

Asthma and Suicide: Current Knowledge and Future Directions

Renee D. Goodwin

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Abstract The prevalence of asthma has risen dramatically, especially among youth, in recent years, and asthma is now among the most common chronic conditions. Recent studies suggest a relationship between asthma and suicidal ideation, suicide attempt, and death by suicide. This paper reviews the literature, summarizes the weight of evidence, and discusses the clinical implications and future directions for research.

Keywords Asthma · Suicidal ideation · Suicide attempt · Suicide · Epidemiology · Depression · Anxiety

Introduction

Suicide is the fifth-leading cause of death among adults in the United States. Suicide attempt (SA) is one of the strongest risk factors for suicide and is associated with substantial impairment and distress. Findings from several recent studies suggest associations between asthma and suicidal ideation, SA, and death by suicide. The central focus of this paper is to critically review available data on the relationship between asthma and suicidal ideation (thoughts about suicide) and suicide behavior and to evaluate the weight of the evidence in terms of clinical implications. The paper also discusses needs for future investigations into asthma suicide behavior and death by suicide and the potential social and biological mechanisms underlying the relationship between asthma and suicide behavior.

Prevalence and Problem of Suicidal Behavior

Each year, approximately 1 million people die by suicide, accounting for nearly 3% of all deaths and 56% of all violent deaths in the world [1]. For every suicide death, there are an estimated 100 to 200 attempts [2], contributing to significant global morbidity and mortality. In the United States, suicide is the 11th-leading cause of death overall and the 5th-leading cause of death among US adults [2]. Each year, approximately 33,000 Americans die by suicide [3].

Pathways to Suicidal Behavior

There is no single cause of suicidal behavior, as suicide likely results from the interaction of multiple factors [2]. The strongest and most common known risk factors for suicidal behavior are untreated mental disorders—including mood disorders [4, 5], substance use disorders [6, 7], schizophrenia [8]—physical disease [9], history of SAs [10, 11], as well as poor coping skills [12]. SAs are strongly linked to death by suicide and powerfully predict future suicidal behavior [13].

Asthma

Asthma is the most common chronic condition affecting adults in the United States [14–16]. Estimates show that it affects approximately 17.5 million adults [17] and accounts for 1.6 million visits to the emergency department each year [18]. Despite widely available and highly effective treatment strategies [19], asthma morbidity continues to be a very common and serious public health problem; it is a leading cause of missed work and lost work productivity

R. D. Goodwin (✉)
Mailman School of Public Health, Columbia University,
722 West 168th Street, Room 1505,
New York, NY 10032, USA
e-mail: rdg66@columbia.edu

[20] and can place limitations on quality of life [21]. The reasons for continued high rates of asthma morbidity, despite the availability of efficacious treatments, are not entirely clear.

Asthma and Suicidal Ideation

Evidence increasingly suggests a link between asthma and suicidal ideation and suicide behavior [22–25]. Previous studies in the suicide literature have repeatedly documented a link between poor physical health/physical illness—without specifying the type of physical illness—and increased risk of suicidal ideation, SA, and completed suicide [26–29]. More recently, studies in clinical and epidemiologic samples have examined whether and to what degree specific somatic conditions are associated with suicide-related outcomes. Studies to date have consistently found that asthma and other respiratory illnesses (eg, chronic obstructive pulmonary disease) are strongly associated with suicidal ideation [30–34]. For instance, Druss and Pincus [33] documented an association between asthma and suicidal ideation in a cross-sectional sample of adults in the general population that persisted after adjusting for major depression and alcohol dependence. In a subsequent longitudinal study, Goodwin and Eaton [34] demonstrated a relationship between asthma and increased likelihood of suicidal ideation (OR, 2.3; 95% CI, 1.03–5.3). This relationship also remained statistically significant after adjusting for depression and use of asthma medication [34].

Asthma and Suicide Attempts

Several studies have documented statistically significant links between asthma and SAs [9, 33–35]. For instance, one longitudinal study of adults in the United States found that asthma was associated with significantly increased risk of SA (OR, 3.5; 95% CI, 1.4–9.0) several years later in a representative sample [34]. Several studies have also shown that relative to other common, chronic physical conditions, the association between asthma and other respiratory disease and suicide behavior is much stronger [9, 31]. The reasons for this remain unclear. For instance, one investigation showed that adults with lung disease were significantly more likely to have made an SA (OR, 1.8; 95% CI, 1.1–2.7) compared with those without lung disease in the United States; lung disease was among the only specific physical health problems that remained statistically linked with SA after adjusting for a range of mental disorders. A subsequent study found that chronic obstructive pulmonary disease was associated with SA in a nationally representative sample of adults [36]. Still, relatively little progress has

been made toward understanding why this relationship persists and what its potential clinical significance might be.

Quite a bit of debate has occurred as to whether there is a causal mechanism linking respiratory disease and suicidal behavior, and whether their association is a methodologic artifact due to confounding [34], or whether their co-occurrence is related to exposure to a common risk factor for both [35, 37]. Methodologic shortcomings of previous studies, including limited comprehensive measurement of potential confounding and/or mediating factors, lack of investigation into potential biological mediators or modifiers, and absence of comprehensive risk factors for SA (eg, psychiatric disorder, life events, substance use), have hindered progress in clarifying the link between asthma and SA and identifying possible pathways underlying this relationship.

Asthma and Death by Suicide

Early studies have documented physical illness as a risk factor for death by suicide [28], but only two recent investigations have focused on asthma specifically as it relates to death by suicide. One recent study on youth aged 11 to 16 in Taiwan found a significant link between asthma and subsequent increased risk of death by suicide [38•]. Another study found a relationship between asthma and death by suicide (though only one case was statistically significant) after 3 years of follow-up [34]. Unlike recent studies on the relationship between asthma and suicidal ideation/SA, to our knowledge, no population-based study has examined the role of depression or other mood disorders using standardized diagnostic criteria for assessment in the relationship between asthma and death by suicide. A proper examination of these variables is important because asthma is linked to both depression and suicide [31]. As physical health problems are among the most well-documented risk factors for death by suicide [39], and previous studies have examined the roles of self-reported cardiovascular disease [26, 40] and self-reported physical health (ie, good vs poor perceived health) [41], it is imperative that future studies among adults look specifically at asthma in relation to death by suicide.

Asthma and Suicidal Behavior in Clinical Settings

Several clinical studies have shown strong links between asthma and/or respiratory disease and suicide-related outcomes. Two studies using large, systematic samples of waiting room samples of more than 5,000 primary care patients cumulatively showed that asthma/pulmonary disease was associated with increased likelihood of suicidal

ideation (OR, 1.9 in both studies) among adults [31, 42]. These associations remained statistically significant after controlling for depression, anxiety, and substance use disorders and demographic characteristics. In addition, similar to community-based findings, the link between asthma/respiratory disease and suicidal ideation was stronger than any link found between other somatic health problems and suicidal ideation [43]. As these clinical studies used representative waiting room samples from diverse primary care settings rather than selected samples or psychiatric patient samples and found increased odds of suicide-related outcomes associated with asthma, this suggests a need to screen for potential suicide risk among adults in primary care who are seen for asthma/respiratory health problems. As the above findings indicate that this link was independent of major depression or substance use disorders, providers should be aware that the absence of observable depression in patients does not necessarily suggest an absence of risk of suicide-related outcomes. This coupled with the finding that most individuals who attempt suicide will have seen a primary care physician within the past 7 days highlights the importance of screening and detection of suicide potential among patients with asthma.

Asthma and Suicidal Ideation/Suicide Behavior Among Youth

In addition to available data on the observed relationship between asthma and suicidal ideation/behavior among adults, several studies have found a link between asthma and suicide-related outcomes among youth. One community-based study of youth aged 9 to 17 in the United States found an association between asthma and increased suicidal ideation (OR, 3.3; 95% CI, 1.04–10.1) that persisted after adjusting for demographic characteristics and mental disorders among youth who had been hospitalized for asthma [44]. A more recent study showed that the incident rate of death by suicide among Taiwanese youth aged 11 to 16 with current asthma was more than twice that of those without asthma (HR, 2.3; 95% CI, 1.4–3.6) [38•], and that a higher number of asthma symptoms was linked with increased risk of suicide in a dose–response fashion. Although it was impressive in sample size and in the prospective measurement of asthma and suicide outcomes, this study was limited in its adjustment for potential confounders and mediators, as it did not adjust for depression, anxiety, or other mental disorders (they were not measured). Still, both studies suggest that youth with active/symptomatic and/or poorly controlled asthma are at increased risk of suicidal ideation and death by suicide. Another recent study from Denmark showed a similarly consistent association between a clinical visit with a physician and subsequent increased risk of SA;

in the time immediately following an appointment, this study found an association between diagnosis of asthma/treatment for asthma at the visit and increased risk of SA (males: RR, 1.57; 95% CI, 1.2–2.1; females: RR, 1.69; 95% CI, 1.4–2.0) [45•]. As these populations are most likely to have contact with the health care system, but not necessarily with mental health care professionals, it is important that primary, emergent, and specialty pulmonary health care providers be aware of and screen for potential risk of self-harm among youth seen with active and poorly controlled asthma. Future prospective studies are needed to help us better understand possible mechanisms of the link between asthma and suicidal behavior, and how we can improve detection and psychiatric treatment so as to prevent suicide-related outcomes among young people.

Possible Mechanisms

Studies to date have not focused on the possible mechanisms of the association between asthma and suicidal ideation and SA. Several possibilities exist.

Causal Relationship

One possibility is that having asthma—in particular, severe or poorly controlled asthma—causes suicidal ideation or suicide behavior due to hopelessness over the condition or functional limitations associated with a severe, chronic illness. To date, there is not enough evidence to support a causal relationship, but this possibility has not been ruled out. It is also important to note, relatedly, that longitudinal studies suggest a strong, significant, bidirectional relationship between asthma and anxiety and depressive disorders [46–50]. The bulk of the evidence to date suggests that early-onset asthma or respiratory symptoms are associated with increased risk of developing anxiety disorders and depression [47], and some [48], but not all [46], suggest that early mental health problems predict subsequent onset of asthma/respiratory disease.

Unmeasured Confounding

It is conceivable that the observed relationship is due to confounding by major depression, cigarette smoking, demographic differences, or some other factor that has been poorly measured in previous studies or has not been adjusted for. For instance, childhood adversity has been documented as a risk factor for both asthma/respiratory disease in adulthood [34, 44, 51] and a well-known risk factor for anxiety and depressive disorders [52–55]. As such, it is conceivable that childhood adversity is a common risk factor leading to the co-occurrence of asthma

and suicide behavior. Future studies that can investigate this possibility are needed. Future studies will be needed to replicate prior results using even better measures of key confounders to rule out this possibility.

Asthma, Inflammation, and Psychiatric Disorders

The relationship between asthma and suicide behavior may arise from common causal risk factors for both. There is a well-documented relationship between asthma and increased levels of inflammation. A relationship between major depression and inflammation is also well-documented [56–61]. 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 [60]. Major depression is the strongest known risk factor for suicide behavior [62], and suicidal ideation is so entwined with depression that it is part of the diagnostic criteria for major depression [63]. As such, it is reasonable to postulate that inflammation may be related to suicide behavior through similar pathways. Although no previous study has examined the potential role of inflammation in the relationship between asthma and suicide behavior, this seems to be a promising avenue for future work.

Asthma Medication and Death by Suicide

Several recent reports have suggested a relationship between use of specific asthma medicines (eg, montelukast sodium) and increased risk of suicidal ideation and suicide behavior [64]. As a result of several postmarketing suicide-related adverse experience reports, the US Food and Drug Administration reviewed clinical trial data to assess neuropsychiatric events and updated the “precautions” to inform patients using this product about potential behavioral and mood side effects [65]. Extensive reviews of clinical trials of montelukast have failed to find evidence of completed suicide related to use of this medicine [64], yet none of these studies has used representative samples of the general population. Therefore, because participants in clinical trials are highly selected on a number of factors, it is difficult to know to what degree this finding is reflective of the association as it exists in the community. Given the repeatedly replicated association between asthma medicine and suicidal thinking/behaviors, it is reasonable to suspect a possible link between asthma and death by suicide. Furthermore, no prior study on the link between asthma and SA (or death by suicide) has taken medication use into account [34, 38•]; no previous study has comprehensively examined the potential role of specific asthma medication use in the relationship between asthma and SA or death by suicide. This, too, seems to be an understudied problem.

Future Directions

In addition to methodologic limitations, no previous study has put forward and/or tested a theoretical model that could explain the pathway and biological plausibility of the relationship between asthma and suicide-related outcomes. Advances in our understanding of suicide have greatly progressed through use of a neurobiological model of stress-diathesis to understand and empirically test neurobiological factors in the risk of suicide [66]. Research on asthma and its potential physiologic consequences/correlates has necessitated the use of biological models to test how asthma may affect various biological substrates, many of which are also associated with mental disorders (eg, major depression). There is currently a lack of any such model to explicate the mechanism of this frequently studied, yet poorly understood relationship. Based on evidence to date, it is conceivable that asthma medications affect suicide behavior. 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 [60].

One hypothesis is that changes in immune functioning, prompted by physiologic changes due to asthma, may influence brain regions associated with depression/suicidal behavior, which increases the risk of death by suicide. In addition to mechanistic studies, psychological autopsy studies would be helpful in uncovering a potential relationship between asthma and death by suicide. In the meantime, the weight of the evidence clearly suggests that screening for suicide risk among youth and adults with asthma in both inpatient and outpatient treatment settings is indicated.

Conclusions

The prevalence of asthma has risen dramatically, especially among youth, in recent years, and asthma is now the most common chronic condition among youth. Future studies are needed to clarify whether and to what degree asthma severity/persistence is associated with suicide-related outcomes or whether these risks are only associated with more severe asthma (as some evidence to date suggests about the relationship between asthma and mental disorders). New studies are needed to help us better understand the nature of this observed link—whether there may be some sort of causal relationship, or whether the observed association arises due to exposure to a common causal factor for both asthma and suicide-related outcomes. Prospective, longitudinal studies that observe individuals over time will provide opportunities to examine the interplay between asthma and suicide behavior and adjust for a wide range of possible confounders and mediators. Although many questions remain

unanswered at present, the evidence to date is compelling in suggesting that those with asthma appear to represent a high-risk group for suicide from a mental health perspective, and indicates a need for screening in both adults and youth who are treated for asthma; screening may be especially important for individuals who do not appear to be depressed or suffering from another mental disorder.

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