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# Risk of suicide for individuals reporting asthma and atopy in young adulthood: Findings from the Glasgow Alumni study

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ABSTRACT

There is emerging evidence that asthma and atopy may be associated with a higher risk of suicide. We investigated the association of asthma and atopy with mortality from suicide ($n=32$) in the Glasgow Alumni cohort, adjusting for the key confounders of socioeconomic position and smoking. We found no evidence of an association in our a priori atopy phenotypes with suicide, and there were insufficient suicides in the asthma phenotypes to draw any conclusions. In additional analyses, individuals reporting both eczema–urticaria and hay fever and those with family history of atopy were at higher risk of suicide. As these were secondary analyses and based on small numbers of events we cannot rule out chance findings. The lack of evidence in our main hypothesis may be due to the small number of suicides or reported associations between asthma and atopy may be confounded.



## 1. Introduction

In 1966 Paffenbarger reported a higher percentage of allergic reaction to irritants and a consistent, "although not statistically significant", higher percentage of asthma, among students who had died by suicide compared to controls (Paffenbarger and Asnes, 1966). Since then, a systematic review (Iessa et al., 2011) and additional papers (Timonen et al., 2001; Kuo et al., 2010; Qin et al., 2011; Loerbroks et al., 2012) have documented a higher risk of suicide ideation, attempt or death as well as depression among asthmatics and/or people with reported or measured atopy. Despite this increasing evidence, important confounders such as socioeconomic position (SEP), smoking and comorbidities were not available in all studies and so may have confounded these reported associations (Woo et al., 2012). Few studies include actual deaths by suicide (Paffenbarger and Asnes, 1966; Kuo et al., 2010; Qin et al., 2011), some with a very small number of deaths (Goodwin and Eaton, 2005). Other studies have amalgamated different asthma/atopy phenotypes making it difficult to investigate whether there is a common aetiological pathway between asthma/atopy and suicide. The Glasgow Alumni study is a historical cohort of university students, with relatively homogenous SEP in adulthood, and information available on smoking in early adulthood (McCarron et al., 1999). In addition, a subsample of the cohort provided data on depression and mental health. The aim of this study was to investigate the association of pre-defined asthma and atopy phenotypes reported in young adulthood with later suicide.

## 2. Methods

Students who attended the University of Glasgow between 1948 and 1968 were invited to an annual medical examination at the Student Health Service with approximately 50% of the students attending ($n=15,322$, 77% male, mean age 20.9 years (S.D. 4.0)) (McCarron et al., 1999). Sociodemographic and medical data were collected through a physician administered questionnaire and physical examination. Students reported "Past Medical History" of, among other conditions, having ever had i) asthma, ii) eczema–urticaria, and iii) hay fever. Eczema and urticaria were asked jointly in the questionnaire and could not be separated in the analysis. The following asthma and atopy phenotypes were initially investigated: asthma (regardless of atopic status), atopy (eczema–urticaria and/or hay fever, regardless of asthma status), and phenotypes based on the combination of these two conditions: asthma with atopy (asthma and eczema–urticaria or hay fever), asthma without atopy (asthma without eczema–urticaria or hay fever) and atopy alone (eczema–urticaria or hay fever without asthma). Secondary analyses investigated all combinations of the two atopic conditions, eczema–urticaria and hay fever, as well as family history of these conditions.

Between 2001 and 2002, members of the cohort who were still alive ($n=8410$) were contacted through a postal questionnaire and 5569 (66%) responded to this follow-up. The General Health Questionnaire (GHQ-12) (Goldberg, 1978) and history of depression in adulthood were collected in this subsample; a score of four or more on the GHQ-12 was used to indicate poor mental health. We investigated the association of asthma and atopy reported at baseline with the

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GHQ-12 and history of depression in adulthood in the sub-sample of questionnaire respondents. The National Health Service Central Register (NHSCR) carried out tracing of the students and provided notification of the date and cause of death, area of current residence, and emigration details. Deaths up until the end of 2012 were included. ICD-9 and ICD-10 codes were used to classify suicides into intentional self harm (ICD9: E950–E959; ICD10: X60–X84) and deaths of undetermined intent (ICD9: E980–E989, excluding E988.8; ICD10: Y10–Y34). Deaths of undetermined cause were also included in our analyses as most such deaths were suicides (Linsley et al., 2001).

Cox proportional hazards regression models were used to investigate the association of asthma and atopy with suicide using age as the time axis. The assumption of proportional hazards across exposure groups was formally tested with the Schoenfeld test. All models were adjusted for year of student examination to control for potential confounding from the change over time of disease prevalence or definitions. The final model contained terms for year of student examination, sex, height, number of siblings, birth order, father's social class measured with occupational class using the Registrar's Social class classification, body mass index (BMI) and smoking. In addition we investigated the association between poor mental health (GHQ-12 score of 4 or more) and suicide in the subsample.

## 3. Results

Students who could not be traced or who had missing exposure data were excluded from this analysis, yielding a total sample of 11,463 (8938 male, 78%) individuals among whom there were 32 suicides (29 male) up to the end of 2012. The incidence of suicide in this study was 5.52 per 100,000/year, which was substantially lower than the UK average (11.8 per 100,000/year) (ONS, 2013). The prevalence of asthma was higher in males than females (3.7% vs. 2.3%, $p=0.001$), while the prevalence of atopy was higher in females than males (12.3% vs. 9.2%, $p<0.001$). The median age of study members at the time of university medical examinations was 19.4 years (range 16–53). We found no evidence of an association of asthma and/or atopy phenotypes in young adulthood with later suicide in our a priori groups (Table 1). However, in additional analysis of secondary outcomes, individuals with a combination of eczema–urticaria and hay fever, and a family history of atopy were associated with higher risk of suicide (Table 2).

Students with missing data in the postal questionnaire were excluded, yielding a total subsample of 4746 (3568 male, 75%; 85% of the 5569 students who responded) individuals among whom there were five suicides (5 male) up to the end of 2012. A greater proportion of females reported a diagnosis of depression (19.5% vs. 14.9%, $p<0.001$), or reported poor mental health (GHQ $\geq 4$) (14.3% vs. 10.0%, $p<0.001$) compared to males. There was no evidence of an association between asthma (OR 1.10, 95%CI 0.66, 1.85, $p=0.71$), atopy (OR 0.89, 95%CI 0.66, 1.22, $p=0.47$), eczema–urticaria and hay fever (OR 0.31, 95%CI 0.04, 2.34, $p=0.26$), family history of atopy (OR 1.12, 95%CI 0.79, 1.59. $p=0.52$), or any other phenotype with a GHQ-12 score of 4 or more, or with history of depression measured in adulthood ($p>0.05$). There was weak evidence that poor mental health (GHQ-12 score of 4 or more) was associated with higher risk of suicide (model 2 adjusted HR 6.14, 95% confidence interval (CI) 0.95, 39.56, $p=0.056$).

## 4. Discussion

Contrary to previous studies (Kuo et al., 2010; Iessa et al., 2011; Qin et al., 2011) we found no evidence for our a priori hypothesis of an association of asthma and/or atopy phenotypes in young adulthood with later suicide. However, individuals with a family history of atopy or both eczema–urticaria and hay fever were associated with a higher risk of suicide. As these were secondary analyses and based on small numbers of events we cannot rule out chance findings.

The selective, relatively well-off population in our study (former university students) meant that residual confounding by SEP in adulthood is unlikely. However, their affluence may have contributed to the low incidence of suicide in this sample and so limited the power to detect clinically important associations with our a priori phenotypes. On the other hand, this is one of the only a few studies to investigate the association between asthma or atopy with death from suicide, as opposed to suicidal ideation or attempted suicide (Paffenbarger and Asnes, 1966; Goodwin and Eaton, 2005; Kuo et al., 2010; Qin et al., 2011, 2013), an approach recommended in a recent review on this topic (Goodwin, 2012).

A small number of suicides in this study limited the power to detect associations increasing our chance of reporting type II errors. In one of our a priori hypotheses there were 5 suicides from 1132 individuals reporting atopy compared with 27 suicides from 10331 individuals not reporting atopy. A retrospective power calculation performed using stata (StataCorp, 2013) calculated we had 25% power at 5% significance level to detect an HR of 1.69 or more. To achieve 80% power at a 5% significance level it would require a total sample size of approximately 34,000 individuals, with equal numbers in the atopy and no atopy groups. Alternatively, given our sample size and the number of suicides in individuals with no atopy, at 80% power and a 5% significance level we were only able to detect an effect size approximately twice the size of that observed (an HR3.23 compared with an HR1.69 observed for atopy analysis). Previous studies have reported that asthma or atopy is associated between a 1.2 and 3.5 times higher odds of suicidal ideation, suicide attempts or completed suicide (Goodwin and Eaton, 2005; Messias et al., 2010; Qin et al., 2011).

A potential source of bias could be due to only half of the students who were invited to the medical examination actually attending. If those who did not attend the medical examination had a higher prevalence of asthma/atopy, and there were more suicides in this group of individuals, then the results of this study would be biased towards the null. This limitation is also relevant to

**Table 1**
Hazard Ratio (HR) and 95% Confidence Interval (CI) of a priori exposures with death from suicide.

| Exposure | Individuals (%) | Suicides (*n*) | Model 1 HR (95% CI) | Model 2 HR (95% CI) |
|---|---|---|---|---|
| Asthma (with or without atopy)[a] | 387 (3.4) | 1 | 0.92 (0.13–6.76) | 0.92 (0.13–6.73) |
| Atopy (with or without asthma)[a] | 1132 (9.9) | 5 | 1.68 (0.65 –4.36) | 1.69 (0.65–4.40) |
| Asthma and atopy phenotypes | | | | |
| No asthma, no atopy (reference group) | 10089 (88.0) | 27 | 1.00 | 1.00 |
| Asthma with atopy | 145 (1.3) | 1 | 2.50 (0.34–18.40) | 2.55 (0.35–18.89) |
| Asthma without atopy | 242 (2.1) | 0 | – | – |
| Atopy without asthma | 987 (8.6) | 4 | 1.51 (0.53–4.32) | 1.51 (0.53–4.34) |

Model 1 adjusted for year of examination. Model 2 also adjusted for sex, height, number of siblings, birth order, fathers social class, body mass index and current smoking.

[a] There were a total of 32 suicides in the cohort of 11,463.