts of interest

None.

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