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ORIGINAL RESEARCH

Onset of depressive symptoms among adults with asthma: results from a longitudinal observational cohort

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Abstract

Aims: Individuals with asthma may be at increased risk of depression, but few studies have identified precursors to the onset of depression. The study goal was to identify risk factors for depression onset among a community-based sample of adults with asthma.

Methods: Data were obtained from three telephone interviews conducted at 2-yearly intervals on a longitudinal cohort of adults with asthma (n=439). The Center for Epidemiologic Studies Depression scale (CESD) was used to measure depressive symptoms. Multiple regression analyses tested associations of sociodemographic and health-related variables with depression prevalence (cross-sectional analyses) and incident depression (longitudinal analyses).

Results: 15% of subjects were classified as "depressed" (CESD≥23) at each interview. Individuals depressed at baseline were more likely to drop out (OR=1.76 [95% CI 1.05, 2.96]). Low perceived control of asthma (measured with the Perceived Control of Asthma Questionnaire [PCAQ]) exhibited the most consistent association with depression. Lower PCAQ was cross-sectionally associated with depression (OR=0.51 per 0.5 SD difference in PCAQ [0.35, 0.75]). Onset of depression was noted in 38 individuals. Decrease in perceived control at follow-up was associated with depression onset (OR=7.47 [2.15, 26.01]).

Conclusions: Low perceived control of asthma predicted depression onset among adults with asthma. This risk factor may respond to self-management education.

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The full version of this paper, with online Appendix, is available at www.thepcrj.org

Introduction

Rates of depression or depressive symptoms are often found to be higher among people with chronic health conditions.[1-3] This finding has been generally substantiated among adults with asthma.[4-9] For example, the odds of major depression and dysthymia among adults with asthma have been reported to be 60-70% higher than among adults without asthma.[8,9] Kovacs *et al*. reported that 20.5% of a sample of adults with asthma were at least moderately depressed, compared to 8.3% of controls.[4] Although not directly compared to referent populations, Lavoie *et al*. found that 19% of a large sample of adults with physician-diagnosed asthma met the criteria for either depressive disorders or depressive disorders plus anxiety disorders,[6] and a similar proportion (18%) was reported by Eisner in a cohort of 743 adults who had been hospitalised for asthma.[7] These rates are considerably higher than 12-month prevalence rates of approximately 7% that have been identified in the general population.[10-12] In contrast, Taitel stated that depression was no more prevalent among adult asthma patients than among "healthy" individuals.[13]

In many chronic health conditions, symptom severity appears to be an important determinant of depression.[14-22] This also appears to be the case in adult asthma. Among adults with asthma, depression appears to be more frequent among people who perceive their asthma to be severe and life-threatening than

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among those who perceive their asthma as less severe.[23] Consistent with this, more frequent and/or severe asthma symptoms have been associated with depression.[7,24] In studies not limited to people with asthma, there also appears to be a relationship between respiratory symptoms and depression.[25]

Although ascertaining rates of depressive symptoms among adults with asthma is important, it is also critical to identify antecedents of change in depressive symptoms. Despite the importance of this question, there have been no studies identifying precursors to the onset of depressive symptoms among people with asthma. Among individuals with other chronic conditions studied longitudinally, increases in symptom frequency or severity (e.g., pain or disability among individuals with rheumatoid arthritis) have been correlated with, or are predictive of, an increase in depression.[7,26-31] Two studies identified functional losses as clearly preceding the onset of new depressive symptoms among a group of women with rheumatoid arthritis.[27,28] However, few studies have been able to identify true precursors to the onset of depressive symptoms in chronic diseases generally, because of the requirements for longitudinal follow-up and a sample large enough to provide adequate numbers of incident cases of depression.

The aims of this analysis therefore were to identify differences among individuals with asthma who were and were not depressed at an initial assessment, and to identify predictors of the onset of depression over time.

Material and methods

Data source

Data were collected during an ongoing longitudinal cohort study of adults with asthma. The principal data source was a recurrent telephone interview. Details of recruitment and the initial follow-up of the cohort have been reported previously.[32-35] Briefly, we first recruited adults with asthma from a random sample of board-certified pulmonary specialists, allergy/immunology specialists, and family practitioners in Northern California. Later, we recruited additional subjects using random-digit telephone dialing to identify people reporting a physician's diagnosis of asthma. In these analyses, we used data from three interview waves conducted approximately two years apart in 2000-2001 (baseline interview for these analyses, when depressive symptoms were first measured; time 1 [T1; n=439]), 2002-2003 (T2; n=347; 77% of those interviewed at T1), and 2004-2005 (T3; n=314; 92% of those interviewed at T2) (See Figure 1). All procedures were approved by the University's Committee on Human Research, and all subjects gave informed consent to participate.

Variables

1. Depressive symptoms

Depressive symptoms were assessed with the 20-item Center for Epidemiologic Studies Depression scale (CESD),[36] which was developed for use as a screening instrument to identify people at risk for clinical depression. It has been shown to be reliable and valid in a wide range of samples.[37] CESD scores range from 0–60; scores ≥16 are considered indicative of possible depression, and scores ≥23 of probable major depressive disorder.[37] In these analyses, we used a CESD score ≥23 as the study definition of depression to increase the specificity of the classification. Thus, although CESD scores ≥23 are not equivalent to a clinical diagnosis of depression, for simplicity of discussion, individuals with CESD scores ≥23 are referred to as "depressed".

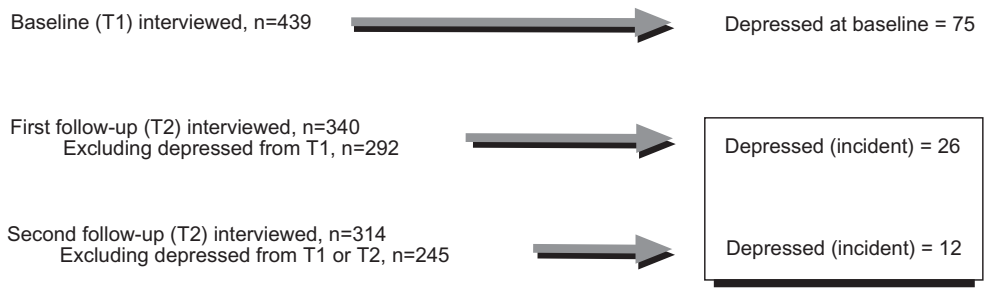
2. Risk indicators/predictors

Potential risk factors for depression were selected *a priori.* Sociodemographic variables examined were: age; sex; educational attainment (less than college degree versus college degree or higher); marital status (married or living with a partner versus other); and race/ethnicity (white, non-Hispanic versus other).

Health-related covariates included smoking status (current, former, or never), co-morbid health conditions (assessed based on self-reports of a physician's diagnosis of the following – high blood pressure, heart disease, diabetes, stomach or intestinal ulcers, arthritis, or osteoporosis), asthma severity, perceived control of asthma, and physical functioning.

Asthma severity was quantified using a previously validated scoring system developed for the assessment of longer-term severity (as opposed to assessment of acute

Figure 1. Subject flow.



symptoms only), based on: asthma symptom frequency over the past two weeks; prior asthma hospitalisation and mechanical ventilatory support for asthma; past and current use of systemic corticosteroids; and use of asthma medications other than systemic steroids.[32,34,38] These asthma severity scores range from 0-28, with higher scores representing more severe asthma, and they have been shown to be correlated with pulmonary function and to predict emergency department utilisation, hospitalisation, restricted activity days, work disability, and mortality.[34,35,39-41]

Perceived control of asthma, or individuals' perceptions of their ability to deal with asthma and its exacerbations, was measured with the 11-item Perceived Control of Asthma Questionnaire (PCAQ).[42] Sample items include: "If I do all the right things, I can successfully manage my asthma," and; "It seems as though fate and other factors beyond my control affect my asthma". Items are rated on a 5-point Likert scale, with total scores ranging from 11-55. For this study, scores were rescaled to range from 0 to 100 for simplicity of interpretation. Four individuals had missing data for one item of the PCAQ in the T2 administration and their scores were calculated without the missing item without extrapolation.

Physical functioning was defined as valued life activity (VLA) disability using a previously validated scale.[43-45] VLAs are defined as a broad spectrum of life activities deemed to be important by the individual.[44] VLA disability has been found to be more closely linked to quality of life among adults with asthma than general physical functioning, and more closely associated with depression and satisfaction with function in other conditions.[43,44,46] VLA disability was assessed by querying the degree to which asthma had affected 16 activity domains such as household work, hobbies, and social activities. Activities not performed for reasons other than asthma as well as activities not important to individuals are not included when summary scores are created. VLA disability is scored as the proportion of rated items that were affected by asthma, and scores range from 0-100. VLA disability was assessed only at T1.

Statistical analysis

Characteristics of individuals who participated through to T3 were compared to those who dropped out of the study using chi-square analyses or t-tests.

To identify cross-sectional correlates of depression at the first assessment (T1), bivariate analyses were first conducted. A multivariate logistic regression analysis was then performed to identify independent correlates of depression at T1. These analyses included the sociodemographic and health-related variables described above.

Chi-square analyses and t-tests were initially used to identify associations between baseline and change variables with the onset of depression. Individuals who were depressed at T1 were excluded from these analyses. Baseline factors considered as predictors of incident depression were sociodemographic and health-related factors from T1. Changes in asthma severity and perceived control from T1 to T2 or T2 to T3 were also considered, depending on the time of onset of depression. For individuals with depression onset at T2, changes from T1 to T2 were examined, while for individuals with depression onset at T3, changes were from T2 to T3 were considered. Change in severity or perceived control was defined as at least a 0.5 standard deviation (SD) worsening (increase for asthma severity; decrease for perceived control scores) from one time period to the next. This degree of change has been shown to approximate to a minimum clinically important difference.[47,48] Multiple logistic regression analysis was then performed to determine independent predictors of depression onset. Among subjects not lost to follow-up, key variables pertinent to the analysis were missing for two individuals who were excluded from the analysis. Goodness of fit of the logistic models was assessed with the Hosmer and Lemeshow goodness-of-fit test.

All analyses were conducted using SAS 9.2 (SAS, Cary, NC).

The STROBE statement of items to be included in reports of observational studies (Appendix A) is available online at www.thepcrj.org.

Results

Subject characteristics

Subject characteristics are shown in Table 1. The mean age of subjects at baseline was approximately 44 years, 70% were female, 44% had at least a college education, and 8% were current smokers.

One hundred and twenty-five individuals were lost from the cohort (declined participation or were lost to follow-up) between T1 and T3. Cohort members who dropped out were younger (42.5 vs. 45.0 years, p=.005), had lower education (32.8% vs. 49.0% with college education, p=.002), and more commonly were current smokers (17.6% vs. 4.5%, p<.0001). Individuals who dropped out also had lower perceived control of their asthma at baseline (66.1 vs. 70.0, p=.003). The odds of dropping out were significantly elevated among individuals depressed at baseline (OR 1.76 [1.05, 2.96]). However, omission of subjects who were depressed at baseline did not substantively change the results of the comparisons between those who were retained and those who were lost from the cohort for the other variables noted above (i.e., demographics, smoking, and perceived control of asthma).

Approximately 15% of the cohort was depressed (CESD $\geq$ 23) at each assessment: 17.1% at T1 (n=75), 14.4% at T2 (n=49), and 15.0% at T3 (n=47). Fifteen individuals (3.4%) were depressed at all three interviews.

Cross-sectional indicators of baseline depression status

In bivariate analyses, current smokers and individuals with

Table 1. Subject characteristics at baseline.

	Total sample (n=439)	Available at T3: Retained (n=314)	Available at T3: Dropped out (n=125)	p*
Sociodemographic				
Age, mean (SD) years	44.3 (8.7)	45.0 (8.5)	42.5 (9.0)	.005
Female, % (n)	70.4 (309)	71.7 (225)	67.2 (84)	.36
Education, college or more, % (n)	44.4 (195)	49.0 (154)	32.8 (41)	.002
Married/with partner, % (n)	69.5 (305)	70.4 (221)	67.2 (84)	.57
White, non-Hispanic, % (n)	69.5 (305)	71.3 (224)	64.8 (81)	.21
Health-related				
Smoking, % (n)				<.0001
Current	8.2 (36)	4.5 (14)	17.6 (22)	
Former	30.1 (132)	29.0 (91)	32.8 (41)	
Any comorbid condition, % (n)	45.3 (199)	43.6 (137)	49.6 (62)	.29
Asthma severity score, mean (SD)	8.4 (5.8)	8.5 (5.8)	8.0 (5.8)	.37
VLA % activities affected, mean (SD)	41.3 (37.8)	42.2 (37.2)	38.9 (39.2)	.40
Perceived control of asthma (PCAQ) score, mean (SD)	68.9 (12.7)	70.0 (12.7)	66.1 (12.2)	.003
Depression				
CESD score, mean (SD)	12.4 (11.4)	11.7 (10.6)	14.2 (13.2)	.06
Depressed (CESD ≥ 23), % (n)	17.1% (75)	14.7% (46)	23.2% (29)	.03

Table 2. Comparisons between non-depressed and depressed subjects: Cross-sectional analyses from T1.

	Bivariate: No depression (n=364, 82.9%)	Bivariate: Depression (n=75, 17.1%)	Bivariate: p*	Multivariate**: OR (95% CI)
Sociodemographic				
Age, years, mean (SD)	44.6 (8.7)	43.0 (8.9)	.17	0.97 (0.94, 1.01)
Female, % (n)	69.0 (251)	77.3 (58)	.17	1.49 (0.78, 2.87)
Education (college or more), % (n)	47.3 (172)	30.7 (23)	.01	0.76 (0.41, 1.42)
White, non-Hispanic, % (n)	71.2 (259)	61.3 (46)	.10	0.67 (0.37, 1.22)
Health-related				
Any comorbid condition, % (n)	43.7 (159)	53.3 (40)	.13	0.82 (0.43, 1.56)
Smoking, % (n)			.02	
Current	6.9 (25)	14.9 (11)		**2.87 (1.14, 7.21)**
Former	28.9 (105)	36.5 (27)		**2.23 (1.17, 4.22)**
Asthma severity score, mean (SD) §	7.9 (5.5)	10.6 (6.6)	<.0001	0.99 (0.84, 1.16)
PCAQ, mean (SD) §	42.0 (5.3)	37.9 (5.6)	<.0001	**0.51 (0.35, 0.75)**
VLA % affected, mean (SD) §	35.4 (35.8)	69.8 (34.1)	<.0001	**1.58 (1.33, 1.87)**
Depressive symptoms				
CESD, Baseline, mean (SD)	8.0 (5.8)	33.6 (8.0)	<.0001	

* p-values from analysis of variance or χ^2 analysis; ** Hosmer and Lemeshow goodness-of-fit test: $\chi^2 = 6.53$, p = .59; § odds per .5 SD-point difference

lower education, greater asthma severity, greater disability, and lower perceived control of asthma were more likely to be depressed (see Table 2).

A multivariate logistic regression analysis was performed to identify independent correlates of depression at baseline (Table 2). Four factors were identified: current smoking (OR 2.87 [95% CI 1.14, 7.21]); former smoking (2.23 [1.17, 4.22]); lower perceived control (PCAQ) score (OR per .5 SD difference in PCAQ 0.51 [0.35, 0.75]); and greater proportion of VLAs affected (OR per .5 standard deviation difference 1.58 [1.33, 1.87]). Higher PCAQ scores reflect perceptions of greater asthma control, so greater perceived control was protective.

Table 3. Comparisons between non-depressed and depressed subjects: Longitudinal analyses of onset of depression at T2 or T3.

	Bivariate			Multivariate**
	No depression (n=233, 86.0%)	Incident depression (n=38, 14.0%)	p*	OR (95% CI)
Baseline sociodemographic				
Age, years, mean (SD)	45.2 (8.6)	45.5 (8.4)	.85	1.00 (0.93, 1.07)
Female, % (n)	68.7 (160)	84.2 (32)	.06	1.87 (0.53, 6.65)
Education (college or more), % (n)	54.9 (128)	34.2 (13)	.02	**0.29 (0.10, 0.90)**
White, non-Hispanic, % (n)	73.8 (172)	65.8 (25)	.33	0.58 (0.19, 1.76)
Baseline health-related				
Any comorbid condition, % (n)	39.9 (93)	71.1 (27)	.0004	**3.29 (0.99, 11.02)**
Smoking, % (n)			.04	
Current	3.4 (8)	10.5 (4)		2.89 (0.48 17.26)
Former	27.0 (63)	36.8 (14)		**4.73 (1.49, 15.06)**
Asthma severity score, mean (SD) §	7.8 (5.5)	9.4 (6.6)	.10	1.02 (0.91, 1.14)
VLA % affected, mean (SD) §	35.3 (35.4)	46.1 (36.2)	.08	0.99 (0.97, 1.01))
PCAQ, mean (SD)§	42.7 (5.2)	39.1 (6.0)	.0002	0.90 (0.80, 1.01)
Baseline CESD, mean (SD)§	7.2 (5.3)	12.4 (6.1)	<.0001	**1.22 (1.11, 1.35)**
Change baseline - follow-up				
Asthma severity score, increase, % (n) †	14.2 (33)	18.4 (7)	.47	1.03 (0.25, 4.27)
PCAQ, decrease, % (n) †	35.6 (83)	61.5 (16)	.02	**7.47 (2.15, 26.01)**

* p-values from analysis of variance or χ^2 analysis; ** Hosmer and Lemeshow goodness-of-fit test: χ^2 = 12.46, p = .13; § odds per .5 SD-point difference; †† Asthma severity score change = increase by .5 standard deviation. PCAQ change = decrease by .5 standard deviation.

Note: Excludes individuals depressed at baseline, even if they were re-interviewed.

Current and former smoking and disability were associated with increased risk. In a secondary analysis excluding PCAQ and VLA disability as potential mediators of disease severity, asthma severity score was significantly associated with depression (OR 1.08 [1.03, 1.13]).

Longitudinal analyses of the onset of depression

Thirty-eight individuals (10.4% of the 364 not depressed at T1) became depressed at one of the follow-up interviews (26 at T2 and 12 at T3 – see Figure 1). Among individuals who became depressed, the mean (±SD) increase in CESD score was 17.6 (±8.8) points. All scores increased by at least 3 points.

In bivariate analyses, individuals who became depressed were more likely to have lower education (34.2% with college education vs. 54.9%, p=.02), to have ≥1 co-morbid condition at baseline (71.1% vs. 39.9%, p=.0004), to be current smokers at baseline (10.5% vs. 3.4%, p=.04), and had lower baseline PCAQ scores, indicating poorer perceived control (42.7 vs. 39.1, p=.0002) (Table 3). In a multiple logistic regression including all variables, decrease in PCAQ score ≥0.5 SD from the preceding interview (OR 7.47 [2.15, 26.01], consistent with worsening perceived control, was associated with onset of depression. Presence of a co-morbid condition at baseline (OR 2.75 [1.21, 6.24]), past smoking (OR 4.73 [1.49, 15.06]), and higher baseline CESD score (OR per CESD point 1.22 [1.11, 1.35]) were also each associated with depression onset.

Discussion

In this study of adults with asthma in the community, depression was approximately twice as common (~15%) as in the general population (~7%). Lower perceived control of asthma, as measured by a validated instrument (PCAQ), was associated with a greater likelihood of depression at the time of first treatment (T1), and a decrease in perceived control coincided with depression onset at follow-up even after controlling for asthma severity and changes in asthma severity. Low perceived control of asthma has previously been linked with lower quality of life, lower asthma-specific health status, greater health care utilisation, and mortality.[41,42,49,50] Our findings are consistent with these observations in suggesting a role for perceived control in depression prevalence and incidence in asthma, and with findings in other chronic conditions.[26,51,52]

Based on previous research, we expected asthma severity to be significantly associated with depression, and this was the case in bivariate analyses, but not in multivariate analyses. Previous studies have shown that lower perceived control is associated with more severe asthma;[49] and in a secondary analysis excluding PCAQ and VLA disability from the

regression model, asthma severity was significantly associated with baseline depression, suggesting that one or both of the latter variables was mediating the effects of disease severity. Thus, while asthma severity may have played a role in depression, it may have been mediated through, and overshadowed by, perceived control of the disease.

Previous studies have shown relationships between disability and depression.[27,28,55-58] In this study, however, there was a strong cross-sectional relationship between VLA disability and depression, but no significant associations between VLA disability and depression onset. VLA disability scores were not available at follow-up, so we could not test whether an increase in disability was associated with depression onset, as has been found in studies of other conditions.[27,28]

Individuals who were depressed were more likely to be lost to follow-up. Such bias through attrition has important implications for future longitudinal studies – particularly those dealing with psychological well-being and distress – and suggests the need for extra vigilance in follow-up or use of data management or analytic approaches to handling such attrition. Since we excluded those with baseline depression from our analysis of depression onset, the effect of such loss to follow-up was minimised in the modeling.

Depression has considerable economic and health costs and exerts a negative influence on health in diverse ways, including increasing the risk of physical decline and the risk of mortality; it is also associated with poor treatment adherence, which may adversely affect treatment and health status.[18,59,61-63] Although we do not have information regarding treatment adherence in this sample, these general findings have been supported in asthma-specific research, with depression being linked to poor asthma control[6,24,64] and risk of hospitalisation.[7] Thus, finding methods to avoid or ameliorate psychological distress among individuals with asthma could play an important role in improving both the health outcomes and quality of life of individuals with asthma, as well as decreasing societal costs.

This study has important limitations. Our measure of depressive symptoms, the CESD, was designed as a screening tool, and is not a diagnostic measure. It is possible that use of a diagnostic measure of depression would affect the analysis of risk factors. Nonetheless, patients with depressive symptoms warrant further evaluation in clinical practice, and treatment for depressive symptoms may be appropriate even in the absence of a diagnosis of major depression.[66] The overall study was powered to look at a variety of physical, social, and environmental factors in asthma. Nevertheless, for the relatively infrequent event of incident depression, the confidence intervals were moderately large for some predictors, even though the observed point estimates were unlikely to be due to chance, based on the exclusion of 1 from these confidence intervals.

The sample may also be biased in ways that make it unrepresentative of all adults with asthma. However, the sample was recruited from a random sample of community allergists, pulmonologists, and family practice physicians, and then further supplemented with a population sample – a heterogeneous approach that probably increases the generalisablity of the results. Furthermore, the attrition between T1 and T3 (28% over three interviews) could bias the results: although there were relatively few differences between individuals who remained in the study compared to those who dropped out, those who dropped out were more likely to be depressed. It is also possible that factors not included in these analyses, such as neighborhood characteristics,[67] could affect the occurrence of depression.

Conclusion

In summary, we found that rates of depression were approximately twice as high in this community-based sample of adults with asthma compared with rates among the general population. Low perceived control of asthma emerged as the most consistent predictor of depression. Previous studies suggest that perceived control may improve with self-management education; for example, receiving instruction on metered-dose inhaler use was associated with increased perceived control,[49] and perceived control increases following asthma self-management education.[50,53,54] Due to the implications of depression – as regards medication adherence and asthma control, general physical health, and health service use, as well as quality of life – identifying the precursors of depression concomitant with asthma is critical. These findings provide a basis for future work examining the role of perceived disease control in the development of depression among adults with asthma.

Acknowledgment

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Difficulties encountered: Individuals who were depressed were more likely to be lost to follow-up.

Alternative methodologies that would have been helpful: Diagnostic clinical interview to assess depression. Verification of asthma diagnosis by medical providers.

New lessons arising from study: Low perceived control of asthma is a consistent predictor of depression.

Lessons for clinical practice as a result of the study: Low perceived control is a strong predictor of depression among adults with asthma. Depression is associated with poor medication adherence and poor outcomes among adults with asthma. There is evidence that perceived control can be improved through self-management education.

Conflict of interest declarations

None of the authors have any conflicts of interest.

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Appendix A. STROBE Statement - checklist of items that should be included in reports of observational studies.

	Item No	Recommendation	
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	√
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	√
Introduction			
Background/ rationale	2	Explain the scientific background and rationale for the investigation being reported	√. p. 1-2
Objectives	3	State specific objectives, including any prespecified hypotheses	√. p. 2. No hypotheses, exploratory
Methods			
Study design	4	Present key elements of study design early in the paper	√. Title and first sentence of methods
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	√. First paragraph of methods
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	(a) √. First paragraph of methods
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	Not applicable
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	√, p. 2-3
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	√. p. 2-3
Bias	9	Describe any efforts to address potential sources of bias	√. Potential confounders addressed in analysis. Potential sources of bias addressed in discussion.
Study size	10	Explain how the study size was arrived at	√. P. 2, Fig. 1
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	√. p. 2, 3
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	√. p. 3
		(*b*) Describe any methods used to examine subgroups and interactions	No subgroups or interactions were examined

		(*c*) Explain how missing data were addressed	√. P. 3
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	√. Cohort study. Loss-to-follow-up was reported for each interview. Longitudinal analyses excluded subjects lost to follow-up, but characteristics of those who were lost were compared to characteristics of those lost.
		(*e*) Describe any sensitivity analyses	Not applicable
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	√. P. 2, Fig. 1. Details of study recruitment presented in previous publications
		(b) Give reasons for non-participation at each stage	√. Number of non-participants provided, with refusals and lost-to-follow-up combined. In interview studies, inability to contact (i.e., lost to follow-up) may be indistinguishable from refusal (phone screening, no return of messages)
		(c) Consider use of a flow diagram	√. Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	√. Table 1
		(b) Indicate number of participants with missing data for each variable of interest	√. Added to Table 1
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	√. 3 telephone interviews, at 2-year intervals
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	√, cross-sectional: Table 1. Incident: Table 3
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	Not applicable
		Cross-sectional study—Report numbers of outcome events or summary measures	Not applicable
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	√. Tables 2 and 3 provide unadjusted and adjusted estimates with 95% CIs. Multivariate models described in methods and tables.
		(*b*) Report category boundaries when continuous variables were categorized	√. "Depression" criterion on p. 2. Other categorical variables described on p. 2, 3.
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Not relevant

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Not applicable
Discussion			
Key results	18	Summarise key results with reference to study objectives	√. p. 5
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	√. p. 6.
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	√
Generalisability	21	Discuss the generalisability (external validity) of the study results	√
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	√

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.