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Migration and autism-spectrum disorder: population-based study

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Background
Migration has been implicated as a risk factor for autism, but evidence is limited and inconsistent.

Aims
To investigate the relationship between parental migration status and risk of autism-spectrum disorder, taking into consideration the importance of region of origin, timing of migration and possible discrepancies in associations between autism subtypes.

Method
Record-linkage study within the total child population of Stockholm County between 2001 and 2007. Individuals with high- and low-functioning autism were defined as having autism-spectrum disorder with and without comorbid intellectual disability, and ascertained via health and habilitation service registers.

Results
In total, 4952 individuals with autism-spectrum disorder were identified, comprising 2855 children with high-functioning autism and 2097 children with low-functioning autism. Children of migrant parents were at increased risk of low-functioning autism (odds ratio (OR) = 1.5, 95% CI 1.3–1.7); this risk was highest when parents migrated from regions with a low human development index, and peaked when migration occurred around pregnancy (OR = 2.3, 95% CI 1.7–3.0). A decreased risk of high-functioning autism was observed in children of migrant parents, regardless of area of origin or timing of migration. Parental age, income or obstetric complications did not fully explain any of these associations.

Conclusions
Environmental factors associated with migration may contribute to the development of autism presenting with comorbid intellectual disability, especially when acting *in utero*. High- and low-functioning autism may have partly different aetiologies, and should be studied separately.

Declaration of interest
None.

Autism-spectrum disorders are a heterogeneous group of pervasive developmental disorders characterised by qualitative impairments in social interaction, communication and restricted and stereotyped patterns of interests and behaviours. Recent studies estimate that about 1% of the child population[1–3] may have an autism-spectrum disorder, representing almost a 20-fold rise in prevalence compared with reports before the 1980s.[4] Although much of this sharp rise in prevalence may be explained by widening of diagnostic criteria and increased recognition, a true increase in incidence of autism cannot be ruled out[4,5] and constitutes an 'urgent public health concern'.[3] Although heritable, the aetiology of autism-spectrum disorder is not well understood. In the context of rising prevalence, the search for environmental risk factors is increasingly important.

Migration is one such factor that has attracted research interest, with vitamin D deficiency and ethnicity suggested as possible explanatory mechanisms.[6,7] However, previous studies on the topic of migration and risk of autism-spectrum disorder vary markedly in quality, sample sizes and definitions of autism. They have also produced inconsistent findings, including reports of an increased,[7–12] similar[8,9,13,14] and even decreased[13,15] risk of autism in children of migrants. There is some evidence that any positive association between parental migration and autism may be confined to autism with comorbid intellectual disability,[6] with at least one study reporting a lowered risk for autism with normal or high intelligence.[16]

Clarification of the role of migration in the development and detection of autism-spectrum disorder may provide aetiological insights and help reveal preventable health inequalities. A focus on the possibility of such health inequalities is particularly important in countries like Sweden where, since the 1970s, migration from outside of Europe has principally consisted of the provision of asylum to people fleeing armed conflict or other extreme adversities. Migration in this context may entail exceptionally stressful circumstances and be linked to social disadvantages both in the home country and during resettlement.[17] We therefore studied the association between migration and autism-spectrum disorder in a large, Swedish total-population-based sample, concentrating on four important aspects that remain unexplored: (a) characteristics of parental region of origin (both geographical region and an index of human development), (b) the importance of timing of migration in relation to the birth of the index child, (c) discrepancies in observed associations between low- and high-functioning autism, and (d) the potentially explanatory role of obstetric and socioeconomic factors.

Method

Study design and study population

We conducted a matched case–control study nested within the Stockholm Youth Cohort, a register-based cohort of all children aged 0–17 years living in Stockholm County between 2001 to 2007 ($n = 589\,114$). Individuals with autism-spectrum disorder (the case group) were ascertained using an exhaustive multisource case ascertainment method through data linkage with official registries covering all pathways of assessment or care of individuals with autism-spectrum disorder in Stockholm County (see Method in the online supplement). All Swedish citizens, including migrants with a residence permit, have unique national identification numbers that allowed record linkage with relevant registers for our study.

In the present study, we excluded children who were adopted, were resident in Stockholm County for less than 4 years, had one parent born abroad or had missing data (online Fig. DS1). Asylum seekers without a residence permit were by default excluded. Ethical approval was given by the research ethics committee at Karolinska Institutet, Stockholm, Sweden.

Case ascertainment

Sweden's child public services system is provided free of charge and used by the overwhelming majority of the population. All infants and pre-school children are offered structured health and developmental assessments to screen for developmental and medical problems in well-baby clinics. Such an assessment with evaluation of social, motor, language and cognitive development is carried out at age 4, in order to ensure timely referral of children with suspected autism to specialist services. Referrals can also be requested by parents, schools and other health or social care agencies. Diagnoses of autism-spectrum disorder in Stockholm County are made by specialist multiprofessional teams at paediatric or child and adolescent mental health services. Guidelines require the use of structured diagnostic assessments covering the child's social, medical and developmental history, observation of the child in naturalistic settings and a structured neuropsychiatric assessment including cognitive testing using standardised and internationally recognised tools (such as Wechsler Intelligence Scale for Children, Wechsler Preschool and Primary Scale of Intelligence, Snijders-Oomen Non-Verbal Intelligence Test (Revised), and Leiter).[18] The County Council offers follow-up care to children with diagnosed autism, which includes special education, occupational therapy, social care or other services through its habilitation services. The habilitation services for children with autism-spectrum disorder in Stockholm County are organised and provide care according to the presence of comorbid intellectual disability (defined as an IQ of 70 or less). We identified children with autism-spectrum disorder via registers covering the above healthcare pathways: that is, child and adolescent mental health, habilitation, paediatric out-patient or in-patient services (see Method in the online supplement).

We studied autism-spectrum disorder as a group and dichotomised into high-functioning autism (defined by the absence of a recorded comorbid intellectual disability, IQ < 70 by international and Swedish convention) and low-functioning autism (defined by the presence of a recorded comorbid intellectual disability). This strategy of subcategorisation was based on literature highlighting these as two key categories for future classification[19] and since the information on DSM-IV[20] subcategories was not readily available in all registers.

Previous studies have validated the diagnostic accuracy of mental health and autism diagnoses recorded in Swedish healthcare registers and have found them to have good validity.[21] Similar findings have also been found in neighbouring Denmark, which has a similar system of healthcare and official registries.[22] We furthermore conducted a validation study, including 200 randomly selected individuals (100 with high- and 100 with low-functioning autism) from the Stockholm Youth Cohort. Case notes were scrutinised by a child and adolescent psychiatrist (S.I.) and a neuropaediatric registrar. An autism-spectrum disorder diagnosis was confirmed in 170 (96%) of these individuals in whom complete records were retrieved ($n = 177$), and clear evidence in support of the high- and low-functioning autism dichotomy based on cognitive assessments was available in 88% and 76% of instances respectively (details available from the author on request). Finally, we cross-validated our case group against information from a national population-based study of twins (the Child and Adolescent Twin study in Sweden (CATSS)).[23] We identified 27 individuals with autism-spectrum disorder among the twins in the Stockholm Youth Cohort and 23 (85%, 95% CI 66–96%) of these had an autism-spectrum disorder confirmed in CATSS (according to parental reports and A-TAC, a screening interview targeting neurodevelopmental disorders).[24] Virtually none (1%) of the non-case twins in our study ($n = 2721$) received an autism-spectrum disorder diagnosis in CATSS.

Exposure and other variables

Prospectively recorded information on children and their parents were retrieved by linkage with registers that contain data based on mandatory reporting. This information included: country of birth; date of immigration to Sweden; family income at birth or (for children born abroad) at the earliest measured point in childhood; and pregnancy outcomes, including birth weight for gestational age, gestational age and Apgar score at 5 min (see Method in the online supplement).

Using mother's country of birth, migration status was first studied by geographical region of birth (United Nations definitions, available at http://unstats.un.org/unsd/methods/m49/m49regin.htm) and then by level of human development (using the UNDP Human Development Index, a composite indicator of development derived using indicators of life expectancy, education and income, available at http://hdr.undp.org/en/statistics/hdi/). These two groupings were employed to capture different dimensions of the parental countries of origin that may be of importance for the development or detection of offspring autism. These dimensions include, for example, ethnicity or environmental factors related to geographical region, as opposed to level of civil unrest or aspects of deprivation related to poor human development. The mother's country of origins was used to characterise parental background, since the paternal and maternal countries of birth were largely identical in children with both parents born abroad.

Data analysis

Ten randomly selected individuals in the control group (that were alive and free of autism) were matched to each individual in the case group by birth date and gender. We conducted conditional logistic regression analyses to estimate crude and adjusted odds ratios (ORs) as estimates of relative risks and their 95% confidence intervals for autism-spectrum disorder according to parental region of birth and the timing of the mother's immigration in relation to the child's birth. We also studied the mutual effect of maternal region of birth and maternal timing of migration in the same model among migrant children only. We tested for trends using the Cochrane-Armitage method.

All models were adjusted for maternal age (< 20, 20–29, 30–39, 40+ years) and paternal age (< 20, 20–29, 30–39, 40–49, 50+ years) at the child's birth, and for family disposable income (in quartiles) at birth or in childhood. To study whether any observed associations between maternal region of birth and low-functioning autism were mediated by birth outcomes, we repeated our analyses with additional adjustment for birth weight for gestational age (being small for gestational age or not), gestational age (< 32, 32–36, 37+ weeks) and Apgar score at 5 min after birth (< 7, ⩾ 7). Since these obstetric data were not available for children born outside Sweden, this analysis was restricted to the subsample of children born in Sweden. All analyses were conducted overall, and according to the gender of child, using SAS 9.2 for Windows.

Results

We identified 4952 individuals with autism-spectrum disorder comprising 2855 children with high-functioning and 2097 with low-functioning autism. Our study population for this paper was restricted to the 3918 children with autism-spectrum disorder meeting our inclusion criteria, comprising 2269 children with high-functioning and 1649 children with low-functioning autism (online Fig. DS1).

A total of 21% of our total study population had both parents born outside of Sweden. The mean duration of residence of the children to migrant parents in Stockholm County varied somewhat with region of origins, but was by definition always over 4 years, and in all age groups exceeded the age and period typically required for detection and diagnosis of autism-spectrum disorder (online Table DS1).

Table 1 depicts the odds ratios for autism-spectrum disorder in relation to maternal geographical region of birth among children with both parents born abroad as compared with children with both parents born in Sweden. As a combined group, autism-spectrum disorder did not appear to have any clear association with migration status. Yet, when this association was examined separately for high- and low-functioning autism, clearly divergent relationships were observed (Table 2). The odds of low-functioning autism was increased in children of migrant parents (crude OR = 1.5, 95% CI 1.3–1.7), and this relationship varied with region of maternal birth. Children of parents born in Sub-Saharan Africa had especially elevated odds, but also those with parental origins in Northern Africa, Latin America, the Caribbean and Southern Asia were more often diagnosed with low-functioning autism than children of Swedish-born parents. In strong contrast, children of migrant parents appeared to have a reduced odds of high-functioning autism (crude OR = 0.5, 95% CI 0.5–0.6) (Table 2). Notably, this inverse association was observed in almost all groups of migrant children, including those in which increased associations with low-functioning autism were not observed.

Table 1 Relative risk of autism-spectrum disorder in relation to maternal geographical region of birth

Migration status	Case group/control group, *n*	OR (95% CI)	Adjusted OR[a] (95% CI)
Both parents born in Sweden	3122/31 445	1.0	1.0
Both parents born abroad	796/8 600	0.9 (0.9–1.0)	0.9 (0.9–1.0)
Maternal country of birth, by geographical subregion[b]			
Northern Africa	31/317	1.0 (0.7–1.4)	1.0 (0.7–1.4)
Eastern Africa	122/933	1.3 (1.1–1.6)	1.1 (0.9–1.4)
Other African	30/168	1.8 (1.2–2.6)	1.5 (1.0–2.2)
Northern America	1/32	N/A	N/A
Latin America/Caribbean	94/759	1.3 (1.0–1.6)	1.1 (0.9–1.4)
Southern Asia	85/988	0.9 (0.7–1.1)	0.8 (0.6–1.0)
Western Asia	181/2848	0.6 (0.5–0.7)	0.6 (0.5–0.7)
Other Asian	26/269	1.0 (0.7–1.5)	0.9 (0.6–1.3)
Northern Europe	114/996	1.1 (0.9–1.4)	1.1 (0.9–1.3)
Eastern Europe	57/531	1.1 (0.8–1.4)	0.9 (0.7–1.3)
Southern Europe	41/612	0.7 (0.5–0.9)	0.6 (0.4–0.9)
Western Europe	14/136	1.1 (0.6–1.8)	1.0 (0.6–1.7)

N/A, not applicable.
a. Adjusted for maternal and paternal age at child's birth and family disposable income at child's birth or in early life, as applicable.
b. Among children with both parents born abroad. Countries contributing the largest number to the case group in each subregion being (when applicable): Northern Africa – Morocco; Eastern Africa – Somalia and Ethiopia; Latin America and the Caribbean – Chile; Southern Asia – Iran; Western Asia – Iraq and Turkey; Northern Europe – Finland; Eastern Europe – Poland; Southern Europe – Former Yugoslavia.

Table 2 Relative risk of high- and low-functioning autism in relation to maternal geographical region of birth

	High-functioning autism			Low-functioning autism		
Migration status	Case group/control group, *n*	OR (95% CI)	Adjusted OR[a] (95% CI)	Case group/control group, *n*	OR (95% CI)	Adjusted OR[a] (95% CI)
Both parents born in Sweden	1963/18 116	1.0	1.0	1159/13 357	1.0	1.0
Both parents born abroad	306/4925	0.5 (0.5–0.6)	0.5 (0.4–0.6)	490/3646	1.5 (1.3–1.7)	1.2 (1.0–1.4)
Maternal country of birth, by geographical subregion[b]						
Northern Africa	8/175	0.4 (0.2–0.8)	0.3 (0.2–0.7)	23/123	2.0 (1.3–3.1)	1.5 (0.9–2.4)
Eastern Africa	26/521	0.4 (0.3–0.6)	0.3 (0.2–0.5)	96/414	2.5 (2.0–3.1)	1.9 (1.5–2.5)
Other African	2/82	0.2 (0.1–0.6)	0.2 (0.0–0.7)	28/66	3.6 (2.4–5.3)	3.5 (2.5–5.6)
Northern America	1/20	N/A	N/A	0/11	N/A	N/A
Latin America/Caribbean	35/456	0.7 (0.5–0.9)	0.5 (0.4–0.8)	59/334	1.9 (1.4–2.4)	1.6 (1.2–2.2)
Southern Asia	26/556	0.5 (0.3–0.6)	0.3 (0.2–0.5)	59/415	1.6 (1.2–2.1)	1.3 (0.9–1.7)
Western Asia	64/1627	0.4 (0.3–0.5)	0.3 (0.2–0.4)	117/1165	1.1 (0.9–1.3)	0.9 (0.7–1.2)
Other Asian	13/160	0.6 (0.4–1.1)	0.6 (0.4–1.1)	13/117	1.1 (0.7–1.9)	1.1 (0.6–2.0)
Northern Europe	74/572	1.2 (0.9–1.5)	1.1 (0.8–1.4)	40/445	1.1 (0.8–1.6)	0.9 (0.6–1.2)
Eastern Europe	35/308	1.0 (0.7–1.3)	0.8 (0.6–1.2)	22/232	1.0 (0.7–1.5)	0.8 (0.5–1.3)
Southern Europe	14/355	0.3 (0.2–0.6)	0.3 (0.2–0.5)	27/251	1.3 (0.9–1.8)	1.1 (0.8–1.7)
Western Europe	8/85	0.9 (0.5–1.8)	0.8 (0.4–1.7)	6/66	1.1 (0.5–2.3)	1.0 (0.4–2.2)

N/A, not applicable.
a. Adjusted for maternal and paternal age at child's birth and family disposable income at child's birth or in early life, as applicable.
b. Among children with both parents born abroad. Countries contributing the largest numbers to the case group in each subregion being (when applicable): Northern Africa – Morocco; Eastern Africa – Somalia and Ethiopia; Latin America and the Caribbean – Chile; Southern Asia – Iran; Western Asia – Iraq and Turkey; Northern Europe – Finland; Eastern Europe – Poland; Southern Europe – Former Yugoslavia.

The odds of low-functioning autism increased with a decreasing human development index in the country of parental origin (P for trend <0.0001, Table 3). For high-functioning autism, the odds in migrant children were instead almost half that of children with parents born in Sweden, except when parents originated from countries with a very high human development index (Table 3).

There was a non-linear association between time since maternal immigration and odds of low-functioning autism (Fig. 1, online Table DS2). Children of mothers who migrated during pregnancy had the highest odds (crude OR = 2.3, 95% CI 1.7–3.0), whereas children born abroad and arriving in Sweden after the age of 4 had an odds ratio below unity. When both the maternal timing of migration and region of birth were considered simultaneously in a mutually adjusted model, both characteristics were independently associated with low-functioning autism (Table 4). No pattern in odds ratios with timing of migration was, however, evident for high-functioning autism.

The relationships reported above were not affected by adjustment for parental age (Tables 1–4), or for obstetric complications (in an analysis restricted to children born in Sweden, see online Table DS3). Adjustment for family disposable income, a characteristic highly correlated with migration from low-income countries, partially attenuated the positive associations between parental migration and low-functioning autism (Tables 1–4). The relationships between maternal geographical region of birth and high-functioning autism as well as low-functioning autism were similar in boys and girls (data not shown).

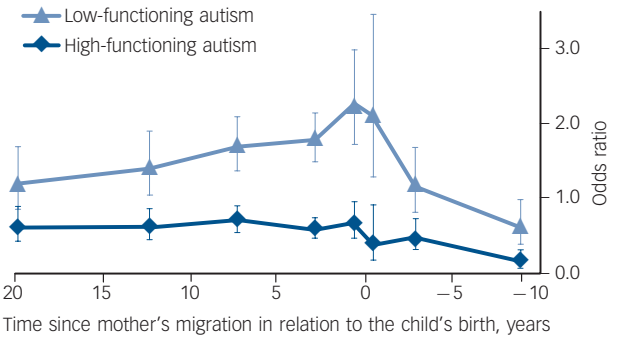

Fig. 1 Relative risk of high- and low-functioning autism in children with both parents born abroad as compared with those with both parents born in Sweden, by time since maternal immigration in relation to the child's birth.

Positive values indicate time since maternal migration to Sweden before the child's birth (in second-generation immigrant children), negative values indicate age of child when the mother migrated to Sweden (in first-generation immigrant children). Bars represent 95% confidence interval.

Discussion

In this large population-based study in Stockholm County, we found children of migrant parents to be at an increased risk of autism with intellectual disability. This risk appeared greatest in children of parents who migrated to Sweden from regions with a low human development index, and peaked when migration occurred around the time of pregnancy. In contrast, the risk of autism without intellectual disability was reduced regardless of timing of migration, and for most regions of parental origin.

Comparison with previous studies

One recent study in Malmö, Sweden, presented separate associations for risks of autism with and without intellectual disability and found results strikingly similar to ours, albeit in a much smaller sample of 250 participants.[16] All other population-based studies with individual-level data have only examined migration as one of several risk factors,[8–11,13] often simply defining migration status as 'mother born abroad'. These studies generated inconsistent findings, with parental migration either not related to autism-spectrum disorder[8,9,13] or associated with a higher[8–11] or lower[13] risk. This inconsistency may be partly explained by differences between studies in their definitions of autism and the proportion of children with associated intellectual disability (online Table DS4). Other studies on this topic lacked individual-level control data[7,12,14,15,25–27] and reported similar or increased risks of autism in children of migrant mothers, except one study from Israel[15] that found a reduced risk in Ethiopian migrants (online Table DS4).

Increased risk of low-functioning autism in children of migrant parents

One possible explanation for the observed association between mother's (employed as a proxy for both parents') country of birth and risk of low-functioning autism is that the underlying autism-spectrum disorder rates vary in different countries of origin. It is difficult to examine this possibility, because very little is known about indigenous prevalence of autism-spectrum disorder in low- and middle-income countries.[28] Difference in risk by ethnicity or skin colour is another possible explanation (for example, reflecting darker skin pigmentation increasing the risk of maternal vitamin D insufficiency during pregnancy[6]), although a British study found little evidence of an independent ethnic

Table 3 Relative risk of high- and low-functioning autism in relation to maternal country of birth categorised according to human development index (HDI)

	High-functioning autism			Low-functioning autism		
Migration status	Case group/control group, *n*	OR	Adjusted OR[a]	Case group/control group, *n*	OR	Adjusted OR[a]
Both parents born in Sweden	1963/18 116	1.0	1.0	1159/13 357	1.0	1.0
Both parents born abroad						
Maternal country of birth, by HDI						
Low	54/1179	0.4 (0.3–0.5)	0.4 (0.3–0.5)	167/898	2.1 (1.8–2.6)	1.9 (1.6–2.3)
Medium	62/1276	0.4 (0.4–0.6)	0.4 (0.3–0.5)	128/933	1.6 (1.3–1.9)	1.4 (1.1–1.7)
High	92/1579	0.5 (0.4–0.6)	0.5 (0.4–0.6)	137/1145	1.4 (1.1–1.7)	1.3 (1.0–1.6)
Very high	98/891	1.0 (0.8–1.2)	1.0 (0.8–1.2)	58/670	1.0 (0.8–1.3)	0.9 (0.7–1.2)

a. Adjusted for maternal and paternal age at child's birth and family disposable income at child's birth or in early life, as applicable.

Table 4 Relative risk of high- and low-functioning autism in relation to mother's region of birth and time since immigration, among children with both parents born abroad only

	High-functioning autism			Low-functioning autism		
Migration status	Case group/control group, *n*	Adjusted OR[a]	Adjusted OR[b]	Case group/control group, *n*	Adjusted OR[a]	Adjusted OR[b]
Mother's geographical subregion of birth[c]						
Northern Africa	8/175	0.3 (0.1–0.6)	0.3 (0.1–0.6)	23/123	1.9 (1.0–3.5)	1.7 (0.9–3.2)
Eastern Africa	26/518	0.3 (0.2–0.5)	0.3 (0.2–0.5)	96/412	2.0 (1.2–3.1)	1.9 (1.2–3.0)
Other African	2/81	0.1 (0.0–0.6)	0.1 (0.0–0.5)	28/66	3.7 (2.0–6.9)	3.6 (1.9–6.9)
Northern America	1/20	N/A	N/A	0/11	N/A	N/A
Latin America/Caribbean	34/451	0.6 (0.4–0.9)	0.6 (0.3–0.9)	59/330	2.0 (1.2–3.1)	2.0 (1.2–3.3)
Southern Asia	26/551	0.3 (0.2–0.5)	0.3 (0.2–0.5)	59/412	1.3 (0.8–2.2)	1.3 (0.8–2.1)
Western Asia	64/1617	0.3 (0.2–0.4)	0.3 (0.2–0.4)	116/1159	1.0 (0.7–1.5)	1.0 (0.6–1.5)
Other Asian	13/158	0.6 (0.3–1.1)	0.5 (0.3–1.1)	13/116	1.0 (0.5–2.1)	1.1 (0.5–2.2)
Northern Europe	67/527	1.0	1.0	37/410	1.0	1.0
Eastern Europe	35/305	0.7 (0.4–1.2)	0.7 (0.4–1.2)	22/230	0.9 (0.5–1.6)	0.8 (0.4–1.5)
Southern Europe	13/349	0.3 (0.1–0.5)	0.2 (0.1–0.5)	27/249	1.1 (0.6–1.9)	1.2 (0.7–2.1)
Western Europe	7/81	0.6 (0.2–1.4)	0.6 (0.2–1.5)	5/63	0.7 (0.3–2.0)	0.8 (0.3–2.1)
Time since mother's immigration to Sweden in relation to the child's birth						
⩾15 years before birth	30/457	1.0	1.0	38/356	1.0	1.0
10–14 years before birth	39/579	1.1 (0.6–1.9)	1.1 (0.6–1.8)	51/413	1.2 (0.7–1.9)	1.2 (0.7–1.9)
5–9 years before birth	74/970	1.5 (0.9–2.5)	1.5 (0.9–2.5)	108/733	1.2 (0.8–1.8)	1.1 (0.7–1.8)
1–4 years before birth	82/1284	1.5 (0.9–2.4)	1.4 (0.9–2.4)	149/966	1.4 (0.9–2.1)	1.4 (0.9–2.1)
Migrated in the year before birth	33/454	1.7 (0.9–3.0)	1.7 (0.9–3.0)	65/333	1.8 (1.1–2.9)	1.9 (1.1–3.1)
Migrated within 1 year after birth	6/138	1.0 (0.4–2.6)	1.0 (0.4–2.6)	19/102	1.2 (0.6–2.4)	1.3 (0.7–2.5)
1–4 years after birth	23/437	1.3 (0.7–2.4)	1.3 (0.7–2.5)	34/334	0.9 (0.5–1.6)	1 (0.6–1.7)
⩾5 years after birth	9/514	0.5 (0.2–1.2)	0.5 (0.2–1.2)	19/344	0.6 (0.3–1.2)	0.7 (0.4–1.3)

N/A, not applicable.
a. Mother's region of birth and time since immigration in relation to child birth mutually adjusted.
b. Additionally adjusted for maternal and paternal age and family disposable income at child's birth or in early life, as applicable.
c. Countries contributing the largest number of cases in each subregion being (when applicable): Northern Africa – Morocco; Eastern Africa – Somalia and Ethiopia; Latin America and the Caribbean – Chile; Southern Asia – Iran; Western Asia – Iraq and Turkey; Northern Europe – Finland; Eastern Europe – Poland; Southern Europe – Former Yugoslavia.

effect on the risk of autism in the absence of maternal migration.[7] Studies from the USA have reported both elevated[13] and reduced[3] risks of autism in non-Hispanic Black and Hispanic children compared with White children, and provided some evidence that Black ethnicity may be linked to autism with, but not without, comorbid intellectual disability.[29] Further research is required, but the above evidence suggests that factors beyond ethnicity may be important in the relationship between migration and low-functioning autism.

In recent decades, many non-European migrants to Sweden have been asylum seekers, often migrating under exceptionally stressful circumstances and often facing social disadvantages both in the home country and during resettlement. To try to capture this dimension of the migration experience we studied whether the association between migration and autism-spectrum disorder varied according to the human development index of the maternal country of birth, and found increasing risks of low-functioning autism with decreasing levels on the human development index.

One key and entirely novel finding of this study was that the risk of low-functioning autism varied with the timing of maternal migration. The risk of low-functioning autism appeared to be highest when migration occurred in the year before birth. This result is important, since it provides further evidence against ethnicity or case ascertainment differences being the main explanations of the parental migration–low-functioning autism association. Furthermore, it indicates that environmental, and hence possibly preventable, factors associated with a stressful parental migration process and acting *in utero* may be implicated in the aetiology of low-functioning autism.

Although we were unable to study many potential causal mechanisms directly, we investigated whether the increased risk of low-functioning autism in migrant children was explained by obstetric complications, parental age or family disposable income. Since we did not have access to obstetric data on children born abroad, these analyses were conducted in the sample of children born in Sweden. Apart from income, consideration of which may have comprised an over-adjustment since low income was almost always a feature of families originating from regions with a low human development index, these factors explained little of the observed associations. Instead, our results are compatible with the 'maternal stress theory'.[30]

Maternal stress during pregnancy is a proposed risk factor for neuropsychiatric disorders in offspring,[31,32] perhaps via impairments in foetal neurodevelopment due to dysregulation of the hypothalamic–pituitary–adrenal axis or epigenetic mechanisms. There is emerging evidence this may be applicable to autism,[30] but further confirmatory research is needed.

Several other hypotheses have also been conceptualised for the role of migration in impaired neurodevelopment and may underlie our findings, but have yet to be rigorously tested. These include maternal vitamin D deficiency,[7] poor maternal nutrition,[33] and early life infections.[34] These theories have also been posited for the effect of migration on psychotic disorders such as schizophrenia, but despite several lines of enquiry for over 40 years, the mechanisms behind these observed associations are unclear.[17,34]

Reduced risk of high-functioning autism in children of migrant parents

Overall, the increased risk of low-functioning autism among migrants was balanced out by a decreased risk of high-functioning autism, such that migration status was not associated with autism-spectrum disorder as a combined category. One intuitive

explanation of this finding is misclassification of high-functioning individuals as low-functioning, due to inter-ethnic bias in diagnostic procedures related to language barriers, cultural misunderstanding, prejudice or differential properties of diagnostic instruments. This explanation is not, however, supported by closer examination of the association between migration status and low-functioning/high-functioning autism status as (a) high-functioning autism was also less common in children to migrants from regions that had no elevated risk of low-functioning autism and (b) the risk of low-functioning autism peaked in children of mothers who migrated during pregnancy, whereas no similar trend with timing of migration was evident for high-functioning autism.

It is impossible to rule out discrete aetiological mechanisms leading to a true protective effect of migration on high-functioning autism, but we consider underdiagnosis of high-functioning autism in migrant children a more plausible explanation of our findings. Unlike intellectual disabilities associated with low-functioning autism, which may be easily recognised, the nuanced social deficits related to high-functioning autism in migrant populations may be missed or attributed to cultural differences. Also, a low perceived need for mental healthcare, stigma and lower awareness of service availability in migrant populations,[35,36] may lead to reduced help-seeking in the absence of overt developmental delays.[37] The cross-cultural validity of assessment tools for autism is another area of future research, but whatever the reason for our results, they mirrored those of a smaller study in a different region of Sweden[16] and provide enough evidence to suggest autism-spectrum disorder with and without intellectual disability should be studied separately.

Strengths and limitations

Our results must be interpreted in light of some limitations. In common with previous studies on this topic, our case ascertainment was based on service use; therefore it is impossible to tease out whether our findings are specific to development or detection of autism-spectrum disorder. We were also unable to study whether the increased risk of low-functioning autism in migrants is unique to autism or reflects risk factors for intellectual disability in general. We also did not have information on current autism-spectrum disorder diagnostic subtypes, although it should be noted that our strategy of treating autism-spectrum disorder as a single group stratified by comorbid intellectual disability is supported by epidemiological evidence and reflects and an approach proposed by the DSM-5 work group for future autism-spectrum disorder classification.[19,38]

The strengths of our study include its large sample and population-based design ensuring high external validity. The universal and free system of mandatory child development assessments in Stockholm County makes it likely that a large proportion of individuals with at least severe autism in the community would have been identified and diagnosed. Furthermore, our multisource case ascertainment, using registries covering all pathways of autism care, warrants that we captured the majority of diagnosed individuals. Furthermore, our validation studies indicated that the case ascertainment had high sensitivity as well as specificity. This is an advantage as few studies use multisource case ascertainment approaches, and often rely on hospital discharge or healthcare records. A majority of children with autism may not have special healthcare needs that require hospital admission (instead more often requiring educational or social interventions).

Implications

In conclusion, our findings suggest that environmental factors associated with migration and acting *in utero* may contribute substantially to the risk of autism with comorbid intellectual disability. They also indicate that high-functioning autism may be underdiagnosed in children of migrant parents. Risk factors for low- and high-functioning autism may be markedly different, implying that these diagnostic subgroups should be studied separately. Migration during pregnancy could entail fetal risks, and policy measures to ensure comprehensive antenatal care for immigrant families from low- and middle-income countries should be a priority.

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EXTRA CONTENT ONLINE

Online supplement

to British Journal of Psychiatry doi: 10.1192/bjp.bp.111.095125

Contents ***1***

A. Method

Swedish registers used for data linkage

The Stockholm County Council Habilitation Services register

Source: Stockholm County Council

Website: http://83.241.200.202/gn/opencms/web/HAB/andra_sprak/english/

Includes all patients treated by Habilitation centers in Stockholm County since 1998, including the Autism Center for Young Children, the Asperger Center, and the Autism Center. The habilitation services are offered free of charge to all children with a diagnosis of autism spectrum disorder in Stockholm County. This register categorizes non-preschool recipients as receiving a service for autism spectrum disorders with or without comorbid intellectual disability.

Pastill - Clinical Database for Child and Adolescent Psychiatry in Stockholm

Source: Stockholm County Council

Website: http://www.bup.se/

Child and adolescent psychiatry, Stockholm County Council, is the main provider of autism diagnostic assessments in Stockholm County, and their register comprises all public mental health service utilization since 2001. It holds diagnostic information at the DSM-IV group level for the majority of treatment episodes.

The Stockholm County Council VAL Database

Source: Stockholm County Council

The VAL database is a County Council administrative register covering the date, venue and diagnosis of all publicly financed health services used in the County since 1990; diagnostic information is recorded according to ICD 9/10 but with incomplete data. Used for supplementing case ascertainment.

The National Patient Register

Source: National Board of Health and Welfare

Website:http://www.socialstyrelsen.se/register/halsodataregister/patientregistret/inenglish

This register includes discharge diagnoses according to ICD 7-10 for all inpatient treatment episodes for psychiatric disorders in Sweden since 1973.

The Multi-Generation Register:

Source: Statistics Sweden

Website: http://www.scb.se/default____2154.aspx

This register includes all individuals born in Sweden since 1932, registered as living in Sweden after 1960, and their parents. First-degree biological relatives and their date of birth were identified through this source.

Integrated Database for Labour Market Research

Source: Statistics Sweden

Website: http://www.scb.se/Pages/List____257743.aspx

Country of birth, family disposable income, education and other demographic variables for parents at birth of child or early in life as applicable were identified from this register.

Medical Birth Register

Source: National Board of Health and Welfare

Website:

http://www.socialstyrelsen.se/register/halsodataregister/medicinskafodelseregistret/inenglish

This register holds prospectively collected data from antenatal and obstetric care on 99% of all Swedish births since 1973. Pregnancy outcomes, including growth for gestational age and Apgar score at 5 minutes, were retrieved using this source.

B. Supplementary tables and figure

TABLE DS1. Average duration of residence in Stockholm County by maternal geographical region of birth among control children

Migration status	**Duration of residence**		
	N	Mean (years)	SD
Both parents Sweden born	31580	13.8	5.0
Both parents born abroad, *by maternal geographical sub-region of mothers birth:*			
Northern Africa	342	13.1	4.5
Eastern Africa	1078	10.9	4.2
Other African	258	11.1	4.7
Northern America	41	9.8	4.4
Latin America/Caribbean	915	12.9	4.8
Southern Asia	1196	11.6	4.7
Western Asia	3315	12.2	4.8
Other Asian	386	11.1	4.7
Northern Europe	1110	14.8	5.3
Eastern Europe	648	13.1	5.2
Southern Europe	698	12.6	4.9
Western Europe	164	10.6	4.6

TABLE DS2. Relative risk of high-functioning autism and low-functioning autism in relation to maternal time since immigration as compared to children of parents born in Sweden

Migration status	High Functioning Autism			Low Functioning Autism		
	Cases/Controls	OR(95% CI)	OR[a](95% CI)	Cases/Controls	OR(95% CI)	OR[a] (95% CI)
Both parents Sweden born	1963/18116	1.0 (ref)	1.0 (ref)	1159/13357	1.0 (ref)	1.0 (ref)
Both parents born abroad, by time since maternal immigration:						
15 years before birth	30/458	0.6 (0.4-0.9)	0.6 (0.4-0.8)	38/357	1.2 (0.9-1.7)	1.1 (0.7-1.5)
10 – 14 before birth	39/581	0.6 (0.5-0.9)	0.6 (0.4-0.8)	51/413	1.4 (1.0-1.9)	1.2 (0.9-1.7)
5 – 9 years before birth	74/970	0.7 (0.6-0.9)	0.6 (0.5-0.8)	108/733	1.7 (1.4-2.1)	1.5 (1.2-1.8)
1 – 4 years before birth	82/1285	0.6 (0.5-0.7)	0.5 (0.4-0.7)	149/968	1.8 (1.5-2.1)	1.6 (1.3-1.9)
Migrated in the year before birth	33/454	0.7 (0.5-1.0)	0.6 (0.4-0.9)	65/333	2.3 (1.7-3.0)	2.1 (1.5-2.8)
Migrated within one year after birth	6/139	0.4 (0.2-0.9)	0.4 (0.2-0.8)	19/102	2.1 (1.3-3.5)	1.9 (1.2-3.2)
1-4 years after birth	23/438	0.5 (0.3-0.7)	0.4 (0.3-0.7)	34/336	1.2 (0.8-1.7)	1.1 (0.8-1.6)
≥ 5 years after birth	9/515	0.2 (0.1-0.3)	0.2 (0.1-0.3)	19/345	0.6 (0.4-1.0)	0.6 (0.4-1.0)

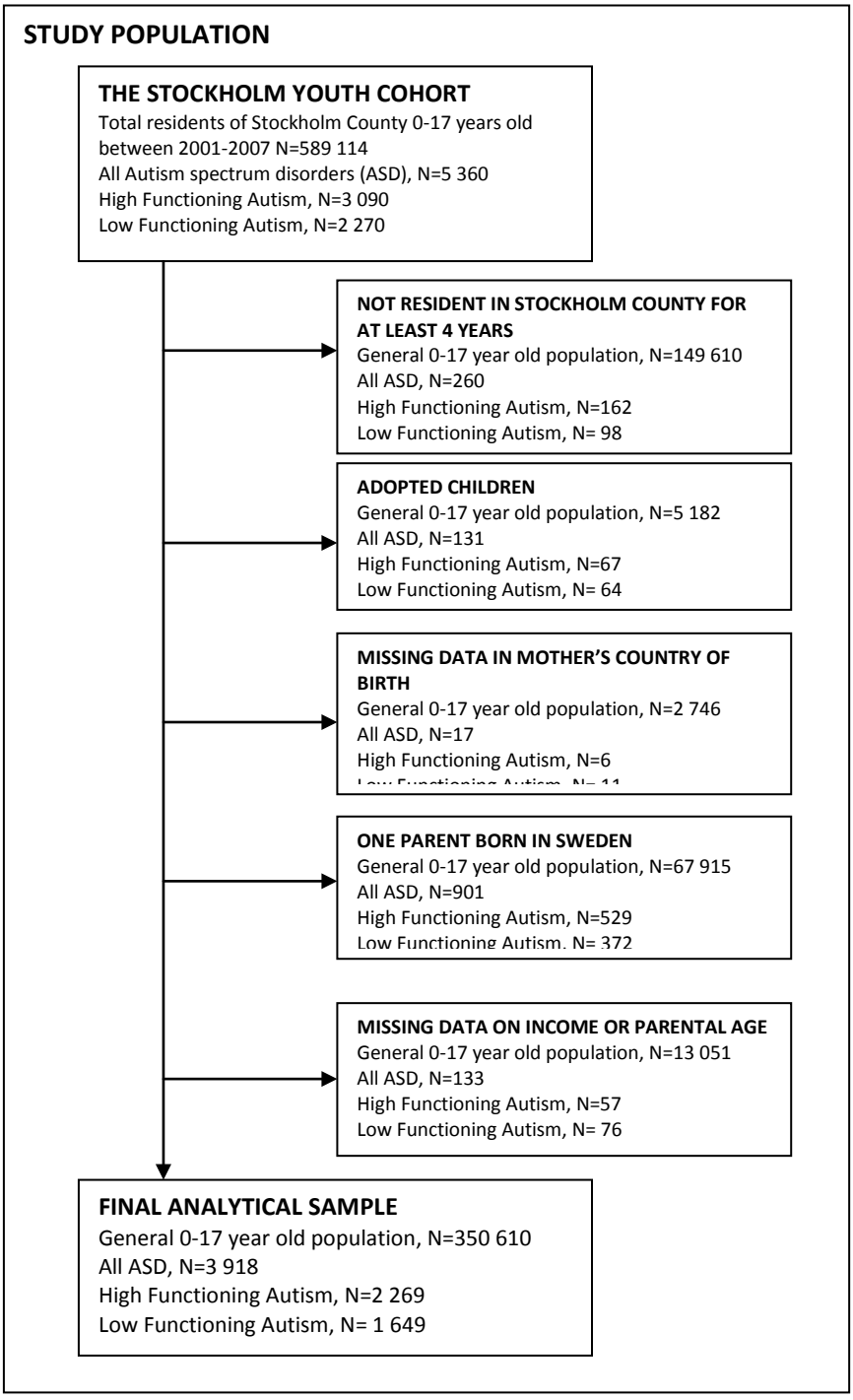
OR= odds ratio. CI = confidence interval. [a]Adjusted for maternal and paternal age and earliest estimate of family income.

TABLE DS3. Relative risk of low-functioning autism among children born in Sweden in relation to maternal geographical region of birth, with and without adjustment for obstetric complications, parental age and family disposable income

Migration status	Low Functioning Autism			
	Cases/Controls	OR (95% CI)	OR[a](95% CI)	OR[b](95% CI)
Both parents born in Sweden	1103/12658	1.0 (ref)	1.0 (ref)	1.0 (ref)
Both parents born abroad				
All countries	399/2776	1.6 (1.5-1.9)	1.6 (1.4-1.8)	1.4 (1.2-1.6)
Maternal country of birth, by geographical sub-region[c]:				
Northern Africa	23/121	2.1 (1.3-3.3)	2.1 (1.3-3.3)	1.7 (1.1-2.7)
Eastern Africa	84/321	3.0 (2.4-3.9)	3.0 (2.3-3.8)	2.5 (1.9-3.3)
Other African	24/52	5.1 (3.1-8.4)	5.0 (3.1-8.3)	4.3 (2.6-7.1)
Northern America	0/8	N/A	N/A	N/A
Latin America and the Caribbean	47/272	2.1 (1.5-2.9)	2.1 (1.5-2.8)	1.8 (1.3-2.6)
Southern Asia	44/298	1.7 (1.2-2.3)	1.6 (1.2-2.3)	1.4 (1.0-2.0)
Western Asia	92/838	1.3 (1.0-1.6)	1.3 (1.0-1.6)	1.1 (0.9-1.4)
Other Asian	11/89	1.4 (0.8-2.7)	1.4 (0.8-2.7)	1.2 (0.7-2.4)
Northern Europe	34/377	1.0 (0.7-1.5)	1.0 (0.7-1.5)	0.9 (0.7-1.3)
Eastern Europe	19/179	1.2 (0.7-1.9)	1.2 (0.7-1.9)	1.0 (0.6-1.7)
Southern Europe	17/173	1.2 (0.7-1.9)	1.2 (0.7-1.9)	1.1 (0.6-1.8)
Western Europe	10/99	1.0 (0.4-2.9)	1.1 (0.4-3.1)	1.0 (0.4-2.8)

OR = odds ratio. CI = confidence interval. N/A = not applicable. [a]Adjusted for birth weight for gestational age, gestational age and Apgar score at 5 minutes. [b]Additionally adjusted for maternal and paternal age at child's birth and family disposable income at child's birth or in early life, as applicable. [c]Among children with both parents born abroad. Countries contributing the largest number of cases in each subregion being (when applicable): Northern Africa – Morocco; Eastern Africa – Somalia and Ethiopia; Latin America and the Caribbean – Chile; Southern Asia – Iran; Western Asia – Iraq and Turkey; Northern Europe – Finland; Eastern Europe – Poland; Southern Europe – Former Yugoslavia.

Figure DS1. Derivation of analytical sample.



C. A systematic review of previous evidence

We aimed to find peer reviewed epidemiological studies studying the association of autism or any of its subtypes with migration of parents.

Method:

Anticipating few studies that specifically study this topic but several with a migration variable in analysis, we derived a broad search strategy in our systematic review of the literature.

We searched Embase (to September 2010), Medline (to September 2010), and Psychinfo (to May 2010) with search terms covering Autism and related terms (see search strategy below) with immigration or migration; or ethnicity/race; or perinatal/prenatal/pregnancy/environmental risk factors.

We excluded non human studies, duplicates, non peer reviewed articles and articles without abstracts and were left with 2 309 unique papers (1 622 in Embase, 298 in Medline, 389 in Psychinfo). The titles or/and abstracts of these were screened and 43 studies required reading to determine relevance for review.

Of these, 11 papers [15-25] discussed relevant issues but were not reports of new data, 16 papers[26-41] did not have a migration variable, one was a case-report of 3 cases[42] and three were reviews.[43-45] References cited in the articles were also cross-checked and 2 further studies were identified.[11,12] Fourteen studies were reviewed in three groups in decreasing order of likelihood of biased estimates- using a population based design with individual level data and attempts at adjustment for confounding, studies that did not have individual level control data but reported population level estimates using ecological/census data, and studies in other groups.

Exact search strategy

Database: EMBASE <1980 to 2010 Week 37>, Medline 1950 to present, PsycINFO <1806 to September Week 3 2010>

Search Strategy:

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1 autism/ or asperger syndrome/ or infantile autism/ or "pervasive developmental disorder not otherwise specified"/ (49038)

2 INFANTILE AUTISM/ or AUTISM/ or autism.mp. (55494)

3 1 or 2 (56423)

4 migration/ or immigration/ (59908)

5 ethnicity.mp. or "ethnic or racial aspects"/ or cultural factor/ or ethnology/ or ethnic difference/ or ethnic group/ or ETHNICITY/ or race/ (310650)

6 PRENATAL DEVELOPMENT/ or PRENATAL STRESS/ or PRENATAL PERIOD/ or prenatal.mp. or PRENATAL EXPOSURE/ (277052)

7 pregnancy.mp. or PREGNANCY/ (1244288)

8 perinatal.mp. or PERINATAL DEVELOPMENT/ or PERINATAL PERIOD/ or PERINATAL STRESS/ (111463)

9 environmental.mp. or "ENVIRONMENTAL ASPECTS AND RELATED PHENOMENA"/ or ENVIRONMENTAL FACTOR/ or ENVIRONMENTAL EXPOSURE/ (692488)

10 RISK FACTOR/ (875600)

11 4 or 5 or 6 or 7 or 8 or 9 or 10 (3149260)

12 3 and 11 (5064)

13 remove duplicates from 12 (3432)

14 limit 13 to human (3124)

15 limit 14 to abstracts (2623)

16 limit 15 to peer reviewed journal [Limit not valid in EMBASE,Ovid MEDLINE(R); records were retained] (2309)

Results:

Only 5 of the 14 studies reviewed (detailed in Table A1) (1 Australian, 2 Danish, 1 USA, and 1 Swedish) were based in the general population with individual level data on cases and comparison groups. Autism was ascertained in all of these from health service use data but no subtypes of autism were studied. Migration history was one of several risk factors studied and generally limited in detail to a measure of 'mother born abroad'. Maternal immigration was associated with either no or a higher risk of autism except the USA study which found children of Mexican mothers to have reduced risk of autism. Seven studies on this topic estimated risk of autism in children of migrant parents as compared to the general population, but lacked individual level control data and instead reporting prevalence or risk estimates from census or ecological data. The results revealed either similar or increased risks of autism in children of migrant mothers except one study from Israel which found a reduced risk in Ethiopian migrants. Keen et al's study in this group is the most detailed study on this topic so far and benefited from a relatively large sample size. All reports before year 2000 had small sample sizes often precluding meaningful statistical analysis.

Our findings in context of previous literature: Our study has several strengths as compared to others. First, all previous studies have used clinical registries or samples for case ascertainment and may under ascertain higher functioning autism cases that are unlikely to present to child psychiatry services or be admitted to hospitals but rather require social, educational or other support as provided by Habilitation services. Secondly, no previous studies have investigated the differential risks of high and low functioning autism simultaneously. No previous studies have investigated the role of time since parental migration in this relationship. Most studies used a variable of mother born abroad in a larger of several other risk factors under study and were not adequately powered to conduct any in depth analysis.

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TABLE DS4. Previous studies on migration and autism

Source (chronological)	Location	Design	Sample	Migration variable	Autism definition	Results
POPULATION-BASED STUDIES INCLUDING INDIVIDUAL CONTROLS						
Williams 2008[1]	NSW, Australia	Surveillance through physician reports. Linkage with midwives data.	182 children with Autism were linked to population data	Mother born in or outside Australia (those born outside Australia were also categorized into born in South East or North-East Asia or not)	DSM-IV autistic disorder	Mother born outside Australia OR=1.5 (95% 1.1-2.1). Adjusted OR=1.4 (95% 1.0-2.0) adjusted for being male, premature, mother≥35 years of age.
Maimberg 2006[2]	Denmark	Population based matched case control study using data likage of Danish Civil Registration, Danish Psychiatric Central Register, Danish Medical Birth Register, and medical birth records.	473 children discharged from a hospital with a diagnosis of Infantile autism (1990-1999). 10 controls matched for date of birth, sex and county of birth. Foreign born children excluded.	Mother with foreign citizenship Father with foreign citizenship	ICD 8-10 diagnosis of Infantile Autism	Mother with foreign citizenship OR=1.7 (95% 1.3-2.5), adjusted OR=1.7 (95% CI 1.3-2.4) adjusted for mothers and fathers age, birth weight, gestational age, Apgar scores <8 at 5 minutes, birth defects and irregular foetal position. Father with foreign citizenship OR=1.1 (95% 0.7-1.6), Adjusted OR= 1.1 (95% CI 0.7-1.7)
Lauritsen 2005[3]	Denmark	Register based cohort study. 943664 children younger than 10 years of age followed up between 1994-2001.	818 children developed autism.	Mothers country of birth in Denmark, In Europe but outside Denmark and outside Europe Child born in Denmark only.	ICD-10 autism codes (F84.0-F84.1) or with broader autistic codes (F84.5, F84.8, F84.9)	Both parents born abroad=RR=1.2 (95% CI 0.9-1.5) Father born abroad RR=1.2 (95% CI 0.8-1.6) Mother born abroad RR=1.8 (95% CI 1.2-2.3) Maternal country of birth as compared to Denmark- Scandinavia or Europe RR=1.0 (95% CI 0.8-1.4), Outside Europe RR=1.4 (95% CI 1.1-1.8), adjusted for maternal and paternal age, maternal, paternal and sibling psychiatric disorder, fathers identity known, urbanization and if mother and father were born in the same country
Croen 2002[4]	California, USA	Population based, all live born children born in California 1988-1994 N=3,497,870	4356 California born children enrolled with Department of Developmental Services as having full syndrome autism.	Mother born in California, other US state, Mexico or 'other'	All children enrolled with 'full syndrome autism', 36% had diagnosed intellectual disability	Mother born in Mexico OR=0.4 (95% CI 0.4-0.5), Adjusted OR=0.6 (95% CI 0.5-0.7), adjusted for child sex, birth weight, plurality, birth order, maternal age, ethnicity and education as compared to mother born in California. Born in 'other country' OR=1.2(95% CI 1.1-1.3), adjusted 1.1 (95% CI 1.0-1.2) Black ethnicity OR=1.2 (95% CI 1.1-1.3), adjusted OR=1.6 (95% CI 1.5-1.8)
Hultman 2002[5]	Sweden	Population based nested case control study	408 children ≤9 years old discharged from Swedish inpatient hospitals with a diagnosis of infantile autism 1987-1994. 2040 controls matched on sex, year and hospital of birth	Mother born in Nordic country, Europe and North America or outside Europe or North America	ICD-9 Autistic Disorder	As compared to being born in a Nordic Country, for Europe or North America OR=1.6 (95% CI 0.9-2.9), adjusted OR=1.1 (95% CI 0.5-2.5), for outside Europe or North America OR=2.9 (95% CI 1.9-4.5), adjusted OR=3.0 (95% CI 1.7-5.2), adjusted for maternal age, parity, smoking during pregnancy, hypertension, diabetes, bleeding in pregnancy, mode of delivery, season of birth, gestational age, birth weight, Apgar score at 5 minutes, congenital malformations.

TABLE DS4 (continued). Previous studies on migration and autism

Source (chronological)	Location	Design	Sample	Migration variable	Autism definition	Results
STUDIES THAT DID NOT HAVE INDIVIDUAL LEVEL INFORMATION ON CONTROLS BUT GENERATED POPULATION BASED ESTIMATES						
Keen 2010[6]	Two boroughs of South London, UK	Retrospective case note review	428 children with autism. Relative risks calculated based on ecological population census data.	Mother born abroad classified into Africe, Caribbean, Asian and elsewhere categories.	Both high and low functioning autism	Mothers born outside Europe had higher risk Caribbean mothers had highest risk in both regions relative to mothers born in UK RR=10.0 (95% CI 5.5-18.1), RR=8.9 (95% CI 5.0-15.5) Effect of Black ethnicity largely explained by immigration status of mother
Barnevic-Olsson 2008[7]	Stockholm County, Sweden	Clinical records from two habilitation centres. Compared with general population.	501 children with autism or PDD-Nos known to one of two habilitation centres and living in Stockholm 2005	Children born in Sweden or abroad, with both parents born abroad and at least one in Somalia	Autism or PDD-NOS, all had intellectual disabilities	Prevalence in Somalian children 0.7% (95% CI 0.37-1.03%) Prevalence in children of non-somali origin= 0.19% (0.18-0.21%)
Kamer 2004[8]	Israel	Population based study of all Jewish population living in Israel born between 1983-1997.	1004 children with PDD born between 1983-1997, population prevalence calculated based on total population 1,113,900	Native children of ethiopian extraction (based on surnames) Immigrants of non ethopian extraction Children born in Ethiopia	Pervasive developmental disorder	No children born in Ethopia had PDD Non-Ethiopian children born in Israel had elevated rate of PDD as compared to Ethopian children born in Israel OR=1.7 (95% CI 1.3-2.2)
Gillberg 1996[9]	Goteburg and Bohuslan, Sweden	Several sources of data collection.	55 children with autistic disorder, compared with total population demographic data from record linkage	At least one parent born abroad	Autistic disorder (DSMIII TR)	15 of 55 (27%) children had one parent born abroad, 26.2% of general population had at least one parent born abroad. 11 of 15 (20%) children with autism had one immigrant parent from outside Northern Europe as compared to records suggesting 3.2% in general (Goteburg) population.
Gillberg 1987[10]	Goteburg and Bohuslan, Sweden	Population based	20 children with infantile autism	Immigrant parents	Autistic disorder (DSMIII)	30% (6/20) autistic children in Goteburg had one parent born abroad as compared to 25.7% in general population (NS) 0/15 children from the rural county had immigrant parents.
Wing 1980[11]	Camberwell	Population based	17 children with autism in Camberwell, among 914 children under 15 years of age living in Camberwell	'New commonwealth fathers' (mainly from Carribeans), Eurpoean father	Autism (nuclear and non-nuclear)	Prevalence of autism in European fathers 4.4/10,000 Prevalence in children of new commonwealth fathers 6.3/10,000
Harper 1979[12]	New South Wales, Australia	not available at time of review	not available at time of review	not available at time of review	not available at time of review	21.9% of all children diagnosed with autism belonged to parents not born in Australia. Greek and German nationalities over represented
STUDIES NOT BASED IN THE GENERAL POPULATION						
Stein 2006[13]	Tel Aviv, Israel	Case-control Healthy controls with mothers who were employees of a health centre	226 mothers of children with autism known to a voluntary organisation 152 control	Mother's country of birth Israel/Asia, Europe/Africa, USA/	Autistic disorder DSM-IV (other PDD excluded)	Mother's country of birth (Israel/Asia, Europe/Africa, USA) in cases 115/55/36, in controls 80/41/31. Chi sq=0.2, p non significant.
Goodman 1995[14]	London, UK	Clinic based study	9 children with Infantile autism, 9 children with other pervasive developmental disorders. 292 children of afro-carribean parents, compared with 1311 children with both parents in Britain	Both parents born in West Indies or Guinea.	ICD 8-10 diagnosis of Infantile Autism	Prevalence of autism and related conditions in afro-carribean group 3.5% Prevalence in comparison group 0.6%