



The relationship between asthma and suicidal behaviours: a systematic literature review



Emma Barker, Kairi Kõlves and Diego De Leo

Affiliation: Australian Institute for Suicide Research and Prevention, National Centre of Excellence in Suicide Prevention, World Health Organization Collaborating Centre for Research and Training in Suicide Prevention, Griffith University, Brisbane, Australia.

Correspondence: Kairi Kõlves, Australian Institute for Suicide Research and Prevention, National Centre of Excellence in Suicide Prevention, World Health Organization Collaborating Centre for Research and Training in Suicide Prevention, Griffith University, Level 1, Building M24 Psychology, 176 Messines Ridge Road, Mt Gravatt Campus, Griffith University QLD 4122, Australia. E-mail: k.kolves@griffith.edu.au

ABSTRACT Asthma is a highly prevalent chronic condition worldwide, and is particularly common in younger people compared to other chronic conditions. Asthma can result in a number of symptoms that are detrimental to the quality of life of sufferers. The aim of the present systematic literature review was to analyse the existing literature on the relationship between asthma and fatal and nonfatal suicidal behaviours.

Articles were retrieved from Scopus, PubMed, ProQuest and Web of Knowledge. We searched for the terms (suicid* OR self-harm) AND (asthma* OR “bronchial hyperreactivity”) published in English-language peer-reviewed journals between 1990 and December 2014. Original research papers providing empirical evidence about the potential link between asthma and suicidal behaviours were included.

The initial search identified 746 articles. Specific limiting criteria reduced the number of articles to the 19 articles that were finally included in the systematic review.

The review found a potential link between asthma and suicide mortality, ideation and attempts across the age groups. Limitations of the review include the restriction to English-language papers published within the chosen time period, the limited number of papers involving suicide mortality, and the fact that the majority of papers originated from the USA.



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Introduction

The World Health Organization (WHO) estimates that approximately 235 million people worldwide suffer from asthma, this being the most common chronic disease suffered by children [1]. The WHO International Statistical Classification of Diseases and Related Health Problems 10th revision asthma (J45) includes allergic asthma, nonallergic asthma, mixed asthma, and asthma, unspecified [2].

The symptoms of asthma are usually well managed with the correct use of medications; however, self-management of asthma can be complicated [3]. Certain factors may potentially exacerbate symptoms in sufferers, including smoking behaviour, stress, particular environment triggers (mould, pollen, dust mites and pet hair), exercise and changes in the weather [4]. These symptoms may have a considerable detrimental effect on the quality of life of those suffering from severe and even mild cases of asthma [5].

A link between asthma morbidity, risk-taking behaviour and depression has been presented in previous research, although the reasons and direction of this association are not clear [6]. Four pathways leading to the association have been suggested: 1) particular symptoms of asthma cause distress leading to psychological problems [6]; 2) depression may lead to increased asthma symptoms through risk-taking behaviour (smoking, drinking, nonadherence to medication and poor illness control in general) [6]; 3) depression and psychological stress may be associated with immune system alteration, increased airway inflammation and the initial onset of asthma symptoms in children [7]; and 4) that there may be a common genetic link leading to susceptibility to asthma, atopy and mood disorders [8].

Another potential cause of depression in asthma sufferers is the use of particular medications, including corticosteroids, which, while reducing the symptoms of asthma, have also been linked to mood disturbances similar to the symptoms of major depression [9]. In 2008, the US Food and Drug Administration introduced new warnings about the potential adverse psychiatric symptoms of leukotriene-modifying medications, used in the treatment of asthma. However, as a recent review has shown, research in this area to date has produced very mixed findings [10] and the full extent of the relationship between asthma medications and psychiatric symptoms is yet to be completely understood [10, 11].

As well as being linked to poor physical and mental health, asthma has been associated with suicidal behaviour. In a review of six observational studies, IESSA *et al.* [12] found an association between asthma and suicide ideation, attempts and mortality in adults and suicide ideation and mortality in children. The aim of the current review is to present a more comprehensive systematic review of the literature about the relationship between asthma and suicidal behaviour.

Method

The current review was conducted in accordance with the Preferred Reporting Items For Systematic Reviews And Meta-analyses (PRISMA) statement (table 1) [13].

Search strategy

A systematic search of Scopus, PubMed, ProQuest and Web of Knowledge was conducted for English-language articles published from January 1990 to December 2014. The search terms used were (suicid* OR self-harm) AND (asthma* OR “bronchial hyperreactivity”).

Inclusion criteria

The initial search retrieved 746 articles before the removal of duplicates and 534 articles after the removal of duplicates. These were limited to 51 potentially relevant papers after perusal of the titles and abstracts to review their relevance to the link between asthma and suicidal behaviours (suicide, suicide attempts and self-harm and suicidal ideation). After reading the full text of these 51 papers, 19 papers presenting original research empirically analysing the potential link between asthma and suicidal behaviour were selected for inclusion in the body of the review. Figure 1 shows a summary of the selection process for papers.

In this article, suicidal behaviour refers to a range of phenomena that include suicide ideation, planning for suicide, self-harming, attempting suicide and suicide. The latter is also defined interchangeably as “fatal suicidal behaviour”, while all other phenomena are considered to be “nonfatal suicidal behaviour” [14].

Data extraction

The following information was extracted for all studies included: author(s) and year of publication; sample size, country and time of the study; study design; measures (asthma and suicidal behaviour); main findings; and quality scores. With regards to the findings, risk ratios, odds ratios (including adjusted odds ratios) and differences in prevalence measured using statistical tests were examined.

TABLE 1 Checklist of preferred reporting items for systematic reviews and meta-analyses (PRISMA)

Section/topic	Checklist item	Reported on page
Title		
Title	Identify the report as a systematic review, meta-analysis or both	96
Abstract		
Structured summary	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; and systematic review registration number	96
Introduction		
Rationale	Describe the rationale for the review in the context of what is already known	97
Objectives	Provide an explicit statement of questions being addressed with reference to PICOS	97
Protocol and registration	Indicate if a review protocol exists, if and where it can be accessed (e.g. web address), and, if available, provide registration information including registration number	N/A
Eligibility criteria	Specify study characteristics (e.g. PICOS and length of follow-up) and report characteristics (e.g. years considered, language and publication status) used as criteria for eligibility, giving rationale	97
Information sources	Describe all information sources (e.g. databases with dates of coverage and contact with study authors to identify additional studies) in the search and date last searched	97
Search	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated	97
Results		
Study selection	State the process for selecting studies (i.e. screening and eligibility) included in systematic review, and, if applicable, included in the meta-analysis	97
Data collection process	Describe method of data extraction from reports (e.g. piloted forms, independently and in duplicate) and any processes for obtaining and confirming data from investigators	97
Data items	List and define all variables for which data were sought (e.g. PICOS and funding sources) and any assumptions and simplifications made	98
Risk of bias in individual studies	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was performed at the study or outcome level), and how this information is to be used in any data synthesis	105
Discussion		
Summary measures	State the principal summary measures (e.g. risk ratio and difference in means)	98
Synthesis of results	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g. I ²) for each meta-analysis	98

PICOS: participants, interventions, comparisons, outcomes and study design; N/A: not applicable. Information from [13].

Quality scores

The 19 studies included in the review were each given a quality score (adapted from POMPILI *et al.* [15]) by two of the authors (E. Barker and K. Kølves). This method allocated each paper a score ranging from 0 to 6 based on the representativeness of the sample, presence of a control/comparison group, number of participants with the condition (asthma), being longitudinal (having a follow-up) and data presentation. More information regarding the determination of these scores is presented in table 2.

Results

Table 2 presents a summary of the 19 studies reviewed which involved asthma and suicidal behaviour and included risk ratios or odds ratios.

Asthma and suicide mortality

Five out of the 19 studies in the current review analysed the association between asthma and suicide mortality. The papers originated from different locations, namely the UK (n=2), Taiwan, Canada and Sweden. Three of the papers used a cohort study design, while the remaining two papers used a nested case-control study design.

Kuo *et al.* [23] used a cohort of 162 766 high-school students aged between 11 and 16 years in Taiwan to analyse the relationship between suicide mortality and asthma. The authors compared children with current asthma, previous asthma and no asthma, finding significant differences in the percentages of

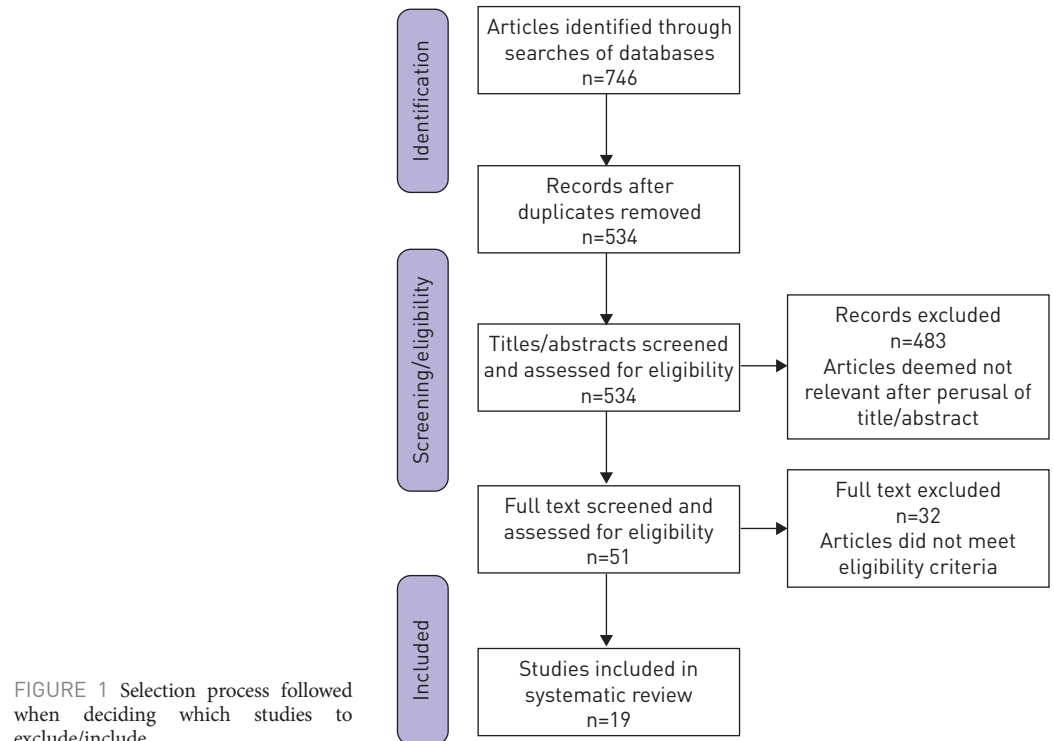


FIGURE 1 Selection process followed when deciding which studies to exclude/include.

children dying by suicide in each of the groups (11% in the current-asthma group, 8.5% in the previous-asthma group and 4.3% in the no-asthma group). When other factors including sex, age, personal and family cigarette smoking behaviour and allergic rhinitis were adjusted for, the current-asthma group still had a significantly higher risk of suicide than the group with no asthma, but the differences between the current- and previous-asthma groups were no longer significant. The authors found that particular symptoms, including wheezing while exercising, coughing at night and severe wheezing were associated with suicide risk, and that the risk increased when a greater number of symptoms were present.

Using a national cohort of 7 140 589 Swedish residents, CRUMP *et al.* [33] found that asthma was more prevalent among women who died by suicide when compared to the general female population. Further analysis revealed that asthma (and a number of other somatic illnesses) was a significant independent risk factor for suicide in both men and women.

In the UK, SINGHAL *et al.* [34] used a retrospective cohort design linking the English Hospital Episode Statistics database with mortality data from 1999 to 2011 to analyse the risk of suicide mortality in people with various psychiatric and physical disorders. 2 500 814 individuals in the cohort suffered from asthma. This UK study indicated that individuals suffering from asthma were significantly more likely to die by suicide than the comparison group.

Also in the UK, WEBB *et al.* [29] used a nested case-control design and data from family medical practices recorded in the General Practice Research Database between 2001 and 2008 to test the association between a number of conditions (including asthma) and suicide mortality. WEBB *et al.* [29] matched 873 adult suicide cases to 17 460 living controls by age and sex. Contrary to the results of the cohort studies, including the UK study by SINGHAL *et al.* [34], this study did not find any increased risk of suicide associated with asthma, or any of the illnesses in the study. However, there was a high percentage of asthma patients reporting depression (64.7%).

In another nested case-control study, BOLTON *et al.* [32] looked at the association between death by suicide and a number of physical disorders, including asthma. Between 1996 and 2009, 2100 individuals who died by suicide were matched to 6300 controls from the Canadian general population. Multivariate analysis indicated that women with asthma were more likely to die by suicide than women who did not have asthma. No significant increased risk was identified in males with asthma in the adjusted model.

Asthma and suicidal ideation/attempts

16 papers in the current review included an analysis of nonfatal suicidal behaviour in individuals suffering from asthma. The majority of these studies (n=10) used cross-sectional study designs, followed by cohort

TABLE 2 Studies of asthma and suicidal behaviour (in chronological order)

Authors	Population, participants and time	Study design	Measures of suicidal behaviour	Measures of asthma	Main findings	Quality score [#]
DRUSS and PINGUS [16]	NHANES study of 7589 individuals aged 17–39 years from 26 states in USA between 1988 and 1994	Cross-sectional	Suicidal ideation and attempts	Self-reported asthma	Asthma, chronic bronchitis and cancer showed a two-thirds increase in the presence of suicidal ideation. Around 1/5 of respondents with asthma, bronchitis, or cancer reported a past suicide attempt, compared to 1/18 in the general population. After adjusting for psychiatric and demographic factors, people with asthma were still significantly more likely to report a suicide attempt (aOR 4.34, $p < 0.001$) and suicide ideation (aOR 1.69, $p < 0.01$).	5 (I=1, II=1, III=2, IV=0, V=1)
GOODWIN et al. [17]	998 consecutive adult primary care patients aged 18–70 years attending appointments at the Associates in Internal Medicine clinic (Columbia-Presbyterian Medical Centre, Manhattan, NY, USA) between October 1998 and April 1999	Cross-sectional	Suicidal ideation	Asthma diagnosis from primary-care physicians	Asthma was significantly associated with suicidal ideation (OR 1.9, 95% CI 1.03–3.4) and with panic attack after controlling for socio-demographic factors and mental disorders. Asthma was not significantly associated with major depression, generalised anxiety disorder, alcohol, or drug use disorders.	3 (I=0, II=1, III=1, IV=0, V=1)
GOODWIN and MARUSIC [18]	MECA study of 1285 youths aged 9–17 years from four sites in USA	Cross-sectional	Suicidal ideation (“In the past 6 months have you thought about suicide or killing yourself?”)	Parental reports of past hospitalisation for asthma	Youths with asthma were significantly more likely to report suicidal ideation than those without asthma, even when adjusting for sociodemographic characteristics and comorbid mental disorders (aOR 3.25, 95% CI 1.04–10.1).	3 (I=1, II=1, III=0, IV=0, V=1)
GOODWIN and EATON [19]	Baltimore (MD, USA) follow-up of the Epidemiologic Catchment Area Study: 3481 community participants aged ≥ 18 years in USA studied in 1981 (wave 1) and 1982 (wave 2); 1920 individuals (74% of the original sample) followed-up in 1993–1996 (wave 3)	Cohort study	Suicidal ideation and attempts measured at three time points	Self-reported asthma	Several associations between asthma and suicidality at different waves were found to be significant. However, current asthma at wave 1 of the study was associated with a significantly increased risk of suicidal ideation at wave 2, after controlling for sex, age, race, asthma treatment and lifetime major depression (OR 2.3, 95% CI 1.03–5.25). Current asthma at wave 1 was also associated with significantly increased risk of suicide attempts at wave 2 when controlling for the same variables (OR 3.54, 95% CI 1.4–8.99). Analysis at wave 3 of the study was not included as the cell sizes became too small for comparison due to participant attrition.	5 (I=1, II=1, III=1, IV=1, V=1)
BENDER [20]	YRBS study of 13917 youth in school grades 9–12 from 40 states and 21 cities in USA in 2005	Cross-sectional	Suicidal ideation and attempts	Self-reported lifetime diagnosis of asthma and asthma symptoms in past 12 months	Students with asthma were significantly more likely to report depressive symptoms, suicidal thoughts, plans, actions and injuries than their nonasthmatic peers: 31% reported considering suicide compared to 16.2% ($p < 0.001$) and 17.9% had made a suicide attempt compared to 8.5% of the nonasthmatic group ($p < 0.001$).	5 (I=1, II=1, III=2, IV=0, V=1)
NOMURA et al. [21]	Regional random sample of 2694 individuals born between 1960 and 1964 (perinatal conditions measured at delivery); 1525 were followed-up in adulthood (27–33 years in 1992–1994) in Baltimore (MD, USA)	Cohort study	Suicidal ideation	Self-reported current or past asthma	Offspring with suicidal ideation had a significantly increased risk of comorbid asthma when confounding factors were adjusted for (aOR 2.8, 95% CI 1.4–5.8). There was no evidence that perinatal risk factors increased the risk of comorbid suicidal ideation and asthma.	5 (I=1, II=1, III=1, IV=1, V=1)

Continued

TABLE 2 Continued

Authors	Population, participants and time	Study design	Measures of suicidal behaviour	Measures of asthma	Main findings	Quality score [#]
CLARKE <i>et al.</i> [22]	NCS-R study of 5692 English-speaking individuals aged ≥18 years and living in USA between February 2001 and April 2003	Cross-sectional	Suicidal ideation and attempts	Self-reported diagnosed asthma	A statistically significant association between asthma and suicidal ideation with attempts [OR 1.98, 95% CI 1.42–2.76], but not suicidal ideation alone (OR 1.09, 95% CI 0.81–1.45) was found. After controlling for age, sex and race/ethnicity, the relationship between suicide attempts and asthma reduced by 6.1% reducing by a further 16% when smoking and nicotine dependence was accounted for. In addition, the association decreased by 12.4% when depression, panic disorder and alcohol dependence or abuse were adjusted for; however, the association remained significant [aOR 1.53, 95% CI 1.06–2.21].	5 (I=1, II=1, III=2, IV=0, V=1)
Kuo <i>et al.</i> [23]	The Study of Asthma and Allergy of 162766 high-school students aged 11–16 years in October 1995–June 1996 and their parents was linked with the national death certification system in Taiwan up to December 2007	Cohort study	Suicide mortality	Self-reported current and previous asthma symptoms	When comparing groups with current asthma, previous asthma and no asthma, the only significant between-group effect was observed in suicide deaths: 11 per 100 000 person-years, 8.5 per 100 000 person-years and 4.3 per 100 000 person-years, respectively (p<0.001). There were no significant differences in natural deaths between the three groups. After adjusting for sex, age, personal and family cigarette smoking and allergic rhinitis, the current-asthma group had a significantly higher likelihood of suicide mortality than the no-asthma group [HR 2.26, 95% CI 1.43–3.43], but not the previous-asthma group. Particular symptoms of asthma [exercise wheezing, night cough and severe wheezing] were significantly associated with suicide risk after adjusting for covariates. Having a greater number of symptoms increased risk of suicide.	6 (I=1, II=1, III=2, IV=1, V=1)
BAE <i>et al.</i> [24]	The 2008 KYRBWS study of 75 238 Korean youths attending middle or high school	Cross-sectional	Self-reported suicidal ideation and attempts	Self-reported diagnosis and treatment of asthma	The results of the study showed higher prevalence of suicidal ideation and attempts in current and former asthmatics when compared to their peers without asthma. These results remained significant when controlling for confounding factors for both considering suicide (OR 1.36, 95% CI 1.19–1.55 and OR 1.40, 95% CI 1.27–1.54, respectively) and attempting suicide (OR 1.55, 95% CI 1.25–1.92 and OR 1.54, 95% CI 1.29–1.84, respectively). aOR also showed a significant relationship between current or former asthma, suicidal ideation and current cigarette use and cigarette use before the age of 13 years. Suicidal ideation was an effect modifier of the relationship between asthma and cigarette use.	5 (I=1, II=1, III=2, IV=0, V=1)
CHAN <i>et al.</i> [25]	National Survey of Health Promotion Knowledge, Attitudes, and Practice of 3853 elderly adults aged >65 years in Taiwan in 2002–2003	Cross-sectional	Suicidal ideation	Self-reported diagnosis of asthma	Univariate analysis showed significant association between suicidal ideation and asthma [OR 2.84, 95% CI 1.76–4.58]. Asthma did not remain a significant predictor of suicidal behaviours in a multivariate logistic regression analysis.	4 (I=1, II=1, III=1, IV=0, V=1)

Continued

TABLE 2 Continued

Authors	Population, participants and time	Study design	Measures of suicidal behaviour	Measures of asthma	Main findings	Quality score [#]
CHRISTIANSEN and STENAGER [26]	3465 children and youths born between 1983 and 1989 who attempted suicide were matched with 20 population controls with identical age and sex (69300 controls) using Danish national population registers and followed until 2005	Nested case-control	Suicide attempt	Hospital records of asthma treated in a somatic hospital	For both male and female patients, treatment for asthma was a significant risk factor for attempted suicide (rate ratio [95% CI] 1.57 [1.15–2.14] ($p < 0.05$) and 1.88 [1.49–2.35] ($p < 0.0001$), respectively). The risk of suicide was greatest in the first couple of weeks after contact with the somatic department. When adjusting for possible confounding variables (<i>i.e.</i> child's psychiatric history, parent's psychiatric history, level of income and education) asthma was not an independent risk factor for suicide (rate ratio [95% CI] for males 1.11 [0.78–1.59] and females 1.02 [0.83–1.24]).	6 (I=1, II=1, III=2, IV=1, V=1)
CHUNG and JOUNG [27]	13958 youths in USA who completed the YRBS and 48814 Korean youths who completed the Korean Youth Behavioral Risk Factor Surveillance Survey aged 12–18 years in 2007	Cross-sectional	Suicidal ideation and attempts	Self-reported diagnosis of asthma	Results indicated that a medical diagnosis of asthma was a significant risk factor for both suicidal ideation (aOR 1.15, 95% CI 1.06–1.25) and attempt (aOR 1.44, 95% CI 1.28–1.63) in the Korean youth sample, but not in the USA youth sample.	5 (I=1, II=1, III=2, IV=0, V=1)
GOODWIN et al. [28]	6584 adults aged 20–39 years who participated in NHANES III between 1988 and 1994 in USA	Cross-sectional	Suicidal ideation and attempts	Self-reported diagnosed asthma	Compared to individuals without asthma, current asthma status was associated with higher risk of suicidal ideation (OR 2.07, 95% CI 1.28–3.34) and suicide attempt (OR 3.83, 95% CI 2.32–6.34), which remained statistically significant (although somewhat reduced) after controlling for demographic characteristics, smoking, depression, dysthymia, mania and allergy (suicide ideation OR 1.77, 95% CI 1.11–2.84 and suicide attempt OR 3.26, 95% CI 1.97–5.39). There was no significant relationship between former asthma and suicide ideation or attempt when the same variables were adjusted for.	4 (I=1, II=1, III=1, IV=0, V=1)
WEBB et al. [29]	Data from UK family practices registered with the GPRD, linked with national mortality records of 873 adult suicide cases matched by age and sex with 17460 living controls between 2001 and 2008	Nested case-control	Suicide mortality	Asthma diagnosis from primary-care records	Overall, there was no higher suicide risk in those with any of the 11 physical illnesses studied combined (aOR 0.89, 95% CI 0.75–1.04). Asthma was not significantly associated with increased suicide mortality before or after controlling for depression (aOR 0.84, 95% CI 0.66–1.08). 64.7% of asthma cases had depression, which was the second most frequent comorbidity after back pain.	6 (I=1, II=1, III=2, IV=1, V=1)
WEBB et al. [30]	Routinely collected UK primary-care records of 2306 self-harm cases and 46120 age- and sex-matched controls from the GPRD between 2001 and 2008 Age at first episode of self-harm ranged from 17 to 87 years	Nested case-control	Self-harm	Asthma diagnosis from primary-care records	Overall, patients diagnosed with any of the included physical illnesses had almost 50% higher risk of self-harm. Separate analysis showed that 9 out of the 11 illnesses had significantly increased risk; however, when controlling for depression, only asthma (OR 1.17, 95% CI 1.03–1.34), back pain and epilepsy remained significant. Having ≥ 2 comorbid medical conditions significantly increased the risk of self-harm in women but not men when controlling for depression.	6 (I=1, II=1, III=2, IV=1, V=1)

Continued

TABLE 2 Continued

Authors	Population, participants and time	Study design	Measures of suicidal behaviour	Measures of asthma	Main findings	Quality score [#]
BANDIERA <i>et al.</i> [31]	1550 Puerto Rican youths aged 11–16 years and living in the South Bronx (New York, NY, USA), San Juan and Caguas (Puerto Rico) participating in the Boricua Youth Study of antisocial behaviours and other psychiatric disorders (wave 3) in 2000–2004	Cross-sectional	Self-reported suicidal thoughts and ideation, past suicide attempts and suicidal plans within the past year	Parental reports of asthma in past year	Those with asthma were ~1.7 times (95% CI 1.11–2.64) more likely to experience suicidal ideation or behaviour than those without asthma. This association was significant even when controlling for demographics, socioeconomic status, major depression, conduct disorder, PTSD, cigarette smoking and stressful life events.	5 (I=1, II=1, III=1, IV=0, V=1)
BOLTON <i>et al.</i> [32]	2100 individuals from Manitoba (Canada) who died by suicide between 1996 and 2009 were matched with 6300 general population controls 8641 individuals with suicide attempts were compared to 25 923 matched controls Data were obtained from the Population Health Research Data Repository at the Manitoba Centre for Health Policy Ages ranged from those born in 1940 and earlier to those born in 1991 and later	Nested case-control	Suicide mortality and suicide attempts	Physician-diagnosed asthma as recorded in the Manitoba health registry	In unadjusted models, asthma was significantly associated with increased risk of suicide mortality (OR 1.50, 95% CI 1.32–1.71; $p<0.001$). In the adjusted model, asthma was no longer significantly associated with suicide risk overall (aOR 1.03, 95% CI 0.88–1.22); however, the risk remained significant in women (aOR 1.41, 95% CI 1.06–1.86; $p<0.05$). Asthma was associated with risk of suicide attempts after adjusting for ADG count, depression, anxiety disorders, substance abuse, schizophrenia, dementia and all other physical disorders (aOR 0.84, 0.75–0.93; $p<0.001$).	6 (I=1, II=1, III=2, IV=1, V=1)
CRUMP <i>et al.</i> [33]	National cohort of 7 140 589 Swedish adults aged ≥ 18 years were followed for suicide mortality using the Swedish death registry between 2001 and 2008	Cohort study	Suicide mortality	Diagnosed asthma recorded in outpatient and hospital registries	Univariate analysis indicated that asthma ($p=0.02$) was more prevalent among women who died by suicide compared to the rest of the population. Further multivariate analysis indicated that a number of somatic disorders, including asthma, were significant independent risk factors for suicide among both men and women (aHR ~1.4–2.1).	6 (I=1, II=1, III=2, IV=1, V=1)
SINGHAL <i>et al.</i> [34]	Cohort from nationwide dataset of English Hospital Episode Statistics linked with mortality data from 1999 to 2011 2 500 814 individuals with asthma were included and ages ranged from children to adults (10–>65 years)	Cohort study	Self-harm and suicide mortality	Hospital admissions for asthma	Asthma was associated with an increased risk of self-harm (rate ratio 1.8, 95% CI 1.8–1.9), the highest risk being in those aged 45–64 years (rate ratio 2.2, 95% CI 2.1–2.2). Those suffering from asthma were also significantly more likely to die by suicide than those in the reference cohort (rate ratio 1.2, 95% CI 1.1–1.3; $p<0.05$).	6 (I=1, II=1, III=2, IV=1, V=1)

NHANES: National Health and Nutrition Examination Survey; aOR: adjusted odds ratio; MECA: Methods for the Epidemiology of Child and Adolescent Mental Disorders; YRBS: Youth Risk Behavior Survey; NCS-R: National Comorbidity Survey Replication; HR: hazard ratio; KYRBWS: Korea Youth Risk Behaviour Web-based Survey; GPRD: General Practice Research Database; PTSD: post-traumatic stress disorder; ADG: Johns Hopkins Aggregated Diagnosis Groups; aHR: adjusted hazard ratio. [#]: Quality ratings have a maximum score of 6. The following criteria were used to assess quality. I: representativeness of the sample to the general population (0=not representative, 1=representative); II: presence of a control/comparison group (0=no control/comparison group, 1=control/comparison group); III: number of participants with history of the condition (asthma) (0=<100, 1=<500, 2=>500); IV: longitudinal (follow-up) (0=no, 1=yes); V: data presentation (0=unclear data presentation, 1=clear data presentation) (adapted from POMPILI *et al.* [15]).

study designs (n=3) and nested case-control study designs (n=3). Studies originated from a relatively wide range of countries/areas including USA (n=9), UK (n=2), USA/Korea (n=1), Korea (n=1), Taiwan (n=1), Denmark (n=1) and Canada (n=1).

Seven of the studies using cross-sectional designs included measures of both suicidal ideation and attempts in people suffering from asthma, while another three studies focused solely on suicidal ideation. The three papers focusing solely on suicidal ideation found significant associations between asthma and suicidal ideation in children [17], adults [18] and elderly adults aged >65 years [25]. The majority of studies including both suicidal ideation and attempts found that asthma was associated with increased risk of both ideation and attempts in adults [16, 28] and children [20, 24, 31]. Two of the papers reported less conclusive results: the study by CLARKE *et al.* [22] was the only one to find that asthma was associated with suicidal ideation including attempt(s), but not with suicidal ideation alone. The study performed in both USA and Korea found an association between suicidal ideation and attempts in Korean youth but not American youth [27]. Two cohort studies from USA found that asthma was significantly associated with suicidal ideation in adults [19, 21]. GOODWIN and EATON [19] also found that asthma was associated with increased risk of suicide attempts, which remained significant when controlling for sex, age, race, asthma treatment and lifetime major depression. The cohort study from the UK found that asthma was significantly associated with an increased risk of self-harm, particularly in the 45–64 year age group [34]. Significantly increased risk was not found in those suffering from cancer, congenital heart disease, ulcerative colitis, sickle-cell anaemia or Down's syndrome. Three nested case-control designs focused on self-harm [30] and suicide attempts [26, 32]. WEBB *et al.* [30] included a number of different somatic conditions, finding that after controlling for depression, only asthma, back pain and epilepsy were significant predictors of self-harm. BOLTON *et al.* [32] found that asthma was significantly associated with attempted suicide after controlling for Johns Hopkins Aggregated Diagnosis Groups count, depression, anxiety disorders, substance abuse/dependence, schizophrenia, dementia, other psychosocial disorders and all physical disorders. Conversely, while CHRISTIANSEN and STENAGER [26] found that individuals treated for asthma were at a higher risk of suicide attempt, particularly within the first couple of weeks of contact with the somatic department, this result did not remain significant after controlling for other factors.

Discussion

Suicidal behaviour has been associated with poor physical health status [35], depression [36] and risk-taking behaviour [37], factors which are all commonly seen in asthma sufferers. It has been hypothesised that the presence of these risk factors in asthma sufferers may interact to result in an increased risk of suicidal behaviour in these individuals. In addition, recent research by DARLINGTON *et al.* [38] has suggested that there may be a common genetic link between asthma and suicidality. The current review supports the association between asthma and suicidality, with a number of studies finding an increased risk of suicide mortality [23, 33] and nonfatal suicidal behaviour [16, 19–22, 27, 30, 31] in asthma sufferers. Only two of the studies failed to find any significant association between asthma and suicidality [26, 29]. The results of studies including a number of different physical illnesses suggested that asthma may present a higher risk than a number of other somatic conditions [30, 33].

There have been some suggestions that medications used to treat the symptoms of asthma may help to explain the increased risk of suicidal behaviours in asthmatics. However, the research pertaining to the use of asthma medications and suicide risk has returned very mixed findings, with a number of studies failing to find an increased risk in individuals using these medications [39–41]. One study indicated that risk associated with asthma medications may be higher than certain types of medications for other conditions (selective serotonin reuptake inhibitors), but that risk may depend on the type of asthma medication used [42]. The other finding, that increased suicide risk was in association only with the use of theophylline for asthma, but not with another type of asthma medication (long-acting β -agonists), supported this possibility [43]. While there are currently not enough available studies in this area to analyse suicide risk depending on the particular asthma medication used, this may be a useful topic to explore in the future.

Asthma is a chronic condition which is very prevalent in younger age groups [1]. A number of studies in the current review focused on the risk of suicide and suicidal behaviour in children and adolescents suffering from asthma, and indicated that young individuals who are suffering from asthma may be at an increased risk of suicide mortality [23], ideation [18] and attempts [20, 24, 31]. Studies also explored the potential impact of risk-taking behaviours in this age group, finding that a large percentage of children who experienced suicidal behaviour had engaged in cigarette smoking (40%), marijuana use (60%) and binge drinking (37%) [20]. The findings of BAE *et al.* [24] supported this, finding significant interactions between asthma, suicidal ideation and cigarette smoking behaviours in youth. Despite these findings, there is no evidence to suggest that children and adolescents are particularly at-risk compared to other age groups, as asthmatic adults and elderly individuals have also been found to have an increased risk of suicidal behaviour.

While there is too little information available to determine if there are any clear sex differences, CLARKE *et al.* [22] did find that risk of suicidality was increased when asthma sufferers were female, depressed, anxious, smokers, abusers of alcohol or nicotine dependent. WEBB *et al.* [30] found that having two or more comorbid medical conditions increased the risk of self-harm in women, but not in men. Furthermore, after adjusting for mental disorders, BOLTON *et al.* [32] found that asthma remained significantly associated with suicide in women, but not in men. Based on these limited findings, more research exploring the potential for sex differences may be warranted.

Implications

The findings of the current review lend support to the existence of a link between suicidal behaviour and asthma in adults and children/adolescents. In particular, young people who engage in risky behaviour including smoking and alcohol/drug use appear to be especially susceptible, and it may be prudent for individuals caring for these children to be wary of the potential for suicidal behaviours in this group [20, 24]. Furthermore, it is likely that these risky behaviours result in poor asthma control and medication adherence, suggesting the need to ensure that young individuals are treating their asthma appropriately [6].

It is possible that the severity and timing of asthma symptoms increases the chances of suicidal behaviour, shown by the findings that particular symptoms or a number of different symptoms may present a greater risk [23]. Furthermore, it appears that risk may be highest in the weeks after medical treatment is sought [33]. As a result, it may be important for medical practitioners to be aware of this potential risk while treating individuals with severe asthma symptoms.

The findings of studies regarding asthma medication and suicide risk have produced mixed results and there appears to be little conclusive evidence consistently linking these medications to suicidal behaviour. It may be possible that particular medications are associated with suicide risk while others are not; however, it is clear that more research is needed on this topic before the safety of these medications can be determined.

Limitations

The limitations and potential for bias of both the current review and the individual studies in the review has been assessed. The current review was restricted to English-language articles published in peer-reviewed journals at the time of the searches. Therefore data published in grey literature (*i.e.* government reports) or in other languages are not included, which may have resulted in the exclusion of some potentially relevant papers. Only five studies involved suicide mortality. A large number of papers on nonfatal suicidal behaviour originated from the USA, a fact that may limit the generalisability of findings to other countries. Studies used varying methodology to determine whether participants suffered from asthma and/or suicidal behaviour, which may affect the ability to compare results from single contributions. For example, a number of studies relied on self-reported indications of asthma and/or suicidality, and this will inevitably involve some degree of inaccuracy [16, 18, 20–24, 28, 31]. Conversely, studies including only asthma sufferers who had received hospital or other medical treatments might have excluded those individuals who did not seek that specific treatment for their illness [17, 29, 30]. Lastly, the large number of descriptive cross-sectional study designs used in the reviewed studies makes it difficult to determine the direction of causality in the relationship between suicidal behaviour and asthma.

Conclusions

Asthma is an important chronic condition that has previously been linked to a number of adverse outcomes including depression and risk-taking behaviour. There is currently a body of research suggesting a link between suicidal behaviour and asthma; however, little is known about the direction of this relationship and potential at-risk subgroups. Nevertheless, it appears that asthmatics may be at an increased risk of suicidal behaviour across all ages. The possibility of asthma medications exacerbating suicidal behaviour is still unclear, and more research is needed in this area.

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