

Asthma and atopic diseases in adolescence and antidepressant medication in middle age

Yuki Sato^{1*}, Ayako Hiyoshi^{2*}, Carren Melinder²,
Chieko Suzuki³ and Scott Montgomery^{2,4,5}

Abstract

This Swedish register-based cohort study examined whether asthma, hay fever and allergic dermatitis in late adolescence identified in the early 1970s are associated with antidepressant medication in middle age, between 2006 and 2009. After adjustment for childhood and adulthood sociodemographic characteristics, psychological, cognitive and physical function, and comorbidity, the magnitude of the associations diminished for asthma, while hay fever and atopic dermatitis retained associations. Hay fever and atopic dermatitis in adolescence have potentially important implications for future mental health, while asthma may already have influenced an individual's ability to cope with stress by late adolescence.

Keywords

adolescence, adults, allergy, asthma, cohort, depression

Background

Recent estimates suggest that approximately one-third of children and young adults have asthma and allergic diseases such as hay fever and atopic dermatitis (Eigenmann, 2005). The rates of these diseases have increased in the past three to four decades in many countries (Eigenmann, 2005; Miyashita et al., 2015). Asthma and allergic diseases have been found to be associated with increased depression risk (Chida et al., 2008). However, it is unclear whether diseases present in adolescence among those without depression are associated with subsequent depression risk in middle age. Evidence for the long-term risk of depression among those with childhood or adolescent onset asthma and allergic diseases is limited to studies with relatively short follow-up duration and

retrospective or self-reported information (Chen et al., 2014; Loerbroks et al., 2012). If increased depression risk is observed decades later, this has important implications for future mental health of children and adolescence with

¹Tohoku University, Japan

²Örebro University, Sweden

³Saga University, Japan

⁴Karolinska Institutet, Sweden

⁵University College London, UK

*Yuki Sato and Ayako Hiyoshi contributed equally.

Corresponding author:

Ayako Hiyoshi, Clinical Epidemiology and Biostatistics,
School of Medical Sciences, Örebro University, SE-701 82
Örebro, Sweden.

Email: ayako.hiyoshi@oru.se

these diseases. The aim of this study is therefore to examine whether individuals who had asthma, hay fever and atopic dermatitis but free of psychiatric conditions in adolescence have a higher risk of being prescribed antidepressant medication for an extended period in middle age, using prospectively recorded information.

Methods

Study population

The study population is a cohort of men who were born from 1 January 1952 to 31 December 1956 and underwent military conscription examinations at ages 17–20 years. The assessment was compulsory at that time and fewer than 4 per cent of men with severe illness or disability were exempt (Otto, 1976). Of the 284,257 men who were identified, we analysed data for 201,090 men after exclusions for inconsistencies in vital status ($n=2623$); diagnosis of psychiatric disorders at the conscription examination ($n=34,879$); were not between ages 17 and 20 years ($n=5524$); had height less than 144 cm, weight above 178 kg or body mass index (BMI) below 15 ($n=29,074$); or emigrated or died before the start of follow-up ($n=28,911$). As the Prescription Register became available in Sweden from 1 July 2005, we followed participants from 1 January 2006 to the date of depression, death, emigration or 31 December 2009, whichever occurred first.

Exposure

We defined asthma, hay fever and atopic dermatitis based on the record review and diagnoses conducted by a physician at the conscription assessment. The Swedish International Classification of Diseases (ICD)-8 codes used were for 493 for asthma, 507 for hay fever and 691 for atopic dermatitis.

Outcome

Using the Prescription Register, which holds records for all prescribed drugs dispensed by Swedish pharmacies, the first date on which the

sum of dispensed antidepressant (N06A) became equivalent to the use for more than or equal to 180 days within 365 days was taken as the incidence date, indicating continuous treatment for depression over an extended period.

Potential confounding factors

Potential confounding factors considered included childhood and adulthood sociodemographic circumstances and psychological, cognitive and physical characteristics. Socioeconomic index from the 1960 Population and Housing Census (when these men were on average 6 years of age) was categorised into six levels, and household crowding was divided into less than one, one to two, and more than two persons per room. The Longitudinal Database of Education, Income and Occupation in 2001 (on average aged 52 years) provided the following: duration in education (≤ 9 years, ≤ 12 years or 13+ years); marital status (married, unmarried and divorced/widowed); and individual disposable income divided into quarters. During conscription assessment in the early 1970s (on average aged 18.5 years), psychological stress resilience and cognitive function were assessed by a psychologist, producing nine-level normally distributed standardised scores, which were collapsed into three categories. Physical function, measured by bicycle ergometer endurance test, was also grouped into three levels. Depression may relate to the presence of other diseases; we therefore took this into account using the Charlson comorbidity index which includes up to 17 types of primary diagnosis identified using the Patient Register (inpatient and outpatient diagnoses) from 1987 to 2005. Region of residence was identified using data from the 1970 Population and Housing Census, from around the time of the conscription examination, and 24 counties were grouped into northern, central and southern regions of Sweden.

Statistical analysis

Cox proportional hazards regression examined the relationship between the diseases and antidepressant medication with adjustment for the

potential confounding factors, producing hazard ratios (HRs) and 95 per cent confidence intervals (CIs). Although some variables violated the proportional hazard assumption when the Schoenfeld residual test was employed, the observed and predicted survival curves for these variables were very close; we therefore present results assuming proportionality. The regression models comprised the following: unadjusted model, adjusted for the potential confounding factors in addition to the region of residence and the year of birth (models 1–3), and simultaneous adjustment for asthma, hay fever and dermatitis (model 4). All measures other than the Comorbidity Index were modelled as categorical variables. The analysis was conducted using SAS version 9.4 and Stata V12 statistical software. Ethical approval from Uppsala regional ethics committee has been obtained (Dnr 2014/324).

Results

Table 1 presents the distribution and unadjusted and adjusted HRs for antidepressant medication risk. From the unadjusted estimates, the risk was higher in men with asthma, dermatitis or hay fever (model 1). Unfavourable characteristics such as lower BMI, stress resilience, cognitive and physical function, disadvantageous socioeconomic characteristics and higher number of comorbid diseases were associated with elevated risk of later medication. Adjustment for sociodemographic circumstances, psychological cognitive and physical function and the morbidity score attenuated the association for asthma, but HRs for dermatitis and hay fever were almost unchanged (models 1–3). When asthma and allergic diseases were simultaneously adjusted for, the associations were hardly changed (model 4). Psychological stress resilience explained a large extent of reduction of the association between asthma and antidepressant medication risk, and the morbidity further reduced the risk.

Discussion

In this large cohort study using prospectively recorded data, we found that allergic dermatitis

and hay fever in adolescence were associated with a higher likelihood of prescribed antidepressant medication in middle-aged men. Adjustment for potential confounding factors did not alter the associations substantially for hay fever and atopic dermatitis. Simultaneous adjustment for all allergic diseases and asthma showed that the risks for receiving antidepressant medication associated with dermatitis and hay fever are independent of each other. The diminished association of asthma with antidepressant medication in the adjusted models was mainly explained by psychological stress resilience. We speculate that childhood asthma may impair stress resilience and that the tendency for depression already is more prominent in adolescence due to the experience of asthma; those with low stress resilience had an elevated risk of asthma in adolescence (odds ratio = 1.98 (95% CI = 1.78–2.19)).

Mechanisms linking allergic diseases and asthma to depression may involve physiological, psychosocial and behavioural pathways. Chronic allergic symptoms may lead to depression risk through sleep disturbance, irritability, fatigue and problems in concentration and thus impairment in work and activities (Wertz et al., 2010). Allergic dermatitis have been found to relate to being stigmatised (Schmid-Ott et al., 1999), and this may lead to shame, poor self-image, low self-esteem and social isolation (Jafferany, 2007), thus increasing the risk. Declines in health-related quality of life due to decreased energy and health and social functioning (Meltzer, 2001) have been associated with hay fever.

A potential limitation of this study is that although the use of the Prescription Register allowed us to identify all men being treated for depression pharmaceutically including in primary care, it is likely that there were many other individuals with depression who did not receive treatment. If depressive symptoms were more likely to be found and treated for men with asthma and allergic diseases when they sought health care for asthma and allergic conditions, this may have inflated the effect size (surveillance bias). Air pollution may be linked to elevated risk of atopic dermatitis (Kim, 2015), hay

Table 1. Unadjusted and adjusted Cox proportional hazard regression models for the risk of antidepressant medication after 2006 by asthma, hay fever and atopic dermatitis in adolescence.

	Depression/total subjects	Unadjusted	Model 1	Model 2	Model 3	Model 4
Asthma (conscription)						
Not diagnosed	13,514/197,159	Reference	Reference			Reference
Diagnosed	311/3931	1.16 [1.04–1.30]**	1.09 [0.97–1.22]			1.06 [0.94–1.19]
Hay fever (conscription)						
Not diagnosed	13,080/191,363	Reference	Reference			Reference
Diagnosed	745/9727	1.13 [1.05–1.21]**	1.11 [1.03–1.19]**			1.10 [1.02–1.18]**
Atopic dermatitis (conscription)						
Not diagnosed	13,687/199,651	Reference	Reference			Reference
Diagnosed	138/1439	1.43 [1.21–1.69]**			1.41 [1.19–1.67]**	1.37 [1.16–1.63]**
Childhood household crowding (1960)						
<1	916/12,594	Reference	Reference			Reference
1–2	7141/104,833	0.93 [0.87–1.00]*	0.93 [0.87–1.00]*		0.93 [0.87–1.00]*	0.93 [0.87–1.00]*
2+	5556/80,578	0.95 [0.88–1.01]	0.92 [0.86–0.99]*		0.92 [0.86–0.99]*	0.92 [0.86–0.99]*
Childhood socioeconomic index (1960)						
Business owners/managers	1471/21,471	0.93 [0.88–0.99]*	0.91 [0.86–0.97]**	0.91 [0.86–0.97]**	0.91 [0.86–0.97]**	0.91 [0.86–0.97]**
Office workers	4069/55,492	Reference	Reference	Reference	Reference	Reference
Farm owners/managers	1251/21,018	0.80 [0.75–0.86]**	0.75 [0.71–0.80]**	0.75 [0.71–0.80]**	0.75 [0.71–0.80]**	0.76 [0.71–0.81]**
Manual workers	5550/81,630	0.92 [0.89–0.96]**	0.88 [0.84–0.92]**	0.88 [0.84–0.92]**	0.88 [0.84–0.92]**	0.88 [0.84–0.92]**
Agricultural workers	507/7813	0.88 [0.80–0.97]**	0.83 [0.76–0.91]**	0.83 [0.76–0.91]**	0.83 [0.76–0.91]**	0.83 [0.76–0.92]**
Others (including unknown)	977/13,666	0.97 [0.91–1.04]	0.90 [0.84–0.97]**	0.91 [0.84–0.98]**	0.91 [0.84–0.98]**	0.91 [0.84–0.98]**
Body mass index (conscription)						
15 – <18.5	1710/22,363	1.13 [1.08–1.19]**	1.04 [0.98–1.09]	1.04 [0.98–1.10]	1.04 [0.98–1.10]	1.04 [0.98–1.09]
18.5 – <25.0	11,100/163,699	Reference	Reference	Reference	Reference	Reference
25.0 – <30.0	868/13,100	0.98 [0.91–1.05]	0.94 [0.88–1.01]	0.94 [0.88–1.01]	0.94 [0.88–1.01]	0.94 [0.88–1.01]
30.0+	147/1928	1.14 [0.97–1.35]	0.94 [0.80–1.11]	0.94 [0.80–1.11]	0.94 [0.80–1.11]	0.94 [0.80–1.11]
Stress resilience (conscription)						
High	3081/52,888	Reference	Reference	Reference	Reference	Reference
Moderate	8087/118,815	1.18 [1.13–1.23]**	1.11 [1.06–1.16]**	1.11 [1.06–1.16]**	1.11 [1.06–1.16]**	1.11 [1.06–1.16]**
Low	2578/28,505	1.59 [1.51–1.67]**	1.33 [1.26–1.41]**	1.33 [1.26–1.41]**	1.33 [1.26–1.41]**	1.33 [1.26–1.41]**

Table 1. (Continued)

	Depression/total subjects	Model 1	Model 2	Model 3	Model 4
Cognitive function (conscription)					
High	3532/55,850	Reference	Reference	Reference	Reference
Moderate	7405/107,622	1.09 [1.05–1.14]***	1.06 [1.02–1.11]**	1.06 [1.01–1.11]**	1.06 [1.02–1.11]**
Low	2875/37,416	1.23 [1.17–1.29]***	1.08 [1.02–1.14]**	1.08 [1.02–1.14]**	1.08 [1.02–1.14]**
Physical capacity (conscription)					
High	3514/58,148	Reference	Reference	Reference	Reference
Moderate	4923/72,759	1.13 [1.08–1.18]***	1.05 [1.01–1.10]*	1.05 [1.01–1.10]*	1.05 [1.01–1.10]*
Low	5387/70,177	1.28 [1.23–1.34]***	1.12 [1.07–1.18]***	1.12 [1.07–1.18]***	1.12 [1.07–1.18]***
Marital status (2001)					
Married	7062/115,408	Reference	Reference	Reference	Reference
Single	4523/57,355	1.31 [1.26–1.36]***	1.13 [1.09–1.18]***	1.13 [1.09–1.18]***	1.13 [1.09–1.18]***
Divorced	2184/27,442	1.32 [1.25–1.38]***	1.19 [1.14–1.25]***	1.19 [1.14–1.25]***	1.19 [1.14–1.25]***
Widowed	56/875	1.05 [0.81–1.37]	1.07 [0.82–1.39]	1.07 [0.82–1.39]	1.07 [0.82–1.39]
Income (2001)					
Highest quartile	3042/55,535	Reference	Reference	Reference	Reference
Second highest quartile	3100/54,536	1.04 [0.99–1.09]	1.08 [1.02–1.13]**	1.08 [1.02–1.13]**	1.08 [1.02–1.13]**
Second lowest quartile	3623/51,348	1.30 [1.24–1.36]***	1.34 [1.27–1.41]***	1.34 [1.27–1.41]***	1.34 [1.27–1.41]***
Lowest quartile	4060/39,661	1.94 [1.85–2.03]***	1.89 [1.80–2.00]***	1.90 [1.80–2.00]***	1.90 [1.80–2.00]***
Education (2001)					
Post-secondary education	4267/62,383	Reference	Reference	Reference	Reference
Secondary education	6639/95,362	1.02 [0.98–1.06]	0.84 [0.80–0.88]***	0.84 [0.80–0.88]***	0.84 [0.80–0.88]***
Less than secondary education	2904/43,059	0.99 [0.94–1.03]	0.75 [0.71–0.79]***	0.75 [0.71–0.79]***	0.75 [0.71–0.80]***
Comorbidity index (1987–2005)	0.23 [0.41] ^a	1.59 [1.54–1.65]***	1.51 [1.46–1.56]***	1.51 [1.46–1.56]***	1.51 [1.46–1.56]***

n = 201,090.

a : mean (standard deviation).

*p<0.05, **p<0.01, ***p<0.001.

Unadjusted: the regression model only included one exposure variable.

Models 1–4: all variables presented as well as the year of birth and region of residence were adjusted for simultaneously. In all analyses, region of residence, stress resilience, cognitive function, physical capacity, marital status, income and education included a category for individuals with missing data (not presented in the table), which found 882 individuals for stress resilience and 202 for cognitive function, otherwise less than 10 individuals for each variable.

fever (Janssen et al., 2003) and depression (Cho et al., 2014), particularly among those with underlying conditions such as asthma (Cho et al., 2014). Adjustment for region may to a degree have taken account for difference in depression risk by air quality, but residual confounding is possible. The purpose of this study was to assess the association of the diseases in adolescence with depression treatment, but there will be diagnoses made after adolescence.

The strength of this study was the comparison of exposures and outcomes separated by three decades, and the use of almost all men in Sweden born between 1952 and 1956. The accuracy of identification of asthma and hay fever was found to be fairly high, approximately 80 per cent (Aberg, 1989). Information on psychiatric conditions at conscription assessment enabled us to exclude those individuals from the analysis, and therefore, it is less likely that the observed associations were due to reverse causation (higher asthma and allergic disease risk due to pre-existing depression). Information on psychological, cognitive and physical function, and adulthood sociodemographic circumstances, which may in part be consequences of asthma and allergic diseases, enabled us to adjust for potentially relevant factors that could confound the associations although this might have been over-adjustment.

In this register-based cohort study of Swedish men, hay fever and atopic dermatitis in adolescence were associated with the elevated risk of being prescribed antidepressant three decades later. Hay fever and atopic dermatitis in adolescence have potentially important implications for future mental health and asthma may already have influenced an individual's ability to cope with stress by late adolescence.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or

publication of this article: This study was supported by grants from the Swedish Research Council for Health, Working Life and Welfare (Forskningsrådet för hälsa, arbetsliv och välfärd, Forte in Swedish acronym) (2015-01365), the UK Economic and Social Research Council (ESRC) grants to the International Centre for Life Course Studies (RES-596-28-0001 and ES/J019119/1), Japan Allergy Foundation (2015), Scandinavia-Japan Sasakawa Foundation (15-15) and Lindhés Advokatbyrå AB (LA2015-0219).

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