

Research paper

Allergies, asthma, and psychopathology in a nationally-representative US sample

Kristen Kelly^{a,*}, Scott Ratliff^a, Briana Mezuk^{a,b}^a Department of Epidemiology, School of Public Health, University of Michigan, United States^b Institute for Social Research, University of Michigan, United States

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ABSTRACT

Background: Symptoms of depressed mood and anxiety have been associated with immune dysregulation and atopic disorders, however it is unclear whether this relationship spans other forms of psychopathology. The objective of this study was to use a large, population-based sample to examine the association between several common psychiatric conditions and two atopic disorders: seasonal allergies and asthma. This study also examined whether comorbidity between psychiatric disorders confounded the relationship between atopy and each psychiatric disorder.

Methods: Data come from the Comprehensive Psychiatric Epidemiology Surveys, a nationally-representative sample of US adults ($N = 10,309$). Lifetime history of major depressive disorder (MDD), generalized anxiety disorder (GAD), panic disorder (PD), and post-traumatic stress disorder (PTSD) was assessed using the Composite International Diagnostic Inventory. History of seasonal allergies and asthma were assessed by self-report. Weighted logistic regression was used to evaluate the association between allergies and asthma and psychopathology. Psychiatric comorbidities were also examined as potential confounders.

Results: Approximately 36.6% had a history of allergies and 11.5% a history of asthma. Seasonal allergies were positively associated with odds of MDD (Odds ratio (OR): 1.24, 95% Confidence Interval (CI): 1.06–1.46), GAD (OR: 1.54 (1.28–1.84)), PD (OR: 1.54 (1.24–1.91)), and PTSD (OR: 1.32 (1.09–1.59)). Asthma was not significantly associated with any psychiatric disorder. All significant associations persisted after adjustment for psychiatric comorbidities.

Limitations: Limitations include self-reporting of atopic disorder status and of all disorder ages of onset.

Conclusions: This study confirms the association between MDD and PD and seasonal allergies, and extends this relationship to GAD and PTSD.

Acronyms

MDD	major depressive disorder
GAD	generalized anxiety disorder
PD	panic disorder
PTSD	post-traumatic stress disorder
IPR	income-to-poverty ratio
NIMH	National Institute for Mental Health
RDoC	Research Domain Criteria
CIDI	Composite International Diagnostic Interview

1. Introduction

The term atopy refers to a propensity to develop an immunologic

sensitivity to benign antigens typically tolerated by non-atopic individuals (Johansson et al., 2004). Atopic disorders are a family of disorders including allergic rhinitis, asthma, and some forms of eczema. Atopic disorders are highly heritable (Willemssen et al., 2008; Strachan et al., 2001) and highly comorbid with each other (Ker and Hartert, 2009; Pinart et al., 2014), suggesting they may share or have overlapping genetic susceptibility (Willemssen et al., 2008; Fagnani et al., 2008; Nystad et al., 2005). In susceptible individuals, exposures that trigger an atopic response may result in elevated levels of inflammatory biomarkers such as interleukin-6 (IL-6) and C-reactive protein (CRP) (Wood et al., 2012; Ólafsdóttir et al., 2005; Borish, 2003; Yokoyama et al., 1995; Gosset et al., 1993). Elevated levels of inflammatory markers have been correlated with a range of mental health outcomes (Howren et al., 2009; Dowlati et al., 2010; Raison et al., 2006; Miller

* Correspondence to: Student Mailboxes, 1415 Washington Heights, Ann Arbor, MI 48109, United States.

E-mail address: kellykj@umich.edu (K. Kelly).

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et al., 2009).

Several studies have also suggested a relationship between common psychiatric disorders and atopic conditions. Large community-based studies have shown that major depressive disorder (MDD) is associated with both allergies (Sanna et al., 2014; Hurwitz and Morgenstern, 1999; Chen et al., 2013; Cohen et al., 1998) and asthma (Loerbroks et al., 2010; Goodwin et al., 2003a,b; Scott et al., 2007). A link between panic disorder (PD) and asthma has been widely replicated (Scott et al., 2007; Katon et al., 2004), and this relationship appears to be bidirectional (Hasler et al., 2005); only a handful of studies have examined the link between PD and allergies, but these also suggest a positive association (Goodwin, 2002; Kennedy et al., 2002). Few studies have examined the relationship between generalized anxiety disorder (GAD) and atopic disorders, and results are mixed (Scott et al., 2007; Goodwin, 2002; Goodwin et al., 2003a,b,c; Patten and Williams, 2007). Finally, post-traumatic stress disorder (PTSD) has been associated with history of asthma (Scott et al., 2007; Weisberg et al., 2002; Goodwin et al., 2007), however it is likely that this relationship is at least partially explained by trauma associated with asthma attacks (Kean et al., 2006). There is little known about the relationship between PTSD and seasonal allergies, although one paper has reported an association (Sledjeski et al., 2008). Finally, experimental studies in animals have demonstrated that allergen exposure in sensitized animals can lead to increases in anxiety-like behavior and reductions in social behavior (Tonelli et al., 2009).

In sum, although multiple studies suggest a relationship between atopic disorders and common psychiatric disorders, the strength of this evidence varies across conditions. In some cases, evidence is limited to small, treatment-seeking clinical samples that may differ from the general population on factors such as disease severity and access to medical care (Wang et al., 2007; Du Fort et al., 1993). Existing reports often examine only one atopic or psychiatric disorder in isolation, and thus it is unresolved whether these hypothesized relationships are consistent across a broad range of psychopathology or across multiple atopic conditions. Measurement of psychopathology also varies, limiting the ability to compare and evaluate disparate findings. Finally, because psychiatric conditions are highly comorbid with each other, (Kessler et al., 2005) it is possible that if one psychiatric disorder were associated with atopy it could confound the relationship between other disorders and atopy, an issue that is rarely addressed in existing literature.

The objective of this study was to examine the relationships between two common atopic disorders, seasonal allergies and asthma, and several common psychiatric disorders using a large community-based sample. We hypothesized that both atopic disorders would show an association with a broad range of psychiatric disorders. We also hypothesized that earlier age of the onset for the atopic disorders would be more strongly associated with psychopathology than atopic disorders that onset later in life.

2. Methods

2.1. Sample

Data come from the Collaborative Psychiatric Epidemiology Surveys (CPES) (Alegria et al., 2008). The CPES consists of three nationally-representative household surveys of US adults: the National Comorbidity Survey Replication (NCS-R), the National Latino and Asian American Study (NLAAS), and the National Survey of American Life (NSAL). All three studies were conducted from 2001–2003. All surveys of the CPES employed the Composite International Diagnostic Inventory (CIDI) to assess psychopathology as described below. Additional details of the CPES methodology are described elsewhere (Heeringa et al., 2004).

The analytic sample for this paper is limited to CPES respondents who were asked about lifetime history of allergies and asthma ($N = 10,341$ from the NLAAS and the long form of the NCS-R only). The

sample was further limited to respondents with complete data on the psychiatric disorders of interest (MDD, GAD, PD, PTSD), history of atopic disorders, and model covariates ($N = 10,309$). Of the participants who were excluded for missing data, eight were missing data on lifetime history of allergies or asthma, and 24 were missing data on health insurance status.

For the analysis examining age-of-onset of atopic disorders in relation to psychopathology, the sample was restricted to respondents with a positive history of the atopic disorder in question and who provided valid data on their age at onset for the condition. Of the 3512 individuals with a history of seasonal allergies, 3290 (93.7%) provided a valid age at onset. Of the 1202 individuals with a history of asthma, 1137 (94.6%) provided a valid age at onset.

The institutional review boards at the University of Michigan, Harvard University, Cambridge Health Alliance, and the University of Washington approved the component surveys of the CPES (Pennell et al., 2004). This analysis used only de-identified publicly available data and was exempt from human subjects regulation.

2.2. Measures

2.2.1. History of psychopathology

Lifetime histories of MDD, GAD, PD, and PTSD were assessed using the DSM-IV version of the World Mental Health CIDI. This instrument consists of structured interviews based on the DSM-IV criteria for each disorder assessed (Kessler et al., 2004b), and has been shown to perform well when compared to a clinician-administered semi-structured interview (Kessler et al., 2004a). Respondents were considered to have a lifetime history of a disorder if they reported at least one period in their life during which they met the DSM-IV criteria for the disorder (American Psychiatric Association, 1994). These disorders were selected because (a) they were assessed in both the NCS-R and NLAAS, (b) they were relatively common (had a lifetime prevalence $> 5\%$) (c) they had support from prior literature. Only a limited number of disorders could be selected due to the need to balance the exploratory nature of our research question with the analytic need to account for multiple comparisons.

2.2.2. History of atopic disorders

Lifetime histories of seasonal allergies and asthma were assessed by self-report. For allergies, respondents were asked "Have you ever had seasonal allergies like hay fever?" For asthma, respondents were asked "Did a doctor or other health professional ever tell you that you had asthma?" Although the accuracy of self-report assessment of atopic conditions like these may vary as a function of disease severity, previous studies of depression using clinician-verified asthma and blood measures have produced similar results to studies using self-reported measures (Goodwin et al., 2003a; Torén et al., 2006; Bauchau and Durham, 2004; Manalai et al., 2012). Information about the age at onset of allergies and asthma was also assessed by self-report. Age of onset was categorized as childhood-onset (ages 0–12), teen-onset (ages 13–18), or adult-onset (age 19+). We chose to categorize this variable because our goal is to explore whether there is heterogeneity within the atopic disorder-mental health relationship as a function of the life stage at which the atopic disorder developed (Lupien et al., 2009; Andersen, 2003); as a result, modeling age at onset as a continuous variable would not be appropriate.

2.2.3. Other covariates

Age at time of interview (in years), gender, race, household income-to-poverty ratio (IPR), and health insurance coverage status were assessed by self-report. Initial covariate fit analyses showed that the relationship between age and psychopathology was non-linear. As a result, this variable was categorized as 18–29, 30–44, 45–64, and 65+. Race was categorized as "black", "Hispanic", "other", or "white" based on respondent self-report. IPR is the ratio of annual household income to

the poverty threshold for the respondent's family size as determined by the US Census Bureau (Proctor and Dalaker, 2002). This variable was categorized into three levels: Income at or below the poverty limit, income two to three times the poverty limit, and income four or more times the poverty limit. Health insurance coverage was based on questions about the respondent's receipt of medical coverage through employer-provided health insurance, privately-purchased insurance, military medical coverage, Medicare, Medicaid, or other assistance programs or coverage, with respondents reporting having one or more of these classified as having health coverage, and individuals reporting none of these classified as not covered.

2.3. Analysis

Multivariable logistic regression models were used to assess the association between allergies and asthma and each of the four psychiatric outcomes. Each exposure was assessed in relation to four outcomes (MDD, PD, PTSD, and GAD); a Bonferroni-adjusted significance cutoff of 0.0125 was calculated to account for multiple testing. Initial models were adjusted for age, gender, race, IPR and health insurance coverage. Following this, models were additionally adjusted for comorbid disorders (e.g., models of allergies predicting MDD were adjusted separately for PD, PTSD and GAD), to examine whether the relationships identified in the main model were confounded by psychiatric comorbidity. Controlling separately for each comorbidity increased the number of models from four to sixteen, however we retained our original Bonferroni-adjusted significance cutoff of 0.0125 because only four exposure/outcome associations were being tested. Finally, logistic models were fit to examine whether the age-at-onset of the atopic disorder was associated with odds of the psychiatric disorder.

We then conducted a series of sensitivity analyses to assess the robustness of our findings. First, we expanded the outcome of panic from PD (approximately 4.1% of the sample had PD) to lifetime history of a panic attack (approximately 23.4% of the sample had experienced a panic attack), to assess whether the lack of association with asthma in the initial analysis was due to the small overall number of PD cases. Next, we examined whether the relationship between lifetime psychopathology and lifetime history of seasonal allergies replicated when using past-year history of each exposure and outcome; this analysis was conducted for allergies only, as history of asthma was only assessed over the lifetime, not in the past year. Finally, we examined whether including respondents from the NSAL in the analytic sample for asthma influenced our results; these respondents had been excluded from the main analysis because the NSAL did not include a question about seasonal allergies, but this survey did assess asthma and all the four psychiatric outcomes.

All analyses were conducted in SAS 9.4 using survey procedures to account for complex sample design of the CPES.

3. Results

Table 1 shows descriptive characteristics of the analytic sample by lifetime history of psychopathology. The columns are not mutually exclusive; respondents with more than one psychiatric disorder appear in multiple columns. As expected, psychiatric disorders were highly comorbid. For example, 24.1% of respondents with a history of MDD also had a history of GAD. Approximately one-third (36.6%) of the sample had a lifetime history of seasonal allergies, and 11.5% had a history of asthma. The atopic conditions were also highly comorbid, with 20.5% of respondents with seasonal allergies also reporting asthma, and 60.0% of respondents with asthma also reporting seasonal allergies.

Fig. 1 shows the odds ratios and 95% confidence intervals of the relationships between seasonal allergies (green) and asthma (black) with each of the four psychiatric disorders. *P*-values are also included, to allow for comparison against the Bonferroni-adjusted multiple

testing significance threshold of 0.0125. Seasonal allergies were significantly associated with MDD (Odds ratio (OR): 1.24; 95% Confidence Interval (CI): 1.06–1.46), GAD (OR: 1.54; 95% CI: 1.28–1.84), PD (OR: 1.54, 95% CI: 1.24–1.91), and PTSD (OR: 1.32, 95% CI: 1.09–1.59). While all point estimates for asthma were greater than 1.0, asthma was not statistically significantly associated with any psychiatric outcome after adjustment for multiple comparisons. The sensitivity analysis examining the association between asthma and history of panic attack, instead of PD, also did not reach statistical significance (OR: 1.26, 95% CI: 0.93–1.70). As shown in Table 2 the relationships between allergies and each psychiatric disorder remained after controlling for psychiatric comorbidity. In some cases results were no longer significant after accounting for multiple comparisons, however effect estimates remained similar to those produced by the original models, indicating that adjustment for comorbid conditions did not attenuate the relationship.

We then examined whether age-of-onset (childhood, teen years, or adulthood) of atopy influenced the relationship between the disorder and psychopathology (Table 3). Among people with allergies, those whose allergies began before age 12 were 1.81 times more likely to have a lifetime history of PTSD than those whose allergies began in adulthood. There was no evidence that age of onset of allergies was related to the other three psychiatric conditions after adjustment for multiple comparisons.

Two sensitivity analyses confirmed the robustness of these results. As shown in Supplementary Table S1, all associations between lifetime psychopathology and lifetime history of seasonal allergies replicated when using past-year definitions of the exposure and outcomes. As shown in Supplementary Tables S2 and S3, the relationships between psychopathology and asthma still did not reach statistical significance even after including the NSAL in the analytic sample.

4. Discussion

This study used a large, community-based sample to simultaneously examine the relationship between multiple psychiatric disorders and seasonal allergies and asthma, two common atopic conditions. The primary finding of this study is that a history of seasonal allergies is consistently associated with greater odds of MDD, GAD, PD, and PTSD. Allergies that began earlier in life were more strongly related to likelihood of PTSD than those that began in adulthood. Contrary to expectation, there were no significant associations between asthma and any psychiatric disorder, although all estimates were in the expected direction. The results of this study indicate that the relationship between atopy and psychopathology is more complex and nuanced than previously suggested.

The finding that seasonal allergies are associated with a broad range of psychopathology is consistent with prior literature. There is a widely-replicated association between MDD and allergies, and previous studies have suggested similar associations with allergies may exist for PD (Goodwin, 2002; Kennedy et al., 2002). To our knowledge, this is the first study to report seasonal allergies as a possible risk factor for PTSD. Although trauma and adversity are risk factors for psychopathology in general, PTSD is unique in requiring a precipitating trauma as part of diagnostic criteria (American Psychiatric Association, 1994.). Informed by these results, future studies should explore whether atopy-related inflammation exacerbates psychiatric symptoms following trauma, or whether atopy-related systemic inflammation at the time of the trauma influences susceptibility to developing PTSD.

There are several potential mechanisms that may contribute to the observed relationship between allergies and this broad range of psychopathology. Systemic inflammation due to an atopic response may act on the brain in a manner that produces or exacerbates psychiatric symptoms (15, 16). In addition, inflammation from atopic responses during childhood or adolescence may influence development at critical periods (Buske-Kirschbaum et al., 2003; Hagberg et al., 2012; Calderón-Garcidueñas et al., 2011), consistent with the finding that earlier age of

Table 1
Descriptive characteristics of analytic sample.

	MDD (n = 2129)	GAD (n = 935)	PD (n = 577)	PTSD (n = 771)	Whole sample (n = 10,309)
Age					
18–29	512 (21.9%)	163 (16.6%)	132 (19.7%)	181 (22.1%)	2608 (23.3%)
30–45	755 (33.6%)	321 (33.3%)	208 (37.2%)	266 (33.5%)	3519 (29.3%)
45–64	677 (35.5%)	355 (40.0%)	198 (35.1%)	283 (40.1%)	3082 (30.9%)
65 +	185 (8.9%)	96 (10.1%)	39 (8.0%)	41 (4.3%)	1100 (16.6%)
Gender					
Male	708 (36.7%)	269 (32.7%)	173 (32.2%)	190 (25.4%)	4492 (47.3%)
Female	1421 (63.3%)	555 (67.3%)	404 (67.8%)	581 (74.6%)	5817 (52.7%)
Race					
Black	144 (7.2%)	70 (7.3%)	43 (7.0%)	85 (12.5%)	712 (11.1%)
Hispanic	536 (9.7%)	190 (6.6%)	140 (9.1%)	185 (8.4%)	3072 (11.7%)
Other	271 (5.4%)	91 (5.2%)	66 (6.7%)	73 (5.6%)	2356 (6.4%)
White	1178 (77.7%)	584 (80.9%)	328 (77.2%)	428 (73.6%)	4169 (70.8%)
Income-to-poverty ratio					
At or below poverty	510 (21.8%)	237 (21.8%)	165 (27.2%)	229 (26.3%)	2546 (22.0%)
2–3x poverty	561 (27.0%)	266 (28.7%)	175 (28.6%)	195 (25.6%)	2755 (27.8%)
4+ times poverty	1058 (51.3%)	432 (49.5%)	237 (44.2%)	347 (48.2%)	5008 (50.2%)
Has health insurance	1784 (85.6%)	802 (87.2%)	488 (87.1%)	645 (85.2%)	8518 (86.2%)
History of allergies	873 (43.2%)	429 (49.3%)	249 (49.2%)	339 (45.9%)	3503 (36.6%)
History of asthma	311 (13.4%)	142 (15.2%)	93 (14.4%)	129 (14.7%)	1195 (11.5%)
Allergy onset					
0–12	265 (32.6%)	126 (32.5%)	76 (33.3%)	120 (43.5%)	969 (32.6%)
13–18	125 (15.3%)	64 (16.0%)	48 (20.2%)	53 (15.8%)	543 (17.7%)
19+	423 (52.1%)	209 (51.6%)	110 (46.5%)	140 (40.6%)	1771 (49.7%)
Asthma onset					
0–12	116 (39.3%)	38 (31.2%)	22 (26.1%)	41 (34.9%)	510 (44.3%)
13–18	36 (11.3%)	22 (15.4%)	8 (11.0%)	17 (14.2%)	141 (11.9%)
19+	143 (49.4%)	68 (53.4%)	57 (62.8%)	61 (50.9%)	479 (43.8%)
Comorbid MDD	–	488 (52.2%)	232 (37.8%)	361 (43.7%)	–
Comorbid GAD	488 (24.1%)	–	171 (33.1%)	228 (29.6%)	–
Comorbid PD	232 (10.3%)	171 (19.6%)	–	144 (17.6%)	–
Comorbid PTSD	361 (17.4%)	228 (25.5%)	144 (25.7%)	–	–

Values are unweighted N, weighted percentages.

Individuals with multiple disorders appear in multiple columns. MDD = major depressive disorder, GAD = generalized anxiety disorder, PD = panic disorder, PTSD = post-traumatic stress disorder.

onset of allergies was more strongly associated with PTSD than allergies which onset later. Alternatively, genetic factors associated with propensity towards atopy may also be associated with susceptibility to psychiatric disorders (Wamboldt et al., 2000; Timonen et al., 2003). The finding that allergies are related to range of psychopathology may also suggest that allergies may be associated with an underlying factor common to several disorders, such as one of the domains, systems, or processes described in the National Institute for Mental Health's Research Domain Criteria (RDoC) (Cuthbert and Insel, 2013; Insel et al., 2010).

Contrary to our expectations, asthma was not significantly

associated with any form of psychopathology in our results. There are multiple potential explanations for these findings. It is possible that the differing results for allergies and asthma may result from an underlying biological difference between the two conditions, such as allergies having a greater ability to affect the brain due to the nose-to-brain pathway (Pardeshi and Belgamwar, 2013; Tonelli and Postolache, 2010). However, some of the associations for asthma have replicated across other studies (Goodwin et al., 2003a; Scott et al., 2007), particularly panic symptomology (Katon et al., 2004; Hasler et al., 2005), so the lack of replication in our study requires consideration of other factors that could have led to differing results. First, many prior studies

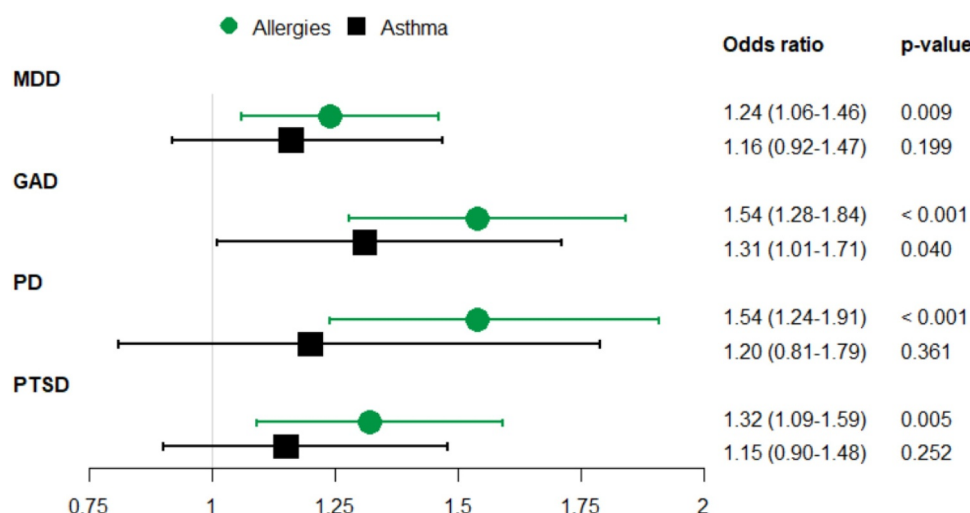


Fig. 1. Odds ratios for associations between atopic disorders and psychiatric disorders.

Note: All models adjusted for age, sex, race income-to-poverty ratio, and health coverage status. All results are given as OR (95% CI). The recommended *P*-value significance threshold is 0.0125, which applies a Bonferroni adjustment to account for the use of four tests per exposure.

MDD = major depressive disorder, GAD = generalized anxiety disorder, PD = panic disorder, PTSD = post-traumatic stress disorder.

Table 2

Association between seasonal allergies and each psychiatric disorder, after controlling for each other psychiatric disorder.

	MDD	GAD	PD	PTSD
Original model	1.24 (1.06–1.46)*	1.54 (1.28–1.84)*	1.54 (1.24–1.91)*	1.32 (1.09–1.59)*
Controlling for MDD	–	1.47 (1.24–1.74)*	1.49 (1.20–1.83)*	1.26 (1.05–1.51)
Controlling for GAD	1.16 (0.98–1.37)	–	1.41 (1.12–1.77)*	1.22 (1.01–1.49)
Controlling for PD	1.21 (1.03–1.43)	1.47 (1.22–1.77)*	–	1.27 (1.05–1.54)
Controlling for PTSD	1.21 (1.03–1.42)	1.49 (1.24–1.79)*	1.47 (1.19–1.81)*	–

Note: All models are adjusted for age, sex, race, income-to-poverty ratio, and health coverage status. MDD = major depressive disorder, GAD = generalized anxiety disorder, PD = panic disorder, PTSD = post-traumatic stress disorder.

* Remains significant after adjustment for multiple comparisons.

Table 3

Timing of atopic onset and risk of psychopathology.

	MDD	GAD	PD	PTSD
Allergy age at onset (ref = 19+)				
0–12	0.93 (0.73–1.20)	1.08 (0.79–1.48)	1.17 (0.84–1.61)	1.81 (1.28–2.55)*
13–18	0.81 (0.61–1.08)	1.01 (0.71–1.44)	1.42 (0.85–2.35)	1.27 (0.83–1.94)
Asthma age at onset (ref 19+)				
0–12	0.64 (0.45–0.92)	0.66 (0.34–1.31)	0.50 (0.23–1.12)	1.03 (0.53–2.01)
13–18	0.62 (0.31–1.25)	1.35 (0.58–3.11)	0.77 (0.28–2.10)	1.67 (0.80–3.50)

Note: This model examines whether, given that an individual has an atopic disorder, a younger age-at-onset of allergies is associated with greater odds of psychopathology. Allergy $N = 3290$, asthma $N = 1137$. Odds ratios are adjusted for age, sex, race, income:poverty ratio, and health coverage status. MDD = major depressive disorder, GAD = generalized anxiety disorder, PD = panic disorder, PTSD = post-traumatic stress disorder.

* Remains significant after adjustment for multiple comparisons.

were conducted with child or adolescent samples (Katon et al., 2007; Ortega et al., 2002; Goodwin et al., 2003c), and our analysis was restricted to adults. If the relationship between asthma and PD was stronger earlier rather than later in the life course, this may contribute to these disparate findings. However, the asthma-PD association has been replicated other large community-based studies of adults (Goodwin et al., 2003a; Scott et al., 2007; Hasler et al., 2005). Another possible reason for the null results may be a result of how history of asthma was assessed, which was dependent on a reporting a physician diagnosis of this condition. This means that assessment of asthma could be correlated with access to medical care, a possibility we attempted to account for by adjusting for health insurance coverage status.

These findings should be interpreted in light of the study strengths and limitations. Data on history of allergies or asthma and their ages at onset was obtained via self-report. It is possible that individuals with a history of psychopathology may be more likely to report health conditions such as seasonal allergies, as has been found in another study of allergies and anxiety (Gregory et al., 2009). While we attempted to use age of onset information to address temporality, the retrospective design of this study (examining lifetime and past-year history) means that we cannot be certain of the directionality and temporality of the observed associations. However, because this design assesses occurrence of disorder in a longer period of time (one lifetime or one year) it avoids the possibility of confounding by seasonality, which would be a concern in a cross-sectional study due to the potential for seasonal patterns in atopic and psychiatric disorders. Finally, we do not adjust for medication use (either antidepressants or antihistamines) because we consider these drugs to be *proxy indicators* of our main exposures and outcome, so adjusting for these medications would both result in multi-collinearity and bias our results towards the null. This study also has several strengths, including the use of a well-validated diagnostic interview to assess a range of psychiatric disorders in a large community-based

sample and multiple sensitivity analyses to assess robustness of the results. By examining multiple psychiatric outcomes assessed using the same instrument in the same sample, this analysis provides among the most complete assessments of the relationship between allergies and asthma with common psychiatric disorders in a manner that allows for direct comparisons across these four conditions.

Further study is needed to understand the relationship between psychopathology and atopy. Longitudinal examination of underlying emotional, behavioral, and biological systems as they relate to atopy, consistent with the RDoC framework, are warranted.

Conflicts of interest

The authors have no conflicts of interest to declare

Authors' contributions

K. Kelly performed the analysis and wrote the initial manuscript.

S. Ratliff assisted with the design and statistical methods.

B. Mezuk provided guidance throughout the analysis and writing, and assisted with revising the manuscript.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.jad.2019.03.026](https://doi.org/10.1016/j.jad.2019.03.026).

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