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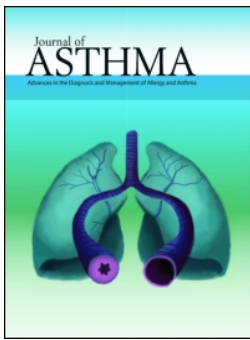
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Abstract

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associated with persistent anxiety, OR=1.26 [1.01, 1.59]. **Conclusions:** In adolescents, asthma is associated with an increased risk of clinically relevant symptoms of depression and food allergy with and increased risk of clinically relevant symptoms of anxiety. Future research is needed to clarify directionality and mechanisms explaining these relationships. Health professionals should be aware of the increased risk of mental health problems in adolescents with asthma or food allergy.



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Condition-Specific Associations of Symptoms of Depression and Anxiety in Adolescents and Young Adults with Asthma and Food Allergy

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Keywords: adolescent; allergic disease; atopic disease; behavior; longitudinal study; young adult

Abstract

Objective: This study examined associations of asthma and food allergy with symptoms of depression and anxiety at 14 and 21 years of age to determine whether condition-specific associations exist. *Methods:* Data come from 4972 adolescents in the Mater University Study of Pregnancy. Symptoms of depression and anxiety were assessed using the Youth Self-Report and Young Adult Self-Report. *Results:* Condition-specific associations between asthma and depression, OR=1.37 [1.12, 1.67] and between food allergy and anxiety, OR=1.26 [1.04, 1.76] were found during adolescence, but not in young adulthood. Whereas asthma was associated with resolved depression, OR=1.70 [1.13, 2.55], food allergy was associated with persistent anxiety, OR=1.26 [1.01, 1.59]. *Conclusions:* In adolescents, asthma is associated with an increased risk of clinically relevant symptoms of depression and food allergy with and increased risk of clinically relevant symptoms of anxiety. Future research is needed to clarify directionality and mechanisms explaining these relationships. Health professionals should be aware of the increased risk of mental health problems in adolescents with asthma or food allergy.

Introduction

Over the past two decades there has been a steady increase in the prevalence of allergic disorders, particularly asthma and food allergy in children and adolescents. As a result, these conditions have become a primary public health concern in developed countries [1-4] and have placed substantial burden on health care systems [5, 6]. North American estimates suggest that 13% and 4% of children have asthma and food allergy, respectively [2, 4]. Asthma and food allergy differ from other childhood-onset chronic conditions (e.g., diabetes, epilepsy) in that affected individuals are typically in relatively good general health, which may be episodically compromised by acute exacerbations that run the full spectrum of clinical severity – from mild to life-threatening [7, 8].

Evidence suggests that asthma and food allergy share some comorbidity with each other [9] and with mental health problems, most notably, depression and anxiety [8, 10-12]. A recent meta-analysis reported that the prevalence of depression and anxiety among adolescents with asthma was 27% and 33% respectively, significantly higher than adolescents without asthma (13% and 21%) [13]. Although research into the mental health of adolescents with food allergy is still in its relative infancy, it appears these adolescents have increased anxiety and lower quality of life than their healthy peers [8, 14, 15].

The apparent increased risk of depression and anxiety among adolescents with asthma or food allergy, as well as condition-specific associations may be at least partially explained by severity and/or poor medical management of the condition [16, 17], shared biological pathways [18], the phenomenon of allostatic load [19], or theories of vulnerability and stress [20]. Although associations between asthma and food allergy with depression and anxiety have been variable [21, 22], some empirical evidence of the specificity of associations between asthma and depression [23] and of food allergy and anxiety [14, 15, 24] has been reported. Emotional burden arising from needing to limit activities or using medication in the presence of peers can negatively impact the health-related quality of life in adolescents with chronic asthma and contribute to symptoms of

depression [25, 26]. Likewise the continual fear of coming in contact with a potentially life-threatening allergen and a learned state of hypervigilance can result in feelings of anxiety and compromises to health-related quality of life among those with food allergies [27, 28].

While findings have suggested that associations between respiratory or allergic disorders and internalizing problems may be specific and/or symptom severity-dependent, many previous studies were cross-sectional and samples were relatively small and homogenous with regards to socioeconomic status [12, 21, 23]. Epidemiological investigations into condition-specific associations between asthma and food allergy with depression and anxiety are important to clarify the pathogenesis of these comorbidities, improve health care delivery and reduce service costs, and ultimately improve the lives of individuals with asthma and food allergy and their families.

In the current study, we aim to build upon previous findings to address important gaps in the literature and to advance this field of study using data from a large population-based birth cohort study of adolescents assessed at 14 and 21 years of age. Specifically, our objective was to examine associations of asthma and food allergy with self-reported symptoms of depression and anxiety in an effort to assess if condition-specific associations are present during adolescence and persist into young adulthood. Based on current theoretical models and previous empirical evidence, we hypothesized that condition-specific associations would be evident such that asthma would be associated with clinically relevant symptoms of depression and food allergy with clinically relevant symptoms of anxiety.

Methods

Participants

Data for this study come from the Mater University Study of Pregnancy (MUSP), a longitudinal birth cohort study of mothers and their offspring designed to examine the factors that influence maternal and child social, psychological, and physical development from the prenatal period through adulthood [29]. Women who received public prenatal care from the Mater Misericordiae Hospital in Brisbane, Australia between 1981 and 1983 were recruited into the study ($N = 8556$) [29, 30]. The MUSP cohort consists of 7223 (84%) live singleton offspring from whom data were available at hospital discharge. Maternal and child assessments were conducted at 3-5 days, six months, and five, 14, 21, and 30 years after birth. A total of $n = 5171$ (72%) mothers and adolescents completed the 14-year follow-up and these data were used for the current analysis. Of these participants, $n = 199$ were excluded because they had missing identifiers needed for data analysis. Thus, $n = 4972$ participants met the eligibility criteria for analysis. Approval to conduct the MUSP was obtained from The University of Queensland's Behavioural and Social Sciences Ethical Review Committee.

Measures

Adolescent Asthma and Food Allergy. Presence of asthma or food allergy in adolescents was based on maternal responses to the question at the 14-year follow-up, "Has your child had any of the following...? [asthma; food allergies]. The reference group was those adolescents whose mothers who did not positively endorse this screening question. To ensure that participants had active conditions that were not outgrown or in remission, lifetime reports of asthma and food allergy were checked against two items from the Youth Self-Report (YSR) and Young Adult Self-Report (YASR) – "I have an allergy" and "I have asthma". This case ascertainment strategy resulted in $n = 3509$ adolescents classified as no asthma/allergy, $n = 1258$ as asthma, and $n = 205$ as food allergy.

Depression and Anxiety in Adolescents. Symptoms of depression and anxiety were measured using the self-reported YSR at 14 years and YASR at 21 years [31]. The DSM-oriented scales derived from these measures were used to increase the clinical utility of the findings [32]. Depression and anxiety were captured using the affective and anxiety problems subscales, respectively. The validity and reliability of the YSR and YASR subscales have been documented in the MUSP and other samples [30, 31, 33, 34]. Responses were coded as: 1 = *often*; 2 = *sometimes*; and, 3 = *rarely/never* such that lower scores indicated more symptoms. The data were then recoded prior to analysis to reflect the original scales, so that higher scores were reflective of more symptoms of depression or anxiety. As reported previously, items for both mental health problems were summed and those scoring above 90th percentile were categorized as having clinically relevant symptoms of depression or anxiety [35].

Adolescent Health Characteristics. Adolescents were dichotomized as to whether they had other health conditions based on maternal reports of the following: acne; epileptic fits; diabetes; a head injury with loss of consciousness; broken bones or fractures; burns requiring hospitalization; poisoning requiring hospitalization. Adolescent body mass index (BMI) was assessed by direct measurement. Current smoking status and alcohol use (defined as consuming alcohol “daily” or “a few time a week”) were categorized as *no* or *yes*.

Maternal and Family Characteristics. Maternal psychological distress was measured using the anxiety and depression subscales of the self-report Delusions-Symptoms-States Inventory (DSSI) [36]. Each subscale consists of seven items which assess recent symptoms of anxiety and depression (more concretely defined as symptoms in the past month). Items were originally assessed using a five-point scale: 1 = *all of the time*; 2 = *most of the time*; 3 = *some of the time*; 4 = *rarely*; and, 5 = *never*. Responses were then recoded by collapsing the *rarely* and *never* options and scores were rescaled and reverse-coded as 0 to 3 to reflect the original DSSI. Total scores on the original DSSI can range from 0 to 42 and scores ≥ 8 indicate psychological distress. The DSSI has been shown to be

valid and reliable [37]. Mothers' scores on the DSSI were included as a potential confounding factor in the regression models.

Maternal marital status was categorized as *married* (includes common-law relationships) or *not married*. Maternal employment status was categorized as *employed* (including full-time, part-time, or self-employed) and *not employed*. Household income was measured using seven pre-specified categories from \$0 to \geq \$36,350 (Australian dollars). These sociodemographic characteristics, in addition to adolescent age and sex, maternal age at child birth and maternal psychological distress, were considered as potential confounding factors in the analyses.

Data Analysis

Data were analyzed using SAS 9.2 (SAS Institute Inc., United States). Univariable statistics were used to describe the study sample. Sociodemographic characteristics were compared across subgroups (no asthma/allergy, asthma, food allergy) using analysis of variance for continuous variables (with post hoc Scheffé tests, where appropriate) and χ^2 test for categorical variables. Frequency distributions were used to estimate the proportion of adolescents with clinically relevant symptoms of depression or anxiety in each subgroup. Logistic regression was used to obtain adjusted estimates (i.e., odds ratio [OR] and associated 95% confidence intervals [CI]) of depression or anxiety for individuals with asthma or food allergy compared to no asthma/allergy adolescents. Multinomial logistic regression was used to examine the association between asthma and food allergy with the course of depression and anxiety between adolescence and young adulthood [*persistent* (90th percentile at 14 and 21 years); *incident* (90th percentile at 21 years only); and, *resolved* (90th percentile at 14 years only)]. Models were adjusted for the potential confounding effects of adolescent, maternal, and family factors.

Multiple imputation was used to account for missing data [38]. Estimates from 20 imputed datasets were combined to provide unbiased estimates. Eight percent of participants had \geq 1 missing

YSR item. Missing data at 14 years was associated with smoking ($p = .026$) and lower household income ($p < .001$). Thirty-three percent of participants had ≥ 1 missing YASR item. Missing data at the 21-year follow-up was associated with being male and with indicators of socioeconomic disadvantage: lower household income, unmarried mother, unemployed mother, and higher maternal psychological distress ($p < .001$ for all). There was no evidence of differential attrition across subgroups of participants.

JUST ACCEPTED

Results

Sample Characteristics

The mean age of adolescents was 13.9 (*SD* 0.3) years at the 14-year follow-up and 51% were male. Eighty-one percent of mothers were married, 59% were employed, and 37% had household incomes in the highest category (\geq \$36,350). Approximately 12% of adolescents were current smokers and 1% consumed alcohol at least weekly. Significant across-group differences were found for adolescent sex, presence of other health conditions, BMI, maternal age at child birth, psychological distress, and marital status (Table 1; $p < .05$ for all). No differences were found between the asthma and food allergy group; however, post hoc comparisons showed significant differences between the no asthma/allergy and asthma group for each of the aforementioned adolescent and maternal characteristics.

At the 21-year follow-up, the mean age of adolescents, now young adults, was 20.6 (0.9) years. As expected, the proportion of individuals who were classified as smokers (37%) or alcohol users (33%) increased from adolescence; however, there were no significant differences across groups. The mean BMI of young adults was 24.1 (5.1); the BMI of young adults with asthma was significant higher than those without asthma or allergy (24.6 vs. 24.0; $p = .012$).

Depression and Anxiety in Adolescents and Young Adults

Estimates of clinically relevant symptoms of depression and anxiety across subgroups are illustrated in Figure 1. The proportion of individuals with anxiety was higher than that of depression at both the 14 and 21-year follow-ups. For all groups, anxiety was less prevalent in young adults compared to adolescents. In adolescence, clinically relevant symptoms of depression were more common in asthma compared to food allergy, whereas for anxiety, the converse was found. Prevalence of persistent symptoms of depression (90th percentile at 14 and 21 years) was 3.0%; incident symptoms of depression (90th percentile at 21 years only) was 10.5%; and, resolved

symptoms of depression (90th percentile at 14 years only) was 8.5%. For persistent, incident, and resolved anxiety, the prevalence was 4.2%, 9.2%, and 17.3%, respectively.

Condition-specific Associations

As shown in Table 2, condition-specific associations were found for YSR-defined clinically relevant symptoms of depression and anxiety during adolescence. Using no asthma/allergy adolescents as the reference group, asthma was associated with increased risk for depression, whereas food allergy was associated with increased risk for anxiety. Estimates of association were robust to adjustment for adolescent, maternal, and family factors, changing minimally after adjusting for the effects of adolescent sex, presence of other health conditions, BMI, smoking status, alcohol use, maternal psychological distress, marital status, and household income. As a result, only the estimates from the fully adjusted logistic regression models are presented. Having asthma was associated with increased risk for clinically relevant symptoms of depression, OR = 1.37 [1.12, 1.67], whereas having food allergy was associated with increased risk for clinically relevant symptoms of anxiety, OR = 1.26 [1.04, 1.76]. In contrast, although associations between asthma or food allergy with depression or anxiety assessed with the YASR during young adulthood were not statistically significant, they were in the same direction as the associations found in adolescence. For asthma and depression, OR = 1.07 [0.87, 1.33] and for food allergy and anxiety, OR = 1.09 [0.70, 1.70]. Results from the multinomial logistic regression models (Table 3), showed that asthma was associated with resolved symptoms of depression, OR = 1.70 [1.13, 2.55], whereas food allergy was associated with persistent symptoms of anxiety, OR = 1.26 [1.01, 1.59].

Discussion

The presence of asthma at age 14 was associated with an increased risk of clinically relevant symptoms of depression while food allergy in adolescence was linked to an elevated risk for clinically relevant symptoms of anxiety compared to adolescents without asthma or food allergies. This study builds on a previous investigation using this birth cohort which showed that children with asthma at the five-year follow-up were at risk for internalizing behavior problems at 14 years [35]. Informed by the results of that study, we investigated specific internalizing problems – symptoms of depression and anxiety at 14 years (adolescence) and again at 21 years (young adulthood). To improve the clinical relevance of the findings we also utilized the DSM-oriented YSR scales [32] and focused our sample on three distinct subgroups of adolescents: no asthma/allergy, asthma-only, and food allergy-only.

Our findings extended those of previous studies providing evidence of specificity of associations between asthma and depression [23, 39] and of food allergy and anxiety [14, 15, 24, 40] among adolescents. These findings contrast a recent study that showed adolescents with asthma had an elevated risk of depression later in life [39], as well as previous work showing an association between asthma and anxiety [12]. These inconsistencies may be at least partly attributable to methodological differences among studies. Chen et al. (2014), used administrative data and diagnoses were classified according to the International Classification of Diseases, whereas our study and that of Slattery and Essex (2011) were based on maternal and self-reports. Furthermore, Slattery and Essex (2011) recruited younger participants (7-13 years) who were part of intact nuclear families which represented a sample of relatively high socioeconomic status whereas our study utilized a sample that represents the full range of socioeconomic status. Finally, these other studies did not explicitly sample adolescents with food allergy, but instead included other allergic disorders, such as allergic rhinitis and atopic dermatitis.

The muted associations between asthma and allergy with symptoms of depression or anxiety during young adulthood supports previous findings [41] and may be the result of adaptive coping and/or natural developmental processes during the transition from adolescence to young adulthood. As adolescents mature, they develop more positive attitudes towards their chronic health condition which has shown to mediate the association between allergic disorders and symptoms of depression and anxiety [42] and confirms the finding of the association between asthma and a resolution of depression from adolescence to young adulthood. Furthermore, evidence shows that among adolescents with and without chronic health conditions, self-concept improves during young adulthood [43] and that improvement in self-concept is antecedent to improvements in symptoms of depression and anxiety [44]. Although, the association between food allergy and persistent anxiety likely reflects a life-long worry and fear of coming into contact with an allergen and potential anaphylactic reaction, some suggest anxiety among adolescents with food allergy may be a normative process [14, 45]. Research has found a positive association between health competence and symptoms of anxiety in young adults with food allergy [27] which possibly reflects increased vigilance as part of adaptive coping [14]. However, due to the cross-sectional nature of the research however, it is not known whether increased competence heightens awareness of the potential perils of exposure to the allergen, thus increasing anxiety, or increased anxiety motivates individuals to become more health competent.

Given the age of adolescents studied, these findings support the need for health professionals to screen for and assess specific aspects of the mental health of adolescents with asthma or food allergy, particularly as they transition from pediatric to adult health services. Transition preparation programs, particularly those that start early and take a proactive, rather than reactive approach to mental health have also shown to be useful in reducing emotional distress among adolescents [46]. Patient-centered approaches to health care should be adopted in practice by recognizing the strengths of individuals and providing supportive tools and resources or targeted clinical services for adolescents (e.g., adolescent medicine clinics with social workers, psychologists,

or specialized nursing staff; transition programs with mental health modules; referral to community agencies) to ensure the optimal health outcomes [47, 48]. Importantly, health professionals should ensure patients have access to evidence-based and guideline-recommended treatments for depression and anxiety. These approaches to health care for adolescents with asthma or food allergy can help accelerate risk reduction from adolescence to young adulthood.

Findings from this study are tempered by some limitations. First, while common in population-based studies, mother-reported diagnoses of asthma or food allergy in adolescents were not validated by medical records or other administrative databases. Instead, we confirmed individuals with current asthma or food allergy using adolescent reports at the 14 and 21-year follow-ups. Second, although other studies have examined potential dose-response effects for adolescents with comorbid asthma and allergies, this type of association was not examined in the current study – asthma and food allergy can be comorbid, but asthma as the only manifestation of food allergy is atypical [9, 49] and the number of individuals with comorbid asthma and food allergy in our study was small and underpowered to detect associations in the multivariable logistic regression and were thus excluded from the analyses. Third, despite evidence showing good concordance between the DSM-oriented YSR and YASR scales with psychiatric diagnoses [34, 50], self-reported symptoms of depression and anxiety may not fully reflect clinical psychiatric disorders. Fourth, no information was available to quantify the severity of asthma or food allergy or the number of food allergies experienced by adolescents – some evidence suggests that severity and medical management of these conditions may be related to symptoms of anxiety or depression [16, 17]. Finally, as observed in other population-based studies, missing data was associated with socioeconomic disadvantage which may give rise to potential selection bias. However, this amount of missingness is similar to other population-based studies [51] and multiple imputation was used to ensure all participant data was included in the analyses to provide as unbiased a set of estimates of association as possible.

Conclusions

Adolescents with asthma were found to be at increased risk for clinically relevant symptoms of depression and those with food allergy for clinically relevant symptoms of anxiety. However, in young adulthood, these associations were no longer present. Instead, asthma was associated with resolved symptoms of depression and food allergy with persistent symptoms of anxiety. As part of a patient-centered approach, health professionals caring for adolescents with these conditions should be aware of the elevated risk of mental health problems and screen for symptoms of depression and anxiety among young people with asthma and food allergy, respectively. Longitudinal studies are needed to clarify the direction of effects between these disorders and mental health problems in an effort to inform medical management of these conditions soon after diagnosis and promote the best possible physical and mental health outcomes. In addition, studies aimed at understanding the mechanisms that contribute to the specificity of associations, as well as understanding the mediating factors contributing to the decline in risk from adolescence to young adulthood can help inform targeted, holistic care for adolescents with respiratory and/or allergic disorders.

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Declaration of Interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

JUST ACCEPTED

Table 1. Characteristics of the Study Sample.

	No Asthma/Allergy (n = 3509)	Asthma (n = 1258)	Food Allergy (n = 205)	<i>F</i> / χ^2	<i>P</i> - value
Adolescent					
Age, years	13.9 (0.3)	13.9 (0.3)	13.9 (0.3)	0.31	.73
Male*, %	50.0	54.4	53.7	7.43	.024
Presence of Other Condition*, %	69.2	75.3	75.6	19.03	<.001
BMI*	20.5 (3.7)	21.0 (4.0)	20.03 (3.7)	6.05	.002
Current Smoker, %	11.6	14.1	10.8	5.68	.06
Consumes Alcohol Weekly, %	1.2	1.2	0.5	0.81	.66
Mother/Family					
Age at Child Birth*, years	25.8 (5.1)	25.4 (4.9)	26.2 (4.7)	4.68	.017
Psychological Distress*, DSSI	3.0 (4.1)	3.5 (4.7)	3.7 (4.7)	7.46	.001
Married*, %	82.2	77.7	82.4	12.28	.002
Employed, %	59.4	58.3	58.6	0.53	.76
Income \geq \$36,350, %	37.8	36.3	38.5	1.04	.60

Note. Adolescent age, maternal age at child birth, and maternal DSSI scores are reported as mean (*SD*).

*Post hoc Scheffé tests suggested a significant difference between the no asthma/allergy and asthma groups.

Table 2. Estimates of Depression and Anxiety During Adolescence (YSR) and Young Adulthood (YASR).

Condition	Asthma	Food Allergy
Depression		
YSR	<i>1.37 [1.12, 1.67]</i>	0.88 [0.53, 1.44]
YASR	1.07 [0.87, 1.33]	1.44 [0.93, 2.23]
Anxiety		
YSR	1.24 [0.98, 1.35]	<i>1.26 [1.04, 1.76]</i>
YASR	0.99 [0.80, 1.22]	1.09 [0.70, 1.70]

Note. Results are presented as OR (95% CI) and those in italics are statistically significant. No asthma/allergy individuals were specified as the reference group. The models adjusted for adolescent sex, presence of other health conditions, BMI, smoking status, alcohol use, maternal psychological distress, marital status, and household income.

Table 3. Associations Between Asthma and Food Allergy With Type of Depression and Anxiety.

	None	Resolved	Incident	Persistent
Depression				
Asthma	1.00	<i>1.70 [1.13, 2.55]</i>	0.98 [0.76, 1.25]	1.15 [0.77, 1.60]
Food Allergy	1.00	1.52 [0.61, 3.76]	1.37 [0.86, 2.18]	0.75 [0.39, 1.43]
Anxiety				
Asthma	1.00	1.23 [0.87, 1.73]	0.92 [0.71, 1.20]	1.12 [0.94, 1.35]
Food Allergy	1.00	1.57 [0.77, 3.18]	0.93 [0.53, 1.64]	<i>1.26 [1.01, 1.59]</i>

Note. Results are presented as OR (95% CI) and those in italics are statistically significant. No asthma/allergy individuals were specified as the reference group. The models adjusted for adolescent sex, presence of other health conditions, BMI, smoking status, alcohol use, maternal psychological distress, marital status, and household income.

Figure 1. Frequency of Depression and Anxiety across Subgroups.

Estimates denote the proportion of adolescents and young adults classified as having depression (top) or anxiety (bottom). Errors bars denote 95% CI.

