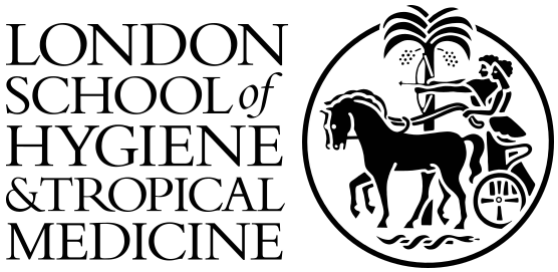

Atopic dermatitis, educational attainment and psychological functioning: a national cohort study

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Manuscript word, table and figure count

Words: 2877 (excluding figure/table legends and references)
Tables: 5
Figures: 0

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Funding sources

This study received support from the UK Economic and Social Research Council (ESRC) as grants to the International Centre for Life Course Studies (grants RES-596-28-0001 and ES/JO19119/1). SML is funded by a Wellcome Senior Clinical Fellowship (205039/Z/16/Z). JS is supported by the Centre for Clinical Research, Värmland County Council.

Conflicts of interest

None declared.

What's already known about this topic?

- Atopic dermatitis can influence quality of life, but little is known about its possible impact on educational attainment.

What does this study add?

- Atopic dermatitis was not associated with lower cognitive function or poorer academic attainment in this large general population-based cohort study of men in Sweden.
- Men with atopic dermatitis had lower stress resilience in late adolescence, which has potential adverse implications for mental and physical health in subsequent adulthood.

Summary

Background Atopic dermatitis (AD) might adversely affect academic performance, possibly through influences on psychological functioning such as stress resilience.

Objectives To investigate the association of atopic dermatitis with stress resilience, cognitive function and educational attainment.

Methods We used data from a national cohort of men who underwent a military conscription examination at ages 17 to 20 years in Sweden between 1969 and 1976. All potential conscripts met a physician who assessed current or previous history of AD. Stress resilience was measured by a psychologist using a semi-structured interview. The conscription assessment included a written cognitive function test. Highest level of achieved education was obtained through record linkage.

Results The study population included 234 715 men, 1 673 (0.7%) had an AD diagnosis. AD was associated with a greater risk of low stress resilience (adjusted relative risk ratio (RRR) 1.60; 95% confidence interval 1.38 to 1.86). AD was associated with higher cognitive function (b coefficient 0.15; 0.05 to 0.24) and higher educational level (RRR 1.29; 1.13 to 1.47) but adjustment for socioeconomic characteristics of the family of origin attenuated the magnitude of the associations and eliminated statistical significance (b coefficient 0.06; -0.03 to 0.15) and (RRR 1.16; 1.00 to 1.35).

Conclusions Swedish males with AD had lower stress resilience in late adolescence but did not have lower cognitive function or poorer educational attainment. The lower stress resilience associated with AD is consistent with an increased risk of possible long-term adverse health outcomes.

Introduction

Atopic dermatitis (AD) is a common inflammatory skin disease that can have a substantial impact on quality of life.[1] AD can result in high social and financial costs and accounts for the largest global health burden due to skin disease.[2] Recently a systematic review highlighted a major research gap with only one population-based study assessing the association between eczema and educational attainment (EA).[3] The only study included in the review did not find an association between childhood AD and school performance at age 11 years.[4]

It is, however, plausible that AD, as it is a chronic disease, might have an adverse impact on educational attainment. AD is characterised by an itchy rash and can lead to pain and sleep loss that could potentially lead to loss of concentration and impaired learning at school. School absenteeism as well as visible lesions and their impact on social interactions could potentially influence school performance detrimentally.

Adverse exposures in childhood and chronic disease are associated with impaired stress resilience: the ability to cope with stressful exposures.[5-6] Some exposures and susceptibility can result in a poorly controlled physiological stress response, involving a greater likelihood of chronic arousal of the hypothalamic-pituitary-adrenal (HPA) axis. If AD has an adverse influence on the experience of daily life, then it may also have implications for stress resilience. Reduced ability to cope with stress might in turn impair cognitive function, and thus educational attainment.

Educational success is important for future health and economic wellbeing.[7] Therefore, it is important to investigate if children with AD are at risk of lower educational attainment and if so to determine the underlying mechanisms. This knowledge will assist in planning interventions to support children during their lives.

We aimed to examine the associations of AD with stress resilience, cognitive function and highest level of education in adolescence, which were measured as part of a compulsory military conscription assessment among a representative sample of men in Sweden.

Materials and methods

This is a cohort study with prospectively recorded data for male Swedish residents who were born between 1952 and 1956 and underwent military conscription examinations at ages 17 – 20 years. At the time, conscription was compulsory for all male citizens, with the exception of individuals with severe disability or who were incarcerated. Inclusion criteria were all men who attended a conscription examination between 1969 and 1976 in Sweden. The conscription examinations included a medical examination, various physical and psychological tests as well as cognitive function tests. Exclusion criteria were men with missing data and those who were not assessed between ages 17 to 20 years.

Information on AD was collected by a physician from a general physical examination based on a clinical evaluation, with a medical history and record review during the conscription assessment. The Swedish International Classification of Diseases (ICD)-8 code 691 was used to identify AD and ICD codes 507 and 493 for rhinitis and asthma diagnoses. A psychological examination using a semi-structured interview was performed to access stress resilience with a score from 1 to 9. Information from a questionnaire and an interview included questions relevant to everyday life aimed to assess the ability to tolerate psychological stress in military service. Stress resilience was categorized in three groups as low (1-3), intermediate (4-6) and high (7-9), as in our previous studies.[8] Cognitive function was assessed by a written test during the conscription examination and recorded using a nine-level normally distributed standardised score. The cognitive function test included questions on logical, spatial, verbal and technical capabilities. High values indicate greater cognitive function. The measures from the Conscription Register used in this study are described in detail elsewhere.[9]

Educational attainment was assessed in 1990 using data from the Longitudinal Integration Database for Health Insurance and Labour Market Studies (Swedish acronym, LISA). Educational attainment was grouped in three categories: compulsory schooling to a maximum of 9 years; post-compulsory secondary education over 2 years but less than 3 years; and subsequent higher/further education.

Other covariates in our study were head of household's occupation and household crowding when cohort members were children using data from the 1960 Population and Housing Census. The head of household's occupation was used to produce a socioeconomic index (SEI), categorised as: manual workers, agricultural workers, farm owners or managers, office workers, business owners or managers and unknown occupation. Household crowding was recorded as the person per habitable room ratio and divided into quarters of the distribution.

Statistical analysis

Cross-tabulation was used to describe the study population for those with and without AD.

The relationship between AD and stress resilience was examined using multinomial regression with high stress resilience as the reference category, with adjustment for parental SEI and household crowding, as well as year and age at conscription assessment in model 1. A further analysis additionally adjusted for cognitive function.

Linear regression was used to assess the association between AD and cognitive function as the dependent variable, with adjustment for parental SEI and household crowding, as well as year and age at conscription, modelled as categorical variables.

The association between AD and highest education level was examined using multinomial regression with compulsory schooling (duration in education ≤9 years) as the reference category, with adjustment for parental SEI and household crowding, as well as year and age at conscription assessment. Further models were additionally adjusted for cognitive function and stress resilience.

Multinomial regression compares each outcome category with a reference category and produces a relative risk ratio (RRR) by exponentiating the regression coefficients. If there were only two categories this would be equivalent to an odds ratio, but as there are more than two, the statistic is termed a relative risk ratio.

A p-value lower than 0.05 or 95% confidence intervals not including 1.00 indicated statistical significance. The analysis was conducted using SPSS 22.0 and Stata V12 statistical software.

Ethical approval from Uppsala regional ethics committee has been obtained (Dnr 2014/324).

Results

In total, 234 715 men were included in analysis. Atopic dermatitis was diagnosed in 1 673 males assessed for military conscription between 1969 and 1976 in Sweden, at ages 17-20 years, representing 0.7% of the study population. Table 1 describes the study population. All covariates were statistically significantly associated with AD. Individuals with AD were more

often from families with parents who were office workers, compared with men without AD, 35% (n=581) and 28% (64 738) respectively and lived in less crowded dwellings. In total, 65 970 (28%) of the men achieved higher education at university level by age of 36 years. Men with AD had higher level education more often than men without AD, 32% (n=538) and 28% (n=65 432) respectively.

The unadjusted analysis found that AD was associated with a statistically significant increased risk of low stress resilience (relative risk ratio (RRR) 1.39; 95% confidence interval 1.21 to 1.60) as shown in table 2. The magnitude of association with AD increased after adjustment for parental SEI and household crowding (RRR 1.52; 1.32 to 1.76), and further increased without loss of statistical significance after additional adjustment for cognitive function (RRR 1.60; 1.38 to 1.86). To adjust for the potential confounding effect of asthma and rhinitis on the association between AD and stress resilience, additional adjustment for these diagnoses was performed. The magnitude of the AD-stress resilience association decreased but remained statistically significant (RRR 1.36; 1.17 to 1.58). Associations of stress resilience with AD, asthma and rhinitis are presented in supplementary table 1. Both asthma and rhinitis are statistically significantly associated with low stress resilience with adjusted RRR of 2.06 (1.87 to 2.26) and 1.43 (1.35 to 1.53), respectively. It is of note that the magnitude of association for asthma is somewhat higher than for AD.

Table 3 shows that in the unadjusted analysis AD is statistically significantly associated with higher cognitive function (b coefficient 0.15 95% CI 0.05 to 0.24). However, adjustment for parental SEI and household crowding attenuated the magnitude of the association between AD and cognitive function and eliminated statistical significance (0.06; -0.03 to 0.15). To aid interpretation, cognitive function was also categorised in three groups as low (1-3), intermediate (4-6) and high (7-9) with analysis using multinomial regression. Compared with low cognitive function, the unadjusted association with AD produced a relative risks ratio of 1.15 (1.01 to 1.32) and 1.26 (1.09 to 1.45) for intermediate and high cognitive function, respectively. After adjustment, these estimates are not statistically significant, producing relative risks ratio of 1.08 (0.94 to 1.23) and 1.07 (0.92 to 1.25) for intermediate and high cognitive function, respectively.

The association between AD and educational attainment is shown in table 4. The unadjusted multinomial regression model showed an increased relative risk of higher level education for individuals with AD (RRR 1.29; 95% CI 1.13 to 1.47). Adjustment for parental SEI and

household crowding attenuated the association between AD and educational attainment and eliminated statistical significance (RRR 1.09; 95% CI 0.95 to 1.25). Further adjustment for cognitive function did not change the association between AD and higher education notably. Adjustment for stress resilience slightly increased the relative risk of higher educational attainment in individuals with AD and attained borderline statistical significance (RRR 1.16; 95% CI 1.00 to 1.35).

Discussion

This large general population-based cohort study of Swedish men showed an association between an AD diagnosis and low stress resilience. Despite having lower stress resilience individuals with AD did not have a risk of lower cognitive function in adolescence or lower level educational attainment by early adulthood.

This study is consistent with the results reported by Ruijsbroek *et al* that did not find an association between AD and educational attainment, in a Dutch birth cohort study examining school performance by age 11 years among more than 1 500 children.[4] Our study population was older and larger and additional information was available on stress resilience. To the best of our knowledge there are no other longitudinal studies that have investigated the association of AD with education.

Several previous studies showed a strong positive association between parental socioeconomic position and the child's educational attainment.[4,10] Childhood AD has been associated with a higher socioeconomic position of parents.[11,12] In contrast with the *a priori* hypothesis, in this study, AD was associated with better cognitive function and higher educational level, which appears to result from confounding by socioeconomic circumstances in childhood: socially advantageous conditions are associated with better cognitive function and educational attainment, but also increase the risk of AD. It is unclear why better socioeconomic position in childhood is associated with higher prevalence rates of AD, but several hypotheses exist. Role of overuse of soaps, differences in health care utilisation, air pollution and maternal diet and age have been suggested.[12,13] A reduced pattern of exposure to environmental microbes at home, the hygiene hypothesis, as a risk for development of AD

might be one of the main possible explanations for the association between parental socioeconomic characteristics and childhood AD.[12-14]

Our study showed a positive association between AD and low stress resilience. Assessments of AD, stress resilience and cognitive function were performed at the same time point during the conscription examination limiting our possibility to identify temporal sequences and thus estimate causation. We speculate that one possibility is that the physical discomfort, sleeping problems and social sequelae of having a disfiguring disease might influence stress resilience. The putative influence of AD on stress resilience might be explained mainly by psychological and psychosocial mechanisms but, underlying neuroendocrine mechanisms, might also play a role, for example, subclinical inflammation related to AD might affect the HPA axis and lead to impaired stress resilience.[15,16] The magnitude of the contemporaneous association between AD and low stress resilience in adolescence is not sufficiently high to suggest it is a significant clinical problem, but it may help to explain some associations of AD with adverse health outcomes in later adulthood. Low stress resilience has been linked to a number of adverse outcomes later in life such as diabetes mellitus, hypertension, stroke and risk of coronary heart disease.[8,17-19] It has also been shown that low stress resilience is associated with an increased risk of subsequent peptic ulcer disease and inflammatory bowel disease.[20,21] Therefore, those with AD may expect a greater disease burden in later adulthood as indicated by their, on average, lower stress resilience. Using the same measure of stress resilience, it has been demonstrated that low resilience in adolescence is associated with a raised risk of adult-onset depression, anxiety and bipolar disorder,[22] as well as with pharmaceutical treatment for anxiety or depression in middle age,[23] indicating a long-term association of stress resilience with mental health. Several other studies support the association and describe possible mechanisms linking stress resilience to depression.[24,25] Another study using these data found AD in adolescence was associated with a greater risk of treatment for depression in middle age.[26] Several other studies have linked AD with depression[27] and it is possible that this association may already have begun in adolescence. If having AD influences stress resilience, this may be due, at least in part, to other atopic diseases, so we additionally adjusted for asthma and allergic rhinitis diagnoses. This only had a modest influence on the magnitude of the AD-stress resilience association. It is of note that the association of asthma with stress resilience was of higher magnitude than for AD. This is in contrast with a study of depression in middle age using these data, which found a higher magnitude association of AD with future depression and not for asthma.[26]

Residual confounding is always a possibility in an observational study. The main objectives here were to assess if AD is associated with *lower* educational attainment and cognitive function: the observed associations were in the opposite direction. Adjustment for markers of socioeconomic circumstances attenuated these associations, so in theory it is possible that more extensive adjustment for family circumstances may show more of an adverse association with education and cognition. However, given the initial direction and magnitude of association a substantially increased risk is unlikely. There is evidence of some confounding by other atopic diseases for the association of AD with stress resilience. However, whatever the causal pathway involves, the on average lower stress resilience among people with AD, still suggests a greater risk of adverse health outcomes in later life.

Our study has a number of strengths, including the use of prospectively recorded data from several linked registers and the large study population of almost all men born between 1952 and 1956 in Sweden. The AD diagnosis as well as stress resilience were assessed by physicians and psychologists. Other variables such as socioeconomic and educational data came from registers, providing a reliable data source with few missing data. We used two complementary outcomes relevant to education, the cognitive function test and highest level of education. The former indicates ability, while the latter both ability and career choices.

A potential limitation is that the prevalence of AD between adults in our study is 0.7%, while most studies report an international prevalence between 3 and 10%. It is expected that individuals with more severe, persistent AD and those with visible lesions on the day of assessment were more likely to have received a diagnosis of AD, while individuals with less severe disease and those with AD which had resolved by adolescence would be missed. It is likely that the study underestimated the number of men who had ever had an AD diagnosis and this misclassification may have caused bias in the results. One possibility is that the results have been diluted by incomplete identification of men with AD, another possibility is that associations are of higher magnitude due to greater likelihood of including men with more severe and persistent disease. AD, asthma and rhinitis were identified using ICD-8 diagnostic codes without further details of diagnoses. Code 691 includes eczema/atopic dermatitis (including infantile onset and similar conditions) and it excludes dermatitis caused by toxins or occupational exposures such as solvents, oils and fats. This a limitation of the AD diagnoses used here, as there is no information on severity or extent and no information on the diagnostic criteria used. Assessment of AD by a physician should result in an acceptably

accurate diagnosis of AD.[28, 29] The conscription examination follows a standardised protocol to evaluate whether a potential conscript is suitable for military service so less severe manifestations of AD may not be considered relevant, so the diagnosis here may be less sensitive. There was no information on AD resolution or information on hospital admissions for AD. A notable limitation is that the study population comprised only males, limiting generalisability of the study results, as the risk and consequences of AD in women may be different. The current study was of men born in the 1950s in Sweden and since then the epidemiology of AD has altered.[14] Therefore, we cannot exclude the possibility that the results may differ in a population born more recently. However, given the direction and magnitude of our results, we believe that AD in adolescence is unlikely to represent a substantial risk for impaired educational performance.

In conclusion, our study did not find AD to be associated with lower educational attainment or cognitive function, but AD was associated with lower stress resilience, signalling a raised risk of adverse psychiatric and somatic outcomes in later adulthood. Risks for comorbidity among those with AD deserves further investigation.

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Table 1 Population characteristics by atopic dermatitis diagnosis for 234 715 male adolescents assessed for military conscription between 1969 and 1976 in Sweden

	Total number in category (% of all in the study)	Atopic dermatitis	
		Yes 1 673 (0.7) n (%)	No 233 042 (99.3) n (%)
Highest level of education			
Compulsory schooling	58 683 (25.0)	373 (22.3)	58 310 (25.0)
Secondary education	110 062 (46.9)	762 (45.5)	109 300 (46.9)
Higher education	65 970 (28.1)	538 (32.2)	65 432 (28.1)
Cognitive function score*	5.2 (2.0)	5.4 (2.0)	5.2 (2.0)
Stress resilience**			
Low (1-3) stress resilience	49 889 (21.3)	432 (25.8)	49 457 (21.2)
Intermediate (4-6) stress resilience	128 843 (54.9)	891 (53.3)	127 952 (54.9)
High (7-9) stress resilience	55 983 (23.9)	350 (20.9)	55 633 (23.9)
Household crowding quarters***			
0.2 – 1.25	60 807 (25.9)	471 (28.2)	60 336 (25.9)
1.29 – 1.67	72 902 (31.1)	582 (34.8)	72 320 (31.0)
1.71 – 2	50 124 (21.4)	340 (20.3)	49 784 (21.4)
2.14 – 13	50 882 (21.7)	280 (16.7)	50 602 (21.7)
The head of household's occupation			
Manual workers	97 230 (41.4)	638 (38.1)	96 592 (41.4)
Agricultural workers	9 081 (3.9)	39 (2.3)	9 042 (3.9)
Farm owners/managers	23 607 (10.1)	128 (7.7)	23 479 (10.1)
Office workers	65 319 (27.8)	581 (34.7)	64 738 (27.8)
Business owners/managers	25 267 (10.8)	210 (12.6)	25 057 (10.8)
Others/unknown	14 211 (6.1)	77 (4.6)	14 134 (6.1)

* Mean (SD). Score from 1 to 9 where higher values indicate higher cognitive function

** Potential ability to cope with stress in military service

*** The number of people per habitable room categorized into equal quarters of the distribution

Table 2 The association between atopic dermatitis and stress resilience in adolescence

	Intermediate stress resilience			Low stress resilience		
	Unadjusted RRR (CI 95%)	Adjusted Model 1 aRRR (CI 95%)	Adjusted Model 2 aRRR (CI 95%)	Unadjusted RRR (CI 95%)	Adjusted Model 1 aRRR (CI 95%)	Adjusted Model 2 aRRR (CI 95%)
Atopic dermatitis						
No	Reference	Reference	Reference	Reference	Reference	Reference
Yes	1.12 (0.98 to 1.25)	1.18 (1.04 to 1.34)	1.21 (1.07 to 1.38)	1.39 (1.21 to 1.60)	1.52 (1.32 to 1.76)	1.60 (1.38 to 1.86)
Household crowding quarters*						
0.2 – 1.25	Reference	Reference	Reference	Reference	Reference	Reference
1.29 – 1.67	1.25 (1.22 to 1.29)	1.19 (1.16 to 1.22)	1.11 (1.08 to 1.14)	1.45 (1.40 to 1.50)	1.31 (1.27 to 1.36)	1.15 (1.11 to 1.19)
1.71 – 2	1.43 (1.39 to 1.47)	1.29 (1.25 to 1.33)	1.16 (1.12 to 1.19)	1.89 (1.82 to 1.95)	1.58 (1.53 to 1.64)	1.27 (1.22 to 1.32)
2.14 – 13	1.81 (1.75 to 1.86)	1.55 (1.50 to 1.60)	1.31 (1.26 to 1.35)	3.00 (2.89 to 3.11)	2.32 (2.23 to 2. 41)	1.62 (1.55 to 1.68)
The head of household's occupation						
Manual workers	Reference	Reference	Reference	Reference	Reference	Reference
Agricultural workers	1.27 (1.19 to 1.35)	1.25 (1.18 to 1.33)	1.16 (1.09 to 1.23)	1.34 (1.25 to 1.43)	1.32 (1.24 to 1.42)	1.10 (1.02 to 1.18)
Farm owners/managers	0.93 (0.90 to 0.97)	0.99 (0.96 to 1.03)	0.99 (0.95 to 1.03)	0.65 (0.62 to 0.68)	0.75 (0.72 to 0.79)	0.74 (0.70 to 0.77)
Office workers	0.58 (0.56 to 0.59)	0.64 (0.62 to 0.65)	0.77 (0.75 to 0.79)	0.43 (0.42 to 0.44)	0.52 (0.50 to 0.54)	0.78 (0.76 to 0.81)
Business owners/managers	0.69 (0.66 to 0.71)	0.76 (0.73 to 0.78)	0.83 (0.81 to 0.86)	0.53 (0.51 to 0.55)	0.64 (0.61 to 0.67)	0.78 (0.74 to 0.82)
Others/unknown	0.82 (0.78 to 0.85)	0.83 (0.79 to 0.87)	0.86 (0.82 to 0.90)	1.06 (1.01 to 1.12)	1.08 (1.03 to 1.14)	1.11 (1.05 to 1.18)

Cognitive function**	0.77 (0.77 to 0.77)	-	0.79 (0.78 to 0.79)	0.58 (0.58 to 0.59)	-	0.60 (0.60 to 0.60)

The analysis used multinomial regression to produce relative risk ratios (RRR)

Model 1: adjusted for household crowding, head of household's occupation, year and age of conscription

Model 2: adjusted as model 1 and cognitive function

* The number of people per habitable room categorized into equal quarters of the distribution

** Score from 1 to 9 where higher values indicate higher cognitive function

Table 3 The association between atopic dermatitis and cognitive function

	Unadjusted		Adjusted	
	b coefficient (95% CI)	p-value	b coefficient (95% CI)	p-value
Atopic dermatitis				
No	Reference	Reference	Reference	Reference
Yes	0.15 (0.05 to 0.24)	0.002	0.06 (-0.03 to 0.15)	0.225
Household crowding quarters*				
0.2 – 1.25	Reference	Reference	Reference	Reference
1.29 – 1.67	-0.44 (-0.46 to -0.42)	<0.001	-0.31 (-0.33 to -0.29)	<0.001
1.71 – 2	-0.74 (-0.76 to -0.72)	<0.001	-0.52 (-0.54 to -0.49)	<0.001
2.14 – 13	-1.19 (-1.21 to -1.16)	<0.001	-0.85 (-0.87 to -0.83)	<0.001
The head of household's occupation				
Manual workers	Reference	Reference	Reference	Reference
Agricultural workers	-0.44 (-0.48 to -0.40)	<0.001	-0.41 (-0.45 to -0.37)	<0.001
Farm owners/managers	0.15 (0.12 to 0.17)	<0.001	-0.00 (-0.03 to 0.02)	0.796
Office workers	1.12 (1.10 to 1.14)	<0.001	0.92 (0.90 to 0.94)	<0.001
Business owners/managers	0.68 (0.66 to 0.71)	<0.001	0.47 (0.45 to 0.50)	<0.001
Others/unknown	0.05 (0.02 to 0.09)	0.002	0.03 (-0.00 to 0.06)	0.067

The analysis used linear regression

Adjusted for household crowding, head of household's occupation and year and age of conscription

* The number of people per habitable room categorized into equal quarters of the distribution

Table 4 The association between atopic dermatitis and education level

	Secondary education (High school)				Higher education (University studies)			
	Unadjusted RRR (CI 95%)	Adjusted Model 1 aRRR (CI 95%)	Adjusted Model 2 aRRR (CI 95%)	Adjusted Model 3 aRRR (CI 95%)	Unadjusted RRR (CI 95%)	Adjusted Model 1 aRRR (CI 95%)	Adjusted Model 2 aRRR (CI 95%)	Adjusted Model 3 aRRR (CI 95%)
Atopic dermatitis								
No	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Yes	1.09 (0.96 to 1.23)	1.02 (0.90 to 1.15)	1.01 (0.89 to 1.15)	1.03 (0.91 to 1.18)	1.29 (1.13 to 1.47)	1.09 (0.95 to 1.25)	1.09 (0.94 to 1.27)	1.16 (1.00 to 1.35)
Household crowding 4 quantiles*								
0.2 – 1.25	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference
1.29 – 1.67	0.88 (0.85 to 0.90)	0.90 (0.87 to 0.93)	0.93 (0.90 to 0.96)	0.93 (0.90 to 0.96)	0.56 (0.54 to 0.58)	0.63 (0.61 to 0.65)	0.72 (0.69 to 0.74)	0.73 (0.70 to 0.75)
1.71 – 2	0.76 (0.74 to 0.79)	0.80 (0.78 to 0.83)	0.85 (0.83 to 0.88)	0.86 (0.83 to 0.89)	0.37 (0.35 to 0.38)	0.46 (0.45 to 0.48)	0.57 (0.55 to 0.60)	0.59 (0.56 to 0.61)
2.14 – 13	0.64 (0.62 to 0.66)	0.70 (0.68 to 0.72)	0.80 (0.77 to 0.82)	0.81 (0.78 to 0.84)	0.20 (0.20 to 0.21)	0.30 (0.29 to 0.31)	0.44 (0.42 to 0.45)	0.46 (0.44 to 0.48)
The head of household's occupation								
Manual workers	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Agricultural workers	0.84 (0.80 to 0.88)	0.83 (0.79 to 0.87)	0.90 (0.86 to 0.94)	0.90 (0.86 to 0.94)	0.55 (0.52 to 0.59)	0.56 (0.52 to 0.60)	0.68 (0.63 to 0.73)	0.68 (0.63 to 0.73)
Farm owners/managers	0.85 (0.82 to 0.88)	0.79 (0.76 to 0.81)	0.77 (0.75 to 0.80)	0.76 (0.74 to 0.79)	0.91 (0.88 to 0.95)	0.73 (0.70 to 0.76)	0.68 (0.65 to 0.71)	0.65 (0.62 to 0.68)
Office workers	1.79 (1.74 to 1.84)	1.64 (1.60 to 1.69)	1.44 (1.39 to 1.48)	1.43 (1.39 to 1.47)	5.21 (5.05 to 5.36)	4.01 (3.89 to 4.14)	2.71 (2.62 to 2.80)	2.65 (2.56 to 2.74)
Business owners/managers	1.09 (1.06 to 1.13)	1.00 (0.97 to 1.04)	0.93 (0.89 to 0.96)	0.92 (0.89 to 0.95)	2.24 (2.16 to 2.33)	1.68 (1.62 to 1.75)	1.32 (1.26 to 1.38)	1.28 (1.23 to 1.34)
Others/unknown	1.00 (0.95 to	0.98 (0.94 to	1.02 (0.97 to	1.03 (0.99 to	1.27 (1.21 to	1.23 (1.17 to	1.22 (1.15 to	1.23 (1.16 to

	1.03)	1.02)	1.06)	1.08)	1.34)	1.29)	1.29)	1.30)
Cognitive function**	1.34 (1.33 to 1.35)	-	1.31 (1.30 to 1.32)	1.28 (1.27 to 1.29)	2.30 (2.28 to 2.32)	-	2.15 (2.13 to 2.17)	2.05 (2.03 to 2.07)
Stress resilience***								
High (7-9)	Reference	-	-	Reference	Reference	-	-	Reference
Low (1-3)	0.42 (0.40 to 0.43)	-	-	0.63 (0.61 to 0.65)	0.11 (0.11 to 0.12)	-	-	0.31 (0.29 to 0.32)
Intermediate (4-6)	0.66 (0.64 to 0.68)	-	-	0.79 (0.77 to 0.82)	0.31 (0.30 to 0.32)	-	-	0.51 (0.50 to 0.53)

The association used multinomial regression to produce relative risk ratios (RRR)

Model 1: adjusted for household crowding, head of household's occupation, year and age of conscription

Model 2: adjusted as model 1 and cognitive function

Model 3: adjusted as model 2 and stress resilience

* The number of people per habitable room categorized into equal quarters of the distribution

** Score from 1 to 9 where higher values indicate higher cognitive function

*** Potential ability to cope with stress in military service

Supplementary table 1 The association between atopic dermatitis, asthma, rhinitis and stress resilience in adolescence

	Total number in category (% of all in the study)	Intermediate stress resilience			Low stress resilience		
		Unadjusted RRR (CI 95%)	Adjusted Model aRRR (CI 95%)	Additional model aRRR (CI 95%)	Unadjusted RRR (CI 95%)	Adjusted Model aRRR (CI 95%)	Additional model aRRR (CI 95%)
Atopic dermatitis							
No	233 042 (99.3)	Reference	Reference	Reference	Reference	Reference	Reference
Yes	1 673 (0.7)	1.12 (0.98 to 1.25)	1.21 (1.07 to 1.38)	1.10 (0.97 to 1.25)	1.39 (1.21 to 1.60)	1.60 (1.38 to 1.86)	1.36 (1.17 to 1.58)
Asthma							
No	230 073 (98.0)	Reference	Reference	Reference	Reference	Reference	Reference
Yes	4 642 (2.0)	1.50 (1.38 to 1.62)	-	1.51 (1.39 to 1.64)	2.01 (1.84 to 2.20)	-	2.06 (1.87 to 2.26)
Rhinitis							
No	223 394 (95.2)	Reference	Reference	Reference	Reference	Reference	Reference
Yes	11 321 (4.8)	1.09 (1.04 to 1.14)	-	1.28 (1.22 to 1.34)	1.06 (1.01 to 1.13)	-	1.43 (1.35 to 1.53)

The analysis used multinomial regression to produce relative risk ratios (RRR)

Adjusted model: adjusted for household crowding, head of household's occupation, year and age of conscription and cognitive function

Additional model: adjusted as "adjusted model" and asthma and rhinitis