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Allergy is associated with suicide completion with a possible mediating role of mood disorder – a population-based study

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Abstract

Background—With increasing research suggesting a role of allergy on suicidality, this study, on a population level, delved into how allergy affects risk for suicide completion in the context of mood disorder and other factors.

Methods—Based on the entire population of Denmark, we included 27,096 completed suicides and 467,571 live controls matched on sex and age with a nested case-control design. We retrieved personal information on hospital contacts for allergy and other variables from various Danish longitudinal registries, and analyzed the data with conditional logistic regression.

Results—We noted that 1.17% suicide victims, compared with 0.79% matched controls, had a history of hospital contact for allergy, and that a history of allergy predicted an increased risk for suicide completion; however, the effect was confined to allergy that led to inpatient treatment (IRR: 1.59, 95% CI: 1.41–1.80). The increased risk was attenuated somewhat but remained significant when adjusted for personal psychiatric history and socioeconomic status. Meanwhile, we observed a non-significantly stronger effect in women than in men, and a significant age-difference with a stronger effect for individuals at high ages. Moreover, we detected a significant interaction between allergy and mood disorder – even an antagonism effect of the two exposures. Allergy increased suicide risk only in persons with no history of mood disorder whereas it eliminated suicide risk in those with a history of mood disorder.

Conclusions—The findings support a link between allergy and suicidality, with a possible mediating role of mood disorder.

Keywords

allergy; mood disorder; population study; suicide risk

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Author's Contribution:

PQ and TTP conceived the idea of this study and obtained the grant for it. PQ designed the study, analyzed the data and wrote the report. All authors contributed to the critical revision and have approved the final version to be published. The guarantor of the paper, Dr Qin P. accepts full responsibility for the work and/or the conduct of the study, had access to the data, and controlled the decision to publish the paper.

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INTRODUCTION

Significant seasonal peaks in suicide incidents have been consistently identified across continents, countries and hemispheres(1–3), but explanations hereof remain unclear. Recent evidence has shown that the seasonality of suicide tends to co-occur with seasonal aeroallergens that dramatically peak in spring (i.e., tree-pollen) and in late summer/early fall (i.e., ragweed)(4;5) and that such a co-occurrence is more prominent for suicide victims with a history of mood disorders(5). A link between depression – the most well-known risk factor for suicide -- and allergy has been consistently reported in recent publications(6–8). Clinical studies have also demonstrated a depressogenic and prosuicidal effect of certain cytokines which are released in a multitude of inflammatory conditions including allergy(9;10). Consequently, there have been increasing speculations and research efforts delving into the hypothesis that allergic reaction to aeroallergens plays a role in suicidality. However, no study, to our awareness, has used individual level data from a large scale population to systematically address the effect of allergy on risk for subsequent suicide completion while taking into account personal history of mood disorder and other risk factors. In the present study, we explored suicide risk in relation to prior hospital contacts for allergic disorders using data from Danish longitudinal population registries with an established nested case control design. We also examined the possible confounding and modification effect of mood disorder in the association between allergy and suicide.

METHODS AND MATERIALS

Settings

We conducted this study based on the entire population of Denmark (5.2 million persons), a country where hospital treatment is free-of-charge for all residents. Individual data were retrieved from several national longitudinal registries and merged using the unique personal identifier (so-called CPR-number) given to all Danes at birth and to new residents of Denmark(11).

The Cause-of-Death Registry(12) contains information on cause and date of all deaths that have occurred in Denmark since 1969. The Danish General Hospital Registry(13) contains personal data on diagnosis and date of treatments at the non-psychiatric hospitals in Denmark since 1977. The Danish Psychiatric Central Registry(14) covers all psychiatric facilities in Denmark and cumulatively records all admission and discharge information since 1969. Data on outpatient contacts (visits to emergency rooms, hospital outpatient clinics or calls for ambulance) were included in the hospital registers from 1995. Diagnoses of illness and causes of death were coded according to the International Classification of Diseases, the 8th revision (ICD-8) until the year 1993 and the 10th revision (ICD-10) thereafter. The ICD-9 has never been introduced in Denmark.

The IDA Database(15) contains personal yearly information on labour market conditions and socio-demographic status for all residents in Denmark. Individual socioeconomic data for a given calendar year are complete only for persons who lived in Denmark on December 31st of the year.

Study Design and Participants

From the Cause-of-Death Registry(12), we identified all definite suicides (codes E950–959 in ICD-8 and X60–84 in ICD-10) that occurred during the period of 1981 to 2006. We adopted a nested case-control design with incidence density sampling(16) to recruit up to 20 live controls per suicide case, matched for date of birth, sex and time of suicide, from a 25 percent representative sample of the national population. The rationale for sampling 20 controls per case is to enable examination of small subgroups on uncommon exposures with

reasonable statistical power. We excluded individuals who were not residing in Denmark on December 31st the preceding year because of the incompleteness of their socio-economic data in the IDA database. We also excluded individuals who were above 90 years old because of too few eligible controls available for them. With this procedure, we finally included 27,096 suicide cases and 467,571 population controls in the present study.

Data assessment

From the Danish General Hospital Registry(13) we retrieved personal history of hospital contacts because of allergic illnesses, as a primary diagnosis, prior to the date of suicide or the matching time of controls. We considered allergy of the following diagnostic groups: allergic rhinitis without bronchial asthma (Codes: 507 in ICD-8 and J30.1, J30.2, J30.3, J30.4 in ICD-10), allergic rhinitis with bronchial asthma (codes: 493 in ICD-8 and J45.0, J45.8 in ICD-10), and atopic dermatitis (codes: 691.0 in ICD-8 and L20 in ICD-10). We assessed the severity of allergy by looking at whether a patient had been treated as an inpatient or only as an outpatient. Upon the results from the preliminary analyses, we constructed a variable summarizing the total number of inpatient treatments for allergy, and a variable indicating the time distance since the recent hospitalization for allergy to the date of suicide.

We obtained personal data on psychiatric history, either as inpatient or outpatient, from the Danish Psychiatric Central Register(14). The diagnosis of interest was primarily mood disorders (affective disorders), (ICD-8: 296, 298.09, 298.19, 300.49, 301.19 and ICD-10: F30-F34, F38, F39), indicating a history of hospital contact for mood disorders. We also constructed a variable referring a hospital contact because of any other psychiatric disorder in order to control for its possible confounding effect.

In addition, we extracted individual data on socioeconomic status from the IDA database(15) based on records in the preceding year of suicide. Considered variables for data adjustment included marital status, annual gross income, place of residence and citizenship(17).

Statistical Analysis

We constructed contingency tables for the main study variables and computed the relative risk of suicide using conditional logistic regression with the PhReg procedure available in SAS version 9(18) with each case forming a separate stratum. Because we sampled controls from individuals at risk for suicide at the time, *i.e.*, incidence density sampling, the estimated odds ratios (OR) in this study were unbiased estimates of incidence rate ratios (IRR)(19). The Wald test was used to determine the variation in risk estimates across diagnostic groups. The interactions between allergy and mood disorder, sex or age of subjects were additionally examined with the likelihood ratio test.

Ethical Issue

We obtained approval from the Danish Data Protection Agency for the present study.

Results

In our study population, 316 (1.17%) suicide cases and 3689 (0.79%) comparison controls had a history of hospital contact because of allergic illnesses, with the majority hospitalized for inpatient treatment. The most common diagnosis was allergic rhinitis with bronchial asthma, followed by allergic rhinitis without asthma and atopic dermatitis. Table 1 presents the distribution of allergic illnesses by diagnoses and the associated crude incident rate ratios (IRR) for suicide.

Overall, a history of allergy predicted suicide completion with an IRR of 1.46 (95% CI: 1.30–1.64); however, the effect was confined to allergy that led to inpatient treatment [IRR=1.59 (CI: 1.41–1.80) for inpatient history; IRR=0.69 (CI: 0.45–1.06) for outpatient history] (Table 1). Moreover, the increased risk associated with an inpatient history of allergy was somewhat eliminated by about 13.8% when the data were adjusted for the effects of mood disorders and other psychiatric history [adjusted IRR: 1.37 (CI: 1.20–1.57)], and then remained almost unchanged when further adjusted for personal marital status, income, citizenship and place of residence [adjusted IRR: 1.31 (CI: 1.15–1.50)] (Table 2).

At the same time, a history of hospitalized allergy tended to increase suicide risk slightly stronger in women than in men; however, the differences were not statistically significant (test of differences by sex: $\chi^2=0.93$, $p=0.335$). Further adjustment for history of mood disorder eliminated the associated risk by 24.4% for women whilst 7.2% for men. Meanwhile, we observed a slightly significant age difference (test of age differences: $\chi^2=7.38$, $p=0.025$) with a tendency of a stronger effect towards individuals at higher ages (Table 2). Adjustment for psychiatric history only eliminated the allergy associated suicide risk in young and middle age people.

When looking at historical hospitalizations for allergy, we noted a substantially high risk for patients with multiple admissions — a likely dose-response relationship. In addition, suicide risk was substantially high during the first three months and remained significantly increased even 3 years after the recent allergy hospitalization (Table 3).

Interestingly, we observed a generally higher prevalence of mood disorder in control subjects with an inpatient history of allergy compared with that in counterpart controls without allergy regardless of sex and age groups (Table 4). Moreover, the influence of inpatient allergy on suicide risk interacted significantly with that of mood disorders (test of interaction: $\chi^2=14.08$, $df=2$, $p<0.001$ for total subjects). Further examinations of effect interdependence between histories of allergy and mood disorder on suicide risk showed that, the two conditions act at the same time to confer a lower risk for suicide than would be expected based on the additive independent effects of the two exposures – indicating an antagonistic relationship between allergy and mood disorder in predicting risk for subsequent suicide. Such observation was consistently present in the analyses stratified by sex and age group of the subjects (Table 4).

DISCUSSION

Findings and explanations

Using data from Danish national longitudinal registries, this large population study confirms our hypothesis demonstrating an increased risk for subsequent suicide completion in individuals with a history of allergic illness. However, the observed elevated risk is confined to severe allergy that leads to inpatient treatment and the effect is, to a certain degree, explained by personal history of mood disorders especially for women and young people. At the same time, a history of hospitalized allergy tends to increase suicide risk non-significantly stronger in women than in men, and significantly more in individuals at higher ages. More interestingly, this study reveals a significant interaction between allergy and mood disorder – even an effect of antagonism of the two exposures, i.e., the increased risk of suicide associated with the co-occurrence of both allergy and mood disorder is smaller than would be expected based on the additive independent effects of allergy and mood disorder alone. This observation is consistently present regardless of sex and age of the subjects. Such results suggest that treatment for allergy may eliminate suicide risk associated with mood disorder or vice versa, treatment for mood disorder may prevent from the effect of allergy.

These findings are evident in supporting a connection between allergy and suicidality. It appears that the connection between allergy and suicide runs deeper than the obvious fact that allergy makes people feel unwell. When allergens activate the immune system, the brain begins to produce pro-inflammatory cytokines – a group of signal proteins that allows cells to communicate with each other(9). The expression of pro-inflammatory cytokines can then lead to reduced activities and social interactions including inhibition of sexual behavior, reduced food intake and increased sleepiness(20). It can also activate the hypothalamic-pituitary-adrenal (HPA) axis in the brain(9;20), which then leads to aberrant responses to stress and further demodulation of immune responses. At the same time, the elevated pro-inflammatory cytokines can activate the indoleamine deoxygenase enzyme, thus reducing serotonin production(9;20) – a well-observed phenomenon among suicidal people. In addition, certain type (Th2-related) pro-inflammatory cytokines can lead to insomnia and sleep loss which may contribute to the increased risk for suicide(21). Briefly to say, allergy increases risk for suicide not only because it makes people feel sick, but also because it affects neuronal function through a number of neuroimmune and general physiopathological interactions, making people lose interest in activities and social interactions or overreact to stressful situations(22;23), which in turn increase the risk for suicide.

These neuro-biological mechanisms well explain the existing reports that patients with allergy are more often to have major depression(24) or sleeping troubles(21), respond more strongly to stressors like back pain(25), and exhibit a higher prevalence of suicide ideation(22). They are also explanatory to our observation of a higher prevalence of mood disorder in the population controls with than without a history of allergy, and in particular, to our finding of a significantly increased risk of suicide completion associated with allergy. In line with these explanations, our results regarding the recentness and frequentness of hospitalization for allergy are therefore expected, simply because the allergy reaction is strong in patients with acute allergy or severe allergy leading to multiple hospitalizations. On the other hand, a general psychological rather than biological explanation is possible. A number of studies have demonstrated a significantly increased risk for suicide among patients diagnosed with medical illness(26). Although there may be explanations specific to certain illnesses, the general worsening of physical function and quality of life due to the illness could be a shared explanation.

There are reports suggesting that the connection between allergy and suicidality may manifest differently by sex, with a stronger association in women than in men(4;8;26). Our estimates are in accordance with these reports although the observed sex differences did not reach a statistically significant level. In the meantime, our results that allergy tends to increase suicide risk stronger in old than young people, and that the increased risk in old age groups is to a less degree explained by psychiatric illness than that in young age groups, are concordance with previous reports that psychiatric illness has a stronger effect in young people while physical illness has a stronger effect in the elderly(26).

One novel and striking finding from the present study is the antagonism effect of allergy and mood disorder, indicating that persons with both allergy and mood disorder have a lower risk of suicide than expected based on their independent effects. This, in another word, means that allergy increases suicide risk only for individuals with no history of mood disorder whereas eliminates suicide risk for those with such a history. Of course, it is possible that patients with co-morbidity of several medical problems, i.e., mood disorder and allergy in this case, receive better attention and treatment. However, this is not sufficient enough to fully explain our observation. We think, it is likely that treatment for mood disorder could prevent from the effect of allergy on suicide risk. This is supported by emerging evidence suggesting that, certain antidepressants such as SSRI, in addition to their antidepressant effects, have also an anti-inflammatory effect by suppressing inflammatory

cytokine production(27;28). On the other hand, in treatment of allergy, the often used intranasal corticosteroids are designed to achieve localized effects with minimal systemic or SNS effects, and thought to reverse the exaggerated Th2-related pro-inflammatory cytokine response(29–31). There are also suggestions(21) that intranasal corticosteroids may have a potent effect on sleep disruption – a common problem for patients suffering from either allergic rhinitis or mood disorders. Therefore, it is our belief that some anti-allergic medications, especially those known to reduce production of allergy-related cytokines, may have an effect of lowering suicide risk in patients with allergy. This speculation could well explain why we did not observe an increased but a likely reduced risk in patients with mild allergic rhinitis that only led to outpatient treatment. As for allergy that is severe enough for inpatient treatment, the protective effect of anti-allergic medications is probably more prominent for patients with than without a co-morbid mood disorder. Although mood disorder is a strong risk factor for suicide on its own, it could act as a mediator for the link between allergy and suicidality through the effect of the allergy-induced cytokines(10). Therefore, medications treating allergy may have a treatment effect on mood disorder thus consequently eliminates the influence of mood disorder on suicide risk. However, this speculation is somewhat against recent concerns on a pro-suicidal effect of anti-allergic treatment(32). Further research is needed to disentangle these therapeutic speculations.

Limitations and Strengths

The present study is, to our knowledge, the first to document an association between a history of allergy and risk for subsequent suicide completion and to explore the modification effect of mood disorder beyond the association. Major strengths include the coverage of the entire national population of Denmark and the precise data collected systematically without a research purpose. This ensures the full representation of a national population and minimizes possible biases often induced by recall of information and selection of access to health care. Moreover, the data were successfully controlled for sex and age differences, and adjusted for important confounders as personal socioeconomic and psychiatric status.

Among limitations, we acknowledge a major under coverage of allergy as we considered only patients with hospital contacts for allergy treatment while the estimated prevalence of allergy is about 25% in the developed countries(33). Similarly, we used psychiatric service contact as a proxy for mood disorder and other psychiatric disorders. This clearly represents a significant underestimate of the full extent of psychiatric disorders, and would reflect more serious disorders(34). At the same time, we were only able to obtain personal historical data on allergy and psychiatric illness when the register data became available, which means that our data cover a relatively long period, but not lifetime for subjects at high ages. Moreover, anti-depressant and anti-allergy treatments and medications are not analyzed because such data were not available for the present study.

Clinical implication and future research

This study expands upon the current knowledge regarding the association between allergy and suicidality, demonstrating that a history of allergy predicts a significantly increased risk for subsequent suicide completion. Although we should not alert the need of assessment for suicidality of all patients with allergy, the results suggest that physicians treating patients with allergic disorders should be vigilant about expressions of suicidal ideation or signs of self-harm, particularly for those with a recent diagnosis or severe allergy.

At the same time, this study adds to existing evidence supporting that allergy, mood disorder and suicide may share underlying pathways in the etiology, including shared inflammatory and stress-response mechanisms as well as psycho-behavioral elements. However, replications of the findings are needed with individually linked epidemiological studies from

various social settings and with randomized clinical trials. Also, it would be of great importance if research could quantify the temporal relationship between allergen exposure and incidents of suicidal behaviour while taking into account personal history of mood disorder and other factors. Cohort studies of patients diagnosed with allergy could be set to document the mediating role of mood disorder and the importance of allergic sensitization on the risk for subsequent suicidal behaviour. Moreover, pharmaco-epidemiological studies are needed to evaluate the interactive effect of psychotropic, antidepressant and anti-allergy medications on risk for subsequent suicidal behaviour. Answers to these questions could help to disentangle the causality of these disorders and may set a new stage for developing innovative treatment targeting these problems concurrently.

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Table 1

Distribution of various allergic illnesses and associated incidence rate ratio for suicide completion, total subjects

Exposures	Number (%)		IRR Crude analysis [§]
	Suicide cases N=27 096	Controls N=467 571	
Inpatient contact for allergic illness	295 (1.09)	3102 (0.66)	1.59 (1.41–1.80) [‡]
Allergy rhinitis without bronchial asthma	23 (0.08)	334 (0.07)	1.31 (0.86–2.01)
Allergy rhinitis with bronchial asthma	266 (0.98)	2626 (0.56)	1.66 (1.46–1.89) [‡]
Atopic dermatitis	15 (0.06)	191 (0.04)	1.49 (0.88–2.52)
Outpatient contact only for allergic illness	22 (0.08)	610 (0.13)	0.69 (0.45–1.06)
Allergy rhinitis without bronchial asthma	9 (0.03)	344 (0.07)	0.51 (0.26–0.99) [‡]
Allergy rhinitis with bronchial asthma	6 (0.02)	208 (0.04)	0.55 (0.24–1.23)
Atopic dermatitis	7 (0.03)	70 (0.01)	1.84 (0.85–4.02)

[§]Crude IRRs were only adjusted for sex-birthday-calendar time through matching.

[‡]p-value <0.05;

[‡]p-value <0.01.

Table 2
History of inpatient treatment for allergic illness and associated incidence rate ratio (IRR) for completed suicide

Exposure in Study Subjects	Number (%)		IRR* (95% Confidence Interval)		
	Suicide cases	Controls	Model I	Model II	Model III
Total subjects					
History of allergy: No	26801 (98.91)	464469 (99.34)	1 (reference)	1 (reference)	1 (reference)
History of allergy: Yes	295 (1.09)	3102 (0.66)	1.59 (1.41–1.80) [‡]	1.37 (1.20–1.57) [‡]	1.31 (1.15–1.50) [‡]
Female subjects					
History of allergy: No	9000 (98.77)	158910 (99.28)	1 (reference)	1 (reference)	1 (reference)
History of allergy: Yes	112 (1.23)	1147 (0.72)	1.72 (1.42–2.09) [‡]	1.30 (1.04–1.63) [‡]	1.20 (0.96–1.51)
Male subjects					
History of allergy: No	17801 (98.98)	305559 (99.36)	1 (reference)	1 (reference)	1 (reference)
History of allergy: Yes	183 (1.02)	1955 (0.64)	1.52 (1.31–1.78) [‡]	1.41 (1.19–1.66) [‡]	1.37 (1.16–1.62) [‡]
Subjects 35 years old					
History of allergy: No	5387 (99.04)	106695 (99.20)	1 (reference)	1 (reference)	1 (reference)
History of allergy: Yes	52 (0.96)	864 (0.88)	1.18 (0.89–1.56)	0.92 (0.67–1.26)	0.88 (0.64–1.22)
Subjects 36–60 years old					
History of allergy: No	12702 (99.16)	244302 (99.48)	1 (reference)	1 (reference)	1 (reference)
History of allergy: Yes	107 (0.84)	1289 (0.52)	1.60 (1.31–1.95) [‡]	1.20 (0.96–1.50)	1.13 (0.90–1.41)
Subjects >60 years old					
History of allergy: No	8712 (98.46)	113472 (99.17)	1 (reference)	1 (reference)	1 (reference)
History of allergy: Yes	136 (1.54)	949 (0.83)	1.86 (1.54–2.23) [‡]	1.85 (1.52–2.26) [‡]	1.81 (1.48–2.21) [‡]

Notes:

* IRRs from model I were only adjusted for sex-birthday-calendar time through matching; model II were further adjusted for history of mood disorder and other psychiatric illness; model III were moreover adjusted for marital status (single or cohabitating vs. married), annual gross income (lowest, second, or third quartile vs. the highest quartile), place of residence (the Capital, provincial cities vs. the rest of Denmark) and citizenship (non-Danish citizen vs. Danish citizen).

[‡] p-value <0.05;

[‡] p-value <0.01.

Test of differences, based upon the crude model: 1) sex differences: x2=0.93, df=1, p=0.335; 2) age differences: x2=7.38, df=2, p=0.025.

Table 3

Hospitalization for allergy and associated incidence rate ratio (IRR) for completed suicide, total subjects

Allergy history	Number (%)		IRR* (95% Confidence Interval)		
	Cases	Controls	Model I	Model II	Model III
Number of hospitalizations					
No history	26801 (98.91)	464469 (99.34)	1 (reference)	1 (reference)	1 (reference)
Once	169 (0.62)	2049 (0.44)	1.39 (1.18–1.63) [‡]	1.26 (1.06–1.50) [‡]	1.22 (1.02–1.45) [‡]
2–3 times	78 (0.29)	734 (0.16)	1.76 (1.39–2.23) [‡]	1.43 (1.09–1.86) [‡]	1.34 (1.02–1.75) [‡]
>3 times	48 (0.18)	319 (0.07)	2.52 (1.85–3.42) [‡]	1.90 (1.34–2.69) [‡]	1.76 (1.24–2.50) [‡]
Time since last hospitalization					
No history	26801 (98.91)	464469 (99.34)	1 (reference)	1 (reference)	1 (reference)
Within 3 months	36 (0.13)	103 (0.02)	5.68 (3.87–8.33) [‡]	5.44 (3.50–8.45) [‡]	4.98 (3.20–7.75) [‡]
3–12 months	27 (0.10)	246 (0.05)	1.79 (1.20–2.68) [‡]	1.52 (0.97–2.37)	1.44 (0.92–2.26)
1–3 years	61 (0.23)	522 (0.11)	1.83 (1.40–2.40) [‡]	1.61 (1.19–2.18) [‡]	1.55 (1.14–2.09) [‡]
>3 years	171 (0.63)	2231 (0.48)	1.31 (1.12–1.53) [‡]	1.11 (0.93–1.32)	1.06 (0.89–1.26)

Notes:

* IRRs from model I were only adjusted for sex-birthday-calendar time through matching; model II were further adjusted for history of mood disorder or other psychiatric illness; model III were moreover adjusted for marital status, annual income, citizenship and place of residence.

[‡] p-value <0.05;

[‡] p-value <0.01.

Table 4

Interdependence between histories of allergy and mood disorder in predicting risk for suicide

History of Affective Disorders	Distribution, cases/controls		IRR* (95% CI)	
	History of allergy No	History of allergy Yes	History of allergy No	History of allergy Yes
Total subjects				
Mood disorder: No	21381 / 457139	239 / 3010	1 (reference)	1.53 (1.33–1.75)
Mood disorder: Yes	5420 / 7330	56 / 92	13.57 (13.02–14.15)	9.71 (6.83–13.79)
Female subjects				
Mood disorder: No	6123 / 155031	76 / 1089	1 (reference)	1.58 (1.25–2.01)
Mood disorder: Yes	2877 / 3879	36 / 58	16.35 (15.40–17.35)	11.53 (7.42–17.90)
Male subjects				
Mood disorder: No	15258 / 302108	163 / 1921	1 (reference)	1.51 (1.28–1.78)
Mood disorder: Yes	2543 / 3451	20 / 34	11.37 (10.72–12.05)	7.63 (4.24–13.75)
Subjects 35 years old				
Mood disorder: No	4755 / 106211	48 / 857	1 (reference)	1.15 (0.85–1.55)
Mood disorder: Yes	632 / 484	4 / 7	22.30 (19.48–25.54)	7.31 (1.97–27.11)
Subjects 36–60 years old				
Mood disorder: No	9810 / 240234	77 / 1236	1 (reference)	1.35 (1.07–1.71)
Mood disorder: Yes	2892 / 4068	30 / 53	13.29 (12.56–14.07)	9.12 (5.70–14.61)
Subjects >60 years old				
Mood disorder: No	6816 / 110694	114 / 917	1 (reference)	2.02 (1.65–2.47)
Mood disorder: Yes	1896 / 2778	22 / 32	12.03 (11.23–12.89)	10.99 (6.22–19.43)

Notes:

* IRRs were derived from stratified analyses and adjusted for marital status, annual income, citizenship and place of residence.

Test of interaction between histories of allergy and mood disorder: All subjects: $\chi^2=14.08$, $df=2$, $p=0.0009$; Female subjects: $\chi^2=8.35$, $df=2$, $p=0.015$; Male subjects: $\chi^2=7.35$, $df=2$, $p=0.025$.