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N.B.: When citing this work, cite the original article.

This is the authors' version of the following article:

L. Braback, Hartmut Vogt and A. Hjern, Migration and asthma medication in international adoptees and immigrant families in Sweden, 2011, *Clinical and Experimental Allergy*, (41), 8, 1108-1115.

which has been published in final form at:

<http://dx.doi.org/10.1111/j.1365-2222.2011.03744.x>

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<http://eu.wiley.com/WileyCDA/Brand/id-35.html>

Postprint available at: Linköping University Electronic Press

<http://urn.kb.se/resolve?urn=urn:nbn:se:liu:diva-69780>

Migration and asthma medication in international adoptees and immigrant families in Sweden

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Running head: *asthma medication and immigration*

Word count 3068

Abstract word count: 263

Key words: *adoptees, asthma, country of birth, environment, inhaled corticosteroids, immigration*

Abstract

Background Studies of asthma in migrant populations illustrate the effects of environmental changes.

Objective In this register study we investigated the importance of exposure to a Western lifestyle in different phases of development in Swedish residents with an origin in regions in the world where asthma usually is less prevalent.

Methods The study population comprised 24 252 international adoptees, 47 986 foreign-born and 40 971 Swedish-born with foreign-born parents and 1 770 092 Swedish-born residents with Swedish-born parents (age 6-25 years). Purchased prescribed inhaled corticosteroids (ICS) during 2006 were used as an indicator of asthma.

Results International adoptees and children born in Sweden by foreign-born parents had three to four fold higher rates of asthma medication compared with foreign-born children. The odds ratios of asthma medication declined persistently with age at immigration. For adoptees the odds ratios (ORs) compared with infant adoptees were 0.78 (95% confidence interval (CI) 0.71-0.85) for those adopted at 1-2 years, 0.51 (0.42-0.61) at 3-4 years and 0.35 (0.27-0.44) after 5 or more years of age. Corresponding ORs for foreign-born children with foreign-born parents immigrating at 0-4 years, at 5-9 years, at 10-14 years and at 15 years or more were 0.73 (0.63-0.86), 0.56 (CI 0.46-0.68) and 0.35 (CI 0.28-0.43), respectively. The odds ratios were only marginally affected by adjustment for region of birth and socioeconomic indicators.

Conclusions and clinical relevance Age at immigration is a more important determinant of purchased ICS than population of origin. This indicates the importance of environmental factors for asthma in schoolchildren and young adults.

Introduction

Recent international studies have demonstrated worldwide variations in the prevalence of asthma both within and between countries [1]. A rising prevalence of asthma occurred particularly in Westernized countries during the second half of the previous century. A more than threefold increase in asthma was observed among male conscripts in Sweden over a period of less than three decades [2]. Genes and environment interact in the development of asthma but changes in prevalence over a short period [2] and geographical differences in asthma within the same ethnic groups [3, 4] must be caused by environmental factors. An increased prevalence of asthma has been linked to urbanization, affluence and changes in diet and microbial contacts [5]. There is some evidence from farm studies that protective exposures act already *in utero* [6].

Studies on migrant populations illustrate the effects of environmental changes. Emigrating from a region with a low prevalence of asthma to a country with a high prevalence could be described as a natural experiment [7]. Migration from a low or middle-income country to a high-income Western country involves substantial environmental changes which may affect the risk of asthma. Migrants adapt to a greater or less extent to life styles in the host society and a protection from asthma related to exposures in the country of birth weakens by duration of residence in the host country. Since 1970 most of the immigrants in Sweden are refugees or relatives of refugees. Foreign-born adoptees differ in several aspects from other immigrants. Many children are adopted from orphanages. Higher social classes are overrepresented among adoptive parents and the children are rapidly integrated into a Swedish lifestyle through their host families.

The aim of this register study in Sweden was to use the large study population available to sort out the independent effects of population of origin and age at immigration/being born in Sweden on the risk of asthma at the age of 6-25 years in international adoptees, raised by Swedish-born parents, and children raised by their foreign-born birth parents. They all had an origin in populations in regions of the world where asthma often is less prevalent than in Sweden. Purchase of prescribed inhaled corticosteroids (ICS) was used as an indicator of asthma and information from the Swedish Prescribed Drug Register was linked to other national registries at an individual level.

Methods

This study was based on Swedish national registers held by the National Board of Health and Welfare and Statistics Sweden. All Swedish residents are assigned a unique ten digit identification (ID) number at birth or immigration. This ID was used to link information from different register sources. The study was approved by the regional ethics committee in Linköping.

Study population

All individuals born 1980-2000, who were alive and registered as residents in Sweden on December 31st 2005 were identified in the Register of the Total Population (RTP). Biological and/or adoptive parents of these individuals were identified in the Multi-Generation Register.

Information about region of birth, date of immigration, sex and year of birth in RTP was linked to the study subjects and their parents. Based on this information we identified three categories of residents with a non-Swedish background; (1) international adoptees, (2) residents born outside of Sweden who immigrated to Sweden with their parents and (3)

residents born in Sweden with two foreign-born parents. We selected four regions of origin where there were considerable numbers of children in all three categories; Eastern Europe, East Asia, South Asia and Latin America. Eastern Europe included the former communist countries in Eastern Europe excluding Yugoslavia; Latin America included all countries in the Americas south of the USA; South Asia included India, Pakistan, Sri Lanka and Bangla Desh. East Asia included all Asian countries east of the Indian peninsula.

This population included 24 252 international adoptees with two Swedish-born adoptive parents, 47 986 foreign-born and 40 971 Swedish-born with two foreign-born parents. To this population we added 1 770 092 Swedish-born residents with two Swedish-born parents as a comparison group.

Demographic variables

Age at adoption/immigration was calculated from year of birth and year of immigration to Sweden according to the RTP. (Adoption in this sense means the time when a child starts to live in the household of the new parents and not the date when the formal adoption procedure is finished). The mean age at adoption was lowest in adoptees from South and East Asia (1.3 years) and highest in adoptees from Eastern Europe (3.2 years). Foreign-born with foreign-born parents had a higher mean age (17-18 years) than Swedish-born with foreign-born parents (12-14 years) in 2006 when purchase of ICS was assessed. The mean age of the adoptees in 2006 varied from 19.4 in adoptees from South Asia to 13.1 in adoptees from Eastern Europe (Table 1).

Sex and geographical residency (urban/rural) were added from RTP. Asian adoptees had a female preponderance, while the opposite was the case for adoptees from Eastern Europe and

Table 1. Socio-demographic characteristics and purchased prescribed inhaled corticosteroids in children and youth (6-25 years) in Sweden in 2006 by own and parental country of birth.

Region of birth of biological parents	Own country of birth	N	Male sex (%)	Mean age at immigration (years)	Mean age in 2006 (years)	Purchased prescribed drugs in 2006	
						inhaled cortisone	beta2-agonists but no inhaled cortisone
Sweden	Sweden	1 770 092	51.5	-	15.1	7.5	2.1
Eastern Europe	Adoptees	3 396	56.7	3.2	13.1	5.9	1.5
	Born in Sweden	15 014	51.4	-	14.3	4.9	1.9
	Immigrants	17 958	46.9	11.4	18.2	1.8	0.1
East Asia	Adoptees	7 464	43.4	1.3	14.6	8.4	3.0
	Born in Sweden	8 261	52.7	-	12.2	7.6	2.4
	Immigrants	11 959	45.2	11.4	17.3	1.4	0.8
South Asia	Adoptees	6 706	37.4	1.3	19.4	10.4	3.0
	Born in Sweden	5 984	51.8	-	12.5	10.2	2.8
	Immigrants	8 058	56.5	13.5	18.1	2.2	1.0
Latin America	Adoptees	6 686	57.8	1.5	17.5	8.7	2.0
	Born in Sweden	11 712	52.1	-	13.9	8.2	2.5
	Immigrants	10 100	52.2	9.4	18.7	3.3	1.9

Latin America. Sex rates were more balanced in the other study groups. The highest completed education of the mother was identified in the Swedish Register of Education in 2005 and categorised as primary school= 9 or less years of primary school, secondary practical= less than 3 years of secondary school, secondary theoretical=3 years of secondary school, and university=at least 3 years of higher education. Income from social assistance was obtained through linkage to the Total Enumeration Income Survey of 2005 and dichotomised as recipient/not recipient of social assistance. Social assistance in Sweden is a form of cash income allowance from local social authorities, after a thorough means investigation, with the purpose to guarantee the applicant a minimum standard of living.

Drug variables

The Swedish Prescribed Drug Register contains data, with unique patient identifiers for all drugs prescribed and dispensed to the whole population of Sweden (more than 9 million inhabitants) since July 2005. Patient identification data are missing for less than 0.3 per cent of all items [8]. The purchase of at least one prescription of a drug with an Anatomical Therapeutic Chemical (ATC)-code that started with R03BA (inhaled corticosteroids) during the calendar year 2006, according to this register, was used to create the outcome variable of the study, *purchased prescribed inhaled corticosteroids (ICS)*. We also collected information on dispensed prescriptions of bronchodilators for inhalation (ATC-code R03AC) to individuals who had not purchased ICS in 2006.

Statistical analysis

Logistic regression was used to calculate odds ratios (ORs) with 95% confidence intervals (CIs), with purchased prescribed ICS, defined above, as the outcome variable. We adjusted all

models to residency as a three-category variable (large city, other city, rural) and to sex. Age was entered as a continuous variable with an interaction term age* sex reflecting the linear age patterns when each sex was analysed separately. In the final model 4 we added maternal education as a four category variable and a dichotomised variable of social assistance as socio-economic indicators. All statistical analyses were performed using SPSS version 18.0 for Windows.

Results

Table 1 demonstrates the prevalence rates of purchased prescribed ICS in 2006 by region of origin and category of immigrant. Purchase of prescribed ICS was much less prevalent in foreign-born with foreign-born parents compared with adoptees and children born in Sweden with foreign-born parents in all four regions ([supporting information, Table S1](#)). Table 2 demonstrates odds ratios for purchased prescribed ICS in 2006 by region of origin after logistic regression with adjustment for sex and age. Significantly lower odds ratios were observed in foreign-born with foreign-born parents in all regions of origin. In contrast, purchase of prescribed ICS varied among Swedish-born subjects with foreign born parents. In comparison with the Swedish majority population, Swedish-born subjects with parents born in Eastern Europe had a decreased risk (OR 0.54) of purchased prescribed ICS whereas those with parents born in South Asia had a slightly increased risk (OR 1.26).

Purchase of prescribed ICS was less likely in adoptees from Eastern Europe when compared with Swedish-born subjects with Swedish-born parents (OR 0.27). In contrast, purchase of prescribed ICS was more likely in adoptees from the other continents. The greatest risk of purchased prescribed ICS was observed in adoptees from South Asia (OR 1.76) (Table 2)

Table 3 demonstrates an inverse dose-response association between age at adoption and the risk of purchased prescribed ICS in 2006 in the unadjusted Model 1. Adjusting for region of birth in Model 3 had nothing but marginal effects on these associations. Region of birth had an influence on the risk of purchased prescribed ICS in the unadjusted Model 2 but these associations became weaker in adoptees from Eastern Europe after adjustment for age at adoption in Model 3 compared with adoptees from Latin America. Adoptees from South Asia had an increased risk, adjusted OR 1.21 in comparison with adoptees from Latin America.

Table 2. Own and parental country of birth as risk factors for purchased prescribed inhaled corticosteroids – odds ratios after logistic regression with adjustment for age and sex

Region of birth of birth parents	Own country of birth	Inhaled cortisone OR (95% CI)
Sweden	Sweden	1
Eastern Europe	Adoptees	0.27 (0.11-0.65)
	Born in Sweden	0.54 (0.40-0.72)
	Immigrants	0.34 (0.25-0.57)
East Asia	Adoptees	1.12 (1.03-1.21)
	Born in Sweden	0.90 (0.82-0.98)
	Immigrants	0.19 (0.16-0.22)
South Asia	Adoptees	1.76 (1.63-1.90)
	Born in Sweden	1.26 (1.16-1.37)
	Immigrants	0.31 (0.27-0.36)
Latin America	Adoptees	1.29 (1.18-1.40)
	Born in Sweden	1.04 (0.98-1.12)
	Immigrants	0.48 (0.43-0.54)

Table 3. Age at adoption, region of birth and purchased prescribed inhaled cortisone in international adoptees, 6-25 years. Odds ratios after logistic regression.

			Model 1* OR (95% CI)	Model 2* OR (95% CI)	Model 3* OR (95% CI)	Model 4 [†] OR (95% CI)
Age at adoption (yr)	0	8 422	1		1	1
	1-2	11 344	0.72 (0.61-0.83)		0.78 (0.71-0.85)	0.80 (0.72-0.88)
	3-4	2 471	0.52 (0.43-0.64)		0.51 (0.42-0.61)	0.55 (0.45-0.67)
	5+	2 015	0.32 (0.26-0.39)		0.35 (0.27-0.44)	0.37 (0.29-0.47)
Region of birth	Latin America	6 686		1	1	1
	Eastern Europe	3 396		0.63 (0.53-0.74)	0.80 (0.67-0.95)	0.72 (0.60-0.86)
	South Asia	6 706		1.26 (1.11-1.41)	1.21 (1.08-1.37)	1.21 (1.07-1.37)
	East Asia	7 464		0.92 (0.82-1.04)	0.90 (0.80-1.02)	0.94 (0.83-1.06)

* Adjusted also for age, sex and rural/urban residency.

[†] Adjusted also for age, sex, rural/urban residency, having received social welfare during 2006 and maternal education.

The odds ratios were only marginally attenuated after adjustment for maternal education and received social assistance in Model 4. The odds ratios in the unadjusted Model 1 and the adjusted Model 3 are also displayed in Figure 1 (a).

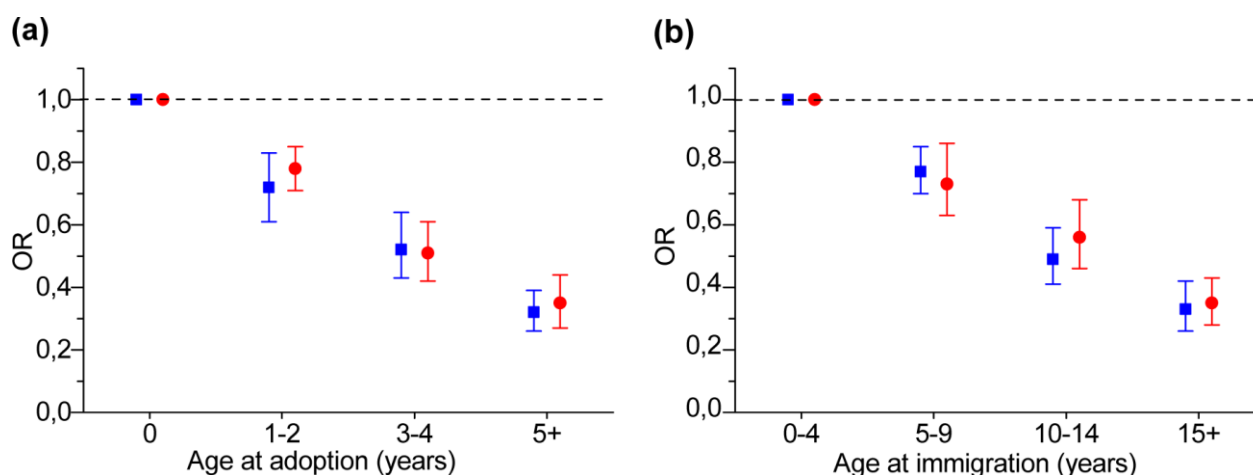


Figure 1.

(a) The risk of purchased prescribed inhaled corticosteroids by age at adoption.

(b) The risk of purchased prescribed inhaled corticosteroids by age at immigration. **Blue squares:** unadjusted odds ratios with 95% confidence intervals. **Red circles:** odds ratios after adjustment for sex, geographical residency (urban/rural) and region of birth.

Table 4 demonstrates the inverse crude dose-response relationship between age at immigration and purchased prescribed ICS in non-adopted foreign-born children (Model 1). This relationship was only marginally affected by adjustment for region of birth (Model 3). The risk of purchased prescribed ICS differed by region of birth (Model 2) but the variability was reduced after adjustment for age at immigration (Model 3). In comparison with immigrants from Latin America, the risk of purchased prescribed ICS in the fully adjusted Model 3 was significantly reduced in immigrants from South Asia (OR 0.84), Eastern Europe (OR 0.61) as well as the East Asia (OR 0.47). Figure 1 (b) depicts the associations between age at migration and purchased prescribed ICS in Model 1 and 3. The associations were only marginally attenuated after adjustment for markers of socioeconomic status in Model 4.

Table 4. Age at immigration, region of birth and purchased prescribed inhaled cortisone in foreign-born offspring with foreign-born parents, 6-25 years. Odds ratios after logistic regression

			Model 1* OR (95% CI)	Model 2* OR (95% CI)	Model 3* OR (95% CI)	Model 4† OR (95% CI)
Age at immigration (yr)	0-4	9 165	1		1	1
	5-9	13 828	0.77 (0.70-0.85)		0.73 (0.63-0.86)	0.79 (0.67-0.93)
	10-14	9 409	0.49 (0.41-0.59)		0.56 (0.46-0.68)	0.58 (0.48-0.71)
	15+	15 528	0.33 (0.26-0.42)		0.35 (0.28-0.43)	0.45 (0.35-0.57)
Region of birth	Latin America	10 100		1	1	1
	Eastern	17 958		0.54 (0.46-0.63)	0.61 (0.52-0.71)	0.56 (0.50-0.66)
	Europe	8 058		0.66 (0.55-0.80)	0.84 (0.69-1.02)	0.87 (0.71-1.06)
	South Asia	11 959		0.40 (0.33-0.49)	0.47 (0.39-0.57)	0.49 (0.40-0.59)
	East Asia					

* Adjusted for age, sex and rural/urban residency.

† Adjusted for age, sex, rural/urban residency, having received social welfare during 2006 and maternal education.

We finally investigated the association between the different immigrant categories and purchased prescribed ICS after logistic regression with adjustment for sex, age and parental region of birth (Results not in tables). In relation to foreign-born subjects with foreign-born parents the adjusted odds ratios for purchased prescribed ICS in adoptees and in Swedish-born subjects with foreign-born parents were 3.94 (95% CI 3.64 – 4.25) and 3.36 (95% CI 3.10 – 3.66), respectively.

Discussion

We investigated purchase of ICS, as an indicator for asthma, after migration to Sweden in migrants from Eastern Europe, South Asia, East Asia and Latin America. To our knowledge, this is the first study to compare the risk of an indicator for asthma in three categories of migrants: international adoptees, foreign-born and Swedish-born with foreign-born parents. The prevalence of purchased prescribed ICS decreased with higher age at migration both in adoptees and in foreign-born immigrants with foreign-born parents and these associations were unchanged after adjustment for region of birth and socio-economic indicators.

Environmental factors related to poverty such as microbial load and diet appear to protect from asthma and allergic diseases in non-affluent areas of the world whereas development of these diseases is promoted in high income countries like Sweden [9]. Previous studies from *e.g.* the US [10-13], the UK [14], Israel [15], Sweden [16, 17] and Australia [18] have demonstrated an association between the risk of asthma and age at migration [11, 15-17] or duration of residence in the new country [11-13, 18]. The new finding in this study is the negative relationship between age at immigration and the risk of purchased prescribed ICS in international adoptees, raised by Swedish parents, as well as in foreign-born children raised by their birth parents. A British study showed a similar risk of asthma in South Asian women who were born in the UK and in women who migrated before five years of age. South Asian women migrating after five years of age had a much lower risk but the risk did not change by increasing age [14]. We have a much larger study population and our findings show a gradually declining risk of purchased prescribed ICS also in individuals migrating after five years of age. In agreement with our study, age at immigration to Israel was inversely related to the risk of asthma at the age of 17 among immigrants from the former Soviet Union and

Ethiopia. In contrast, immigration from Western Europe did not affect the risk of asthma [15].

An increased risk of asthma is a consequence for children in all ages moving from less developed regions with a low prevalence of asthma to more developed regions in the world with a higher prevalence of asthma.

Adoptees had an almost fourfold increased risk of purchased prescribed ICS compared with immigrants from the same region of birth. Mean age at migration among the immigrants in this study was 10 years whereas most adoptees were adopted before two years of age. The highest risk of purchased prescribed ICS in young adults was demonstrated in individuals who had immigrated in early infancy. Conversely, the protective effect on asthma of being born in low or median income regions was closely related to the length of the residency in the native country. A low level of acculturation in immigrants may further counteract the effects of asthma-promoting exposures in the new society [10, 19], in contrast to adoptees who are immediately integrated into a Swedish lifestyle. In comparison with the Swedish majority population and adoptees from other continents, adoptees from Eastern Europe had a decreased risk of purchased prescribed ICS. A lower prevalence of purchased prescribed ICS was to a large extent explained by the higher age at migration in adoptees from Eastern Europe.

Purchase of prescribed ICS was more likely in adoptees from Asia and Latin America than in Swedish born subjects with Swedish-born parents. We could not exclude, that differences in purchase of ICS were related to differences in health seeking behaviour. Adoptive parents could be more eager to seek medical care for their children. The highest rate of purchased prescribed ICS was observed in adoptees from South Asia. Similarly, Swedish-born children with parents from South Asia had slightly increased odds for purchased prescribed ICS compared to Swedish-born children with Swedish-born parents. Such findings may indicate a

genetic propensity to asthma in the South Asian population. Nevertheless, recent multicentre studies have suggested a very low prevalence of asthma in children in some of the centres in India [20, 21]. Certain environments in India may confer a protection from asthma. It has been proposed that populations originating in tropical areas have evolved an immune response with a proinflammatory profile. A strong Th 2 response is crucial in an environment with a high load of worms and other parasites. A similar immune response in temperate areas is deleterious and associated with an increased risk of asthma and allergic diseases [22]. Recent studies on gene-environment interaction have demonstrated that the expression of a specific gene is determined by the context. A genetic variant could be related to an increased risk of asthma in one environment but protect from asthma in another environmental background [23]. In comparison with their white counterparts, south Asian and black Caribbean children born in the UK had a greater risk of asthma [24] and multiple wheeze [25]. South Asian schoolchildren living in the UK also had an increased risk of wheeze triggered by food [26]. Black children in the US have an excess risk of asthma compared with non-Black children and this difference was observed in all income groups [27].

A low prevalence of purchased prescribed ICS does not *per se* imply a low prevalence of asthma. Underdiagnosis of asthma and underuse of prophylactic medication has been reported to be more common in low-income families in Canada [28], the US [29] and New Zealand [30]. It is quite possible that the same pattern exists in Sweden. In 2001, almost 50% of the immigrant children aged less than 17 years was living in relative poverty in Sweden as compared to 8% in Swedish-born children with Swedish-born parents. The proportion of immigrant children living in economic vulnerability was 67.4% among those with less than 2 years of residence in Sweden, and 28.6% among those with 10-12 years in Sweden [31]. Language barriers, health seeking behaviour, low health literacy and inadequate access to

health care contribute to a reduced utilization of ICS in immigrants [32]. It is reasonable to believe that purchased prescribed ICS as a marker of current asthma may underestimate the true prevalence of asthma in immigrants, particularly among those who have recently arrived. Underestimation of asthma may therefore contribute to the much lower purchase of ICS in foreign-born children with foreign-born parents as compared with adoptees and Swedish-born children with foreign-born parents. However, underuse of asthma medication and underdiagnosis of asthma is less likely to explain the similar and inverse association between age at migration and purchased prescribed ICS both in adoptees and foreign-born children with foreign-born parents despite socioeconomic disparities and potential differences in health seeking behaviour between the two groups. Upper social classes are overrepresented in the former group whereas lower social classes are more likely in the latter one. Furthermore, the decreasing risk of purchased prescribed ICS by increasing age at migration persisted after adjustment for socioeconomic indicators.

Asthma medication as a marker of asthma has some other limitations particularly in infants and elderly people [33]. Some children are treated with asthma medication without having received a diagnosis of asthma [34]. In particular, asthma medication is common in preschool children with transient, viral-induced wheeze. A diagnosis of asthma is uncertain before five or six years of age [35, 36]. We have therefore only included children six years and above where ICS prescription tends to be more specific for asthma. Persistent asthma [37] and more severe symptoms [38] are more likely in schoolchildren receiving inhaled corticosteroids. Beta-agonists would be more sensitive yet less specific measure of asthma, and include respiratory conditions which are not asthma. There was no indication in the crosstabulations in Table 1 that including beta-agonists as markers of asthma in the analysis would have changed the patterns of migrants reported in this study,

Conclusions and clinical relevance

Migration from a low or median income region of the world with a low prevalence of asthma to an affluent country like Sweden with a high prevalence of asthma is related to an increased risk of asthma medication in children in immigrant families as well as in international adoptees. This risk declines with higher age at immigration and is highest in adoptees and Swedish-born offspring of foreign-born parents. Adoptees and Swedish-born offspring with an origin in South Asia had the highest risk of purchased prescribed ICS, suggesting a genetic susceptibility for asthma when exposed to the lifestyle and environment of a high income society like Sweden.

Acknowledgement

Lennart Bråbäck was supported by the Umeå SIMSAM Node “Microdata research on childhood for lifelong health and welfare” financed by the Swedish Research Council.

Hartmut Vogt was supported by The Swedish Asthma and Allergy Association (Stockholm, Sweden).

References

1. Pearce N, Sunyer J, Cheng S, Chinn S, Bjorksten B, Burr M, Keil U, Anderson HR, Burney P, Comparison of asthma prevalence in the ISAAC and the ECRHS. ISAAC Steering Committee and the European Community Respiratory Health Survey. International Study of Asthma and Allergies in Childhood. *Eur Respir J* 2000;**16**: 420-426.
2. Bråbäck L, Hjern A, Rasmussen F, Trends in asthma, allergic rhinitis and eczema among Swedish conscripts from farming and non-farming environments. A nationwide study over three decades. *Clin Exp Allergy* 2004;**34**: 38-43.
3. Pekkarinen PT, von Hertzen L, Laatikainen T, Makela MJ, Jousilahti P, Kosunen TU, Pantelejev V, Vartiainen E, Haahtela T, A disparity in the association of asthma, rhinitis, and eczema with allergen-specific IgE between Finnish and Russian Karelia. *Allergy* 2007;**62**: 281-287.
4. von Mutius E, Martinez FD, Fritzsche C, Nicolai T, Roell G, Thiemann HH, Prevalence of asthma and atopy in two areas of West and East Germany. *American journal of respiratory and critical care medicine* 1994;**149**: 358-364.
5. Von Hertzen LC, Haahtela T, Asthma and atopy - the price of affluence? *Allergy* 2004;**59**: 124-137.
6. von Mutius E, 99th Dahlem conference on infection, inflammation and chronic inflammatory disorders: farm lifestyles and the hygiene hypothesis. *Clinical and experimental immunology* 2010;**160**: 130-135.
7. Hjern A, Haglund B, Hedlin G, Ethnicity, childhood environment and atopic disorder. *Clin Exp Allergy* 2000;**30**: 521-528.

8. Wettermark B, Hammar N, Fored CM, Leimanis A, Otterblad Olausson P, Bergman U, Persson I, Sundstrom A, Westerholm B, Rosen M, The new Swedish Prescribed Drug Register--opportunities for pharmacoepidemiological research and experience from the first six months. *Pharmacoepidemiology and drug safety* 2007;**16**: 726-735.
9. Asher MI, Stewart AW, Mallol J, Montefort S, Lai CK, Ait-Khaled N, Odhiambo J, Which population level environmental factors are associated with asthma, rhinoconjunctivitis and eczema? Review of the ecological analyses of ISAAC Phase One. *Respiratory research* 2010;**11**: 8.
10. Eldeirawi KM, Persky VW, Associations of acculturation and country of birth with asthma and wheezing in Mexican American youths. *J Asthma* 2006;**43**: 279-286.
11. Eldeirawi K, McConnell R, Furner S, Freels S, Stayner L, Hernandez E, Amoruso L, Torres S, Persky VW, Associations of doctor-diagnosed asthma with immigration status, age at immigration, and length of residence in the United States in a sample of Mexican American School Children in Chicago. *J Asthma* 2009;**46**: 796-802.
12. Holguin F, Mannino DM, Anto J, Mott J, Ford ES, Teague WG, Redd SC, Romieu I, Country of birth as a risk factor for asthma among Mexican Americans. *American journal of respiratory and critical care medicine* 2005;**171**: 103-108.
13. Joseph SP, Borrell LN, Shapiro A, Self-reported lifetime asthma and nativity status in U.S. children and adolescents: results from the National Health and Nutrition Examination Survey 1999-2004. *Journal of health care for the poor and underserved* 2010;**21**: 125-139.
14. Kuehni CE, Strippoli MP, Low N, Silverman M, Asthma in young south Asian women living in the United Kingdom: the importance of early life. *Clin Exp Allergy* 2007;**37**: 47-53.

15. Pereg D, Tirosh A, Lishner M, Goldberg A, Shochat T, Confino-Cohen R, Prevalence of asthma in a large group of Israeli adolescents: influence of country of birth and age at migration. *Allergy* 2008;**63**: 1040-1045.
16. Hjern A, Rasmussen F, Johansson M, Aberg N, Migration and atopic disorder in Swedish conscripts. *Pediatr Allergy Immunol* 1999;**10**: 209-215.
17. Hjern A, Rasmussen F, Hedlin G, Age at adoption, ethnicity and atopic disorder: a study of internationally adopted young men in Sweden. *Pediatr Allergy Immunol* 1999;**10**: 101-106.
18. Powell CV, Nolan TM, Carlin JB, Bennett CM, Johnson PD, Respiratory symptoms and duration of residence in immigrant teenagers living in Melbourne, Australia. *Archives of disease in childhood* 1999;**81**: 159-162.
19. Grüber C, Illi S, Plieth A, Sommerfeld C, Wahn U, Cultural adaptation is associated with atopy and wheezing among children of Turkish origin living in Germany. *Clin Exp Allergy* 2002;**32**: 526-531.
20. Worldwide variations in the prevalence of asthma symptoms: the International Study of Asthma and Allergies in Childhood (ISAAC). *Eur Respir J* 1998;**12**: 315-335.
21. Lai CK, Beasley R, Crane J, Foliaki S, Shah J, Weiland S, Global variation in the prevalence and severity of asthma symptoms: phase three of the International Study of Asthma and Allergies in Childhood (ISAAC). *Thorax* 2009;**64**: 476-483.
22. Le Souef PN, Goldblatt J, Lynch NR, Evolutionary adaptation of inflammatory immune responses in human beings. *Lancet* 2000;**356**: 242-244.
23. Martinez FD, Gene-environment interactions in asthma: with apologies to William of Ockham. *Proceedings of the American Thoracic Society* 2007;**4**: 26-31.

24. Netuveli G, Hurwitz B, Levy M, Fletcher M, Barnes G, Durham SR, Sheikh A, Ethnic variations in UK asthma frequency, morbidity, and health-service use: a systematic review and meta-analysis. *Lancet* 2005;**365**: 312-317.
25. Kuehni CE, Strippoli MP, Low N, Brooke AM, Silverman M, Wheeze and asthma prevalence and related health-service use in white and south Asian pre-schoolchildren in the United Kingdom. *Clin Exp Allergy* 2007;**37**: 1738-1746.
26. Kuehni CE, Strippoli MP, Silverman M, Food intolerance and wheezing in young South Asian and white children: prevalence and clinical significance. *The Journal of allergy and clinical immunology* 2006;**118**: 528-530.
27. Miller JE, The effects of race/ethnicity and income on early childhood asthma prevalence and health care use. *American journal of public health* 2000;**90**: 428-430.
28. Kozyrskyj AL, Mustard CA, Simons FE, Socioeconomic status, drug insurance benefits, and new prescriptions for inhaled corticosteroids in schoolchildren with asthma. *Archives of pediatrics & adolescent medicine* 2001;**155**: 1219-1224.
29. Adams RJ, Fuhlbrigge A, Guilbert T, Lozano P, Martinez F, Inadequate use of asthma medication in the United States: results of the asthma in America national population survey. *The Journal of allergy and clinical immunology* 2002;**110**: 58-64.
30. Mitchell EA, Stewart AW, Pattemore PK, Asher MI, Harrison AC, Rea HH, Socioeconomic status in childhood asthma. *International journal of epidemiology* 1989;**18**: 888-890.
31. Salonen T, Child poverty in Sweden. Annual Report 2003. Stockholm. In: Save the Children S ed., 2003.
32. Davidson E, Liu JJ, Sheikh A, The impact of ethnicity on asthma care. *Prim Care Respir J* 2010;**19**:202-208.

33. Hoffmann F, Glaeske G, Prescriptions as a proxy for asthma in children: a good choice? *European journal of clinical pharmacology* 2010;**66**: 307-313.
34. Zuidgeest MG, van Dijk L, Smit HA, van der Wouden JC, Brunekreef B, Leufkens HG, Bracke M, Prescription of respiratory medication without an asthma diagnosis in children: a population based study. *BMC health services research* 2008;**8**: 16-24.
35. Global Initiative for Asthma. Global strategy for the diagnosis and management of asthma in children 5 years and younger, 2009; cited 2010 Dec 16. Available from <http://www.ginasthma.org/>
36. Zuidgeest MG, van Dijk L, Spreeuwenberg P, Smit HA, Brunekreef B, Arets HG, Bracke M, Leufkens HG, What drives prescribing of asthma medication to children? A multilevel population-based study. *Annals of family medicine* 2009;**7**: 32-40.
37. Kozyrskyj AL, Mustard CA, Becker AB, Identifying children with persistent asthma from health care administrative records. *Can Respir J* 2004;**11**: 141-145.
38. Andersson M, Bjerg A, Forsberg B, Lundbäck B, Rönmark E, The clinical expression of asthma in schoolchildren has changed between 1996 and 2006. *Pediatr Allergy Immunol* 2010;**21**: 859-866.

Supporting information

Additional supporting information may be found in the online version of this article:

Table S1. Prevalence of purchased prescribed inhaled corticosteroids (ICS) (at least one prescription in 5-year age-groups and at least two prescriptions for all ages) in Sweden in 2006 by own and parental country of birth.

Table S1. Prevalence of purchased prescribed inhaled corticosteroids (ICS) (at least one prescription in 5-year age-groups and at least two prescriptions for all ages) in Sweden in 2006 by own and parental country of birth.

Region of birth of biological parents	Own country of birth	At least one prescription of ICS				Two or more prescriptions of ICS
		6-10 years %	11-15 years %	16-20 years %	21-25 years %	6-25 years %
Sweden	Sweden	9.6	8.2	6.2	5.4	2.4
Eastern Europe	Adoptees	6.0	5.7	4.6	6.0	2.7
	Born in Sweden	5.5	5.2	4.7	3.9	1.9
	Immigrants	2.4	1.6	1.5	1.8	1.0
East Asia	Adoptees	9.0	9.8	7.6	7.9	2.8
	Born in Sweden	8.9	7.6	4.0	4.6	2.0
	Immigrants	1.5	0.9	1.6	1.3	0.4
South Asia	Adoptees	11.2	9.8	10.0	10.7	3.1
	Born in Sweden	14.1	8.7	5.5	7.7	2.5
	Immigrants	2.0	1.6	1.9	2.8	1.0
Latin America	Adoptees	11.5	10.5	7.0	8.0	2.7
	Born in Sweden	10.8	7.9	5.8	5.6	2.0
	Immigrants	5.6	5.0	3.8	2.5	1.8