Acta Psychiatrica Scandinavica

Received: 16 April 2021 | Accepted: 12 July 2021

DOI: 10.1111/acps.13350

Acta Psychiatrica Scandinavica WILEY

ORIGINAL ARTICLE

Migration and risk of intellectual disability with and without autism: A population-based cohort study

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Funding information
This work was supported by the Swedish Research Council (grant number 2015-02529).

Abstract

Objective: To investigate whether parental migration, parental region of origin, timing of child's birth in relation to maternal migration and parental reason for migration are associated with intellectual disability (ID) with and without autism.

Methods: We used a register-based cohort of all individuals aged 0–17 years in Stockholm County during 2001–2011. General estimating equation logistic model and additionally sibling comparison were used to calculate odds ratios (ORs) and 95% confidence intervals (CIs). The models were adjusted for child's sex and birth year and parental age at child's birth, and additionally for migrant-specific variables in the analyses including only children with migrant parent(s).

Results: Within the eligible sample of 670,098 individuals, 3781 (0.6%) had ID with autism, and 5076 (0.8%) had ID without autism. Compared with children with Swedish-born parents, children with both parents born abroad had an increased risk of ID with autism (OR = 1.6, CI 1.5–1.8) and ID without autism (OR = 1.9, CI 1.7–2.0). Among these children with both parents born abroad, it was protective of ID with autism when the child's birth occurred before and later than four years after maternal migration, which was replicated in the sibling comparison. The associations with both conditions were more pronounced with parental origin in regions comprising low- and middle-income countries and with reasons other than work or study.

Conclusions: Parental migration is associated with ID regardless of co-occurrence of autism. Our results indicate an association between environmental factors during pregnancy related to migration and offspring ID with autism, although further confirmative studies are needed.

KEYWORDS

autism spectrum disorder, epidemiology, human migration, intellectual disability

1 | INTRODUCTION

Parental migration has been recognized as a potential factor associated with autism spectrum disorders (henceforth autism) since the 1980s.[1,2] Recent studies considering co-occurrence of intellectual disability (ID) have shown that children with migrant parents have an increased risk of being diagnosed with autism with ID, but a decreased risk of autism without ID.[3–5] This observation may hypothetically suggest that there is a relationship between parental migration and ID or cognitive impairment rather than the autism. However, the link between parental migration and ID is not well examined.[6–8] It is important to study whether parental migration is specifically associated with autism with ID (ie, ID with autism), ID without autism or both conditions, because it may lead to improved understanding about whether the underlying aetiological pathways for these conditions are distinct.

Furthermore, underlying factors explaining the association of ID with autism in children of migrant parents are unknown. The aetiology of ID and autism is complex and only partly understood, although studies have shown an importance of inherited genetic influences, environmental factors and gene-environment interactions in their aetiology.[9–11] As causal explanations of the association between migration and ID with autism, environmental factors acting in pregnancy, genetic factors and selective migration of people with genetic vulnerability to autism have been hypothesized.[3,4,12–15] To explore these hypotheses, indirect evidence from epidemiological data is important but currently lacking. Firstly, the association between different parental migration statuses and ID with autism is not well examined. Children having both migrant parents may have been exposed to different factors than those with one migrant parent. In addition, examining children's exposure to maternal and paternal migration separately may give hints on whether environmental factors acting in utero or early in life are associated with the conditions. Secondly, it is not known how parental region of origin is associated with ID with autism, although such origins may be linked to various exposures. Findings from previous studies, although inconsistent, have suggested a more pronounced risk with parental origins from low-income countries.[3,4,7,12,14] Thirdly, it has not been examined how timing of child's birth in relation to maternal migration is associated with ID with autism. Studying the association might lead to finding a clue on whether exposure to any specific maternal migration phase (eg pre-migration, travel and post-migration phase) during different putative vulnerable periods in life, for example in utero, is associated with the conditions. Fourthly, it is not known whether parental reasons for migration are associated with ID with autism. The reasons for migration, such as a migration for work or study, versus being a refugee, or to join a family member entail different circumstances, while differential patterns in risk may give valuable information about why parental migration is associated with neurodevelopmental conditions. An improved understanding of the association between migration and ID with and without autism may provide valuable clues to modifiable causes of these conditions.

The Stockholm Youth Cohort (SYC) is a register-based total population cohort, established to explore risk factors for autism. Using this cohort, we have previously reported that children of migrant parents from low-income countries had an increased risk of ID with autism, and this risk increase was highest when maternal migration occurred around pregnancy.[4] However, we did not examine the risk of ID without

Significant Outcomes

- We found that parental migration is associated with an intellectual disability regardless of co-occurrence of autism, although underlying factors may differ between the conditions.
- Our results suggested that these associations are partly explained by environmental factors during pregnancy related to circumstances around migration for intellectual disability with autism, and by factors linked to parental origin in low- and middle-income countries for intellectual disability in general, although further studies on these and other factors such as assessment bias and selection are needed.
- To reduce the burden of these conditions, recipient countries should consider policies that lead to increased health literacy and access to antenatal care in migrants.

Limitations

- There was likely non-differential misclassification in the date of maternal migration, especially among refugees who may have arrived as asylum seekers before the date a resident permit is granted, which may have diluted associations with timing of child's birth in relation to maternal migration.
- It is possible that the validity of the tools used to diagnose intellectual disability and autism may have different properties in different migrant groups leading to outcome misclassification.
- The possibility of selection bias because of the exclusion of population cannot be excluded, especially in the analysis for the parental reason for migration, where 26% of the population was excluded because of a lack of data on the exposure variable.

autism in relation to migration, nor whether maternal or paternal migration status mattered most or how parental reason for migration was linked to ID. Here, we, therefore, report on the details of the association between parental migration and risk of ID with and without autism from an updated version of SYC including additional birth cohorts and extended follow-up.

1.1 | Aims of the study

Our aims were to investigate whether (i) parental migration, (ii) parental region of origin, (iii) timing of child's birth in relation to maternal migration and (iv) parental reason for migration are associated with ID with and without autism.

2 | MATERIALS AND METHODS

To examine the association between parental migration and autism and ID, we used a large total population sample in Stockholm County with prospectively recorded detailed information, using logistic regression models and additionally a sibling-comparison design to account for confounding by shared genetic or environmental factors.

2.1 | Study population

The SYC included all individuals aged 0 through 17 years resident in Stockholm County at any time during 2001 through 2011. The individuals were followed until the end of follow-up (31 December 2016), emigration or death, whichever occurred first. We excluded adopted children, who lacked information for biological parents, and children who resided in Sweden <4 years to ensure an enough follow-up time for children to get a diagnosis of the outcome. Those not officially granted residence in Sweden (ie asylum seekers and undocumented migrants) were not part of the cohort, as it was linked with personal identification number only held by those with a resident permit in Sweden. Exposure, outcome and covariate data were extracted through record linkage with a range of national and regional health and administrative registers, described elsewhere.[16]

2.2 | Outcome and case ascertainment

We examined two outcomes separately, ID with autism and ID without autism. Autism case status was ascertained using ICD-9 (299), ICD-10 (all F84s) and DSM-IV (299) codes in national and regional registers covering all the potential pathways of the autism diagnosis and care in Stockholm County; the National Patient Register, the VAL database, and the Clinical Database for Child and Adolescent Psychiatry in Stockholm, and supplemented using the Habilitation Register.[16] Ascertainment of ID status was based on ICD-9 (317–319), ICD-10 (F70–F79) and DSM-IV (317–319) codes in the registers and supplemented with information in the Habilitation Register, which classifies services recipients as having ID or not.[16] Children who ever diagnosed with ID before the end of follow-up were classified as ID cases, and these children were divided into ID with and without autism depending on the co-occurrence of autism, which was assessed for children who ever got a diagnosis of autism. The overall validity of psychiatric diagnoses in Sweden is considered being high.[17,18] A previous validation of autism case ascertainment through review of medical records found that 96.0% and 75.6% cases were consistent with an autism diagnosis and an ID with autism diagnosis, respectively.[16] There is, however, no specific validation study of ID diagnoses in the Swedish healthcare registers.

2.3 | Exposure variables

Our first exposure was parental migration status. Migrants were defined as people who were born abroad and had moved to and settled in Sweden. All individuals were categorized in four groups based on parental migration status using the Multi-generational Register and the Register of Total Population: children with both parents born in Sweden, both parents born abroad, mother born abroad and father born in Sweden and father born abroad and mother born in Sweden.

Our second exposure was parental region of origin. Information of region of origin was obtained from the Register of Total Population and classified into eight regions: Sweden, Other European countries, Middle East and North Africa, Sub-Saharan Africa, Central and South Asia, Latin America and the Caribbean, East Asia and Pacific and North America. For children with both parents born abroad, maternal region of origin was used as parental region of origin if not missing, because maternal and paternal regions of origin were largely identical.

Our third exposure was timing of child's birth in relation to maternal migration, categorized as: ≥5 years before, 0–4 years before, in the year after, 1–4 years after, 5–9 years after, 10–14 years after, 15–19 years after and ≥20 years after maternal migration. In addition, we made subgroups of migrants' children based on timing of child's birth in relation to maternal migration, categorized as children born abroad before maternal migration and those born in Sweden after maternal migration. The date for maternal migration, obtained from the Register of Total Population, was based on the date of registration with the Swedish Tax Agency, which all migrants with a residence permit at migration get shortly

after arriving in Sweden. However, some migrant groups, such as asylum seekers, get a residence permit after having been granted asylum and are hence registered at a later stage. We compared the date of registration with the Swedish Tax Agency with self-reports of migration date collected by the Swedish Migration Agency when migrants apply for a residence permit in Sweden (Table S1). Based on these analyses, we assigned refugees (except for quota refugees) and people who got a residence permit for humanitarian reasons an adjusted migration date corresponding to a date one year before the registration with the Swedish Tax Agency.

Our fourth exposure was parental reason for migration to Sweden, categorized as following according to the Swedish Migration Agency's definition based on Swedish and international conventions: refugee, family reunion of refugee, other family reunion, humanitarian reason, work and study and other reason. The data were obtained via Statistics Sweden's Longitudinal database for studies of the immigrants' integration (STATIV by Swedish acronym)[19] and assigned according to the reason of the father to reflect familial reason for migration.

2.4 | Other covariates

A child's sex and birth year were obtained from the Register of Total Population. Birth year was categorized as follows: 1984–1990, 1991–1997, 1998–2004 and 2005–2011. Data on first-degree biological relatives and their date of birth were identified from the Multi-generation Register. Maternal and paternal age at child's birth were both parameterized as follows: <25, 25–29, 30–34, 35–39 and ≥40 years.

2.5 | Data analysis

All analyses were conducted in SAS version 9.4. To derive robust standard errors, accounting for clustering of children born to the same mother, we calculated odds ratios (ORs) and two-sided 95% confidence intervals (CIs) from general estimating equation logistic models. We conducted several analyses.

Firstly, we analysed parental migration status and parental region of origin among all included children, using children with both parents born in Sweden as the reference. Models were adjusted for possible confounders including child's sex and birth year and maternal and paternal age at child's birth. Furthermore, an additional analysis was conducted to compare children with a mother born abroad and a father born in Sweden with children with a father born abroad and a mother born in Sweden. Including only children with migrant background in the analysis enabled to additionally adjust for potential confounders that are migrant-specific variables such as parental region of origin and timing of child's birth in relation to maternal migration.

Secondly, we examined timing of child's birth in relation to maternal migration among only children with both parents born abroad. We used children born in the year after maternal migration as the reference because this group seemed special according to our previous study.[4] The model was also additionally adjusted for parental region of origin. Furthermore, we conducted an additional analysis to compare migrants' children born abroad before maternal migration and those born in Sweden after maternal migration with children with both parents born in Sweden. As this analysis included children with both parents born in Sweden, we could not adjust for parental region of origin, but only other factors that are not migrant-specific.

Thirdly, we investigated paternal reason for migration among only children with both parents born abroad, additionally adjusting for parental region of origin and timing of child's birth in relation to maternal migration. We used children with refugee parents as the reference, considering that refugees migrated under particularly arduous circumstances and may be exposed to more detrimental migration-related factors compared with other migrants.[20]

2.6 | Sibling analysis

We examined timing of child's birth in relation to maternal migration using sibling comparisons in order to explore the potential residual confounding by shared familial factors.[21] We used conditional logistic regression models, matched on maternal identification number and adjusted for non-shared confounding characteristics including child's sex and birth year and maternal and paternal age at child's birth.

3 | RESULTS

In the total study population of 736,180 individuals in the SYC, we excluded adopted children (n = 7895), children who resided <4 years in Sweden (n = 29,779) and children without data on parental age and/or parental region of origin (n = 28,408), leaving 670,098 individuals for analysis, including 3781 individuals (0.6%) with ID with autism and 5076 individuals (0.8%) with ID without autism (Figure S1). The largest category was children with both parents born in Sweden (n = 420,905), followed by the group with both parents born abroad (n = 143,514), father born abroad and mother born in Sweden (n = 55,984) and mother born abroad and father born in Sweden (n = 49,695). There were some differences in characteristics between these groups (Table 1). Maternal age at birth was lower among children with both parents born abroad. In these children, 43% had parents

TABLE 1 Characteristics of the cohort, shown for each group

	No. (%)					
	Children with both Swedish parents			Children with both parents born abroad		
	Total *n* = 420,905	ID with autism *n* = 1981	ID without autism *n* = 2606	Total *n* = 143,514	ID with autism *n* = 1143	ID without autism *n* = 1711
Child sex						
Male	216,089 (51.3)	1360 (68.7)	1419 (54.5)	73,766 (51.4)	848 (74.2)	1043 (61.0)
Female	204,816 (48.7)	621 (31.3)	1187 (45.5)	69,748 (48.6)	295 (25.8)	668 (39.0)
Child birth year						
1984–1990	95,367 (22.7)	454 (22.9)	824 (31.6)	30,437 (21.2)	168 (14.7)	423 (24.7)
1991–1997	107,571 (25.6)	757 (38.2)	945 (36.3)	37,524 (26.1)	329 (28.8)	563 (32.9)
1998–2004	102,440 (24.3)	476 (24.0)	519 (19.9)	36,204 (25.2)	387 (33.9)	459 (26.8)
2005–2011	115,527 (27.4)	294 (14.8)	318 (12.2)	39,349 (27.4)	259 (22.7)	266 (15.5)
Maternal age at child's birth (years)						
<25	53,764 (12.8)	296 (14.9)	541 (20.8)	38,009 (26.5)	301 (26.3)	459 (26.8)
25–29	123,926 (29.4)	584 (29.5)	809 (31.0)	45,247 (31.5)	333 (29.1)	536 (31.3)
30–34	154,056 (36.6)	636 (32.1)	798 (30.6)	37,074 (25.8)	285 (24.9)	420 (24.5)
35–39	74,733 (17.8)	372 (18.8)	375 (14.4)	18,552 (12.9)	165 (14.4)	224 (13.1)
40+	14,426 (3.4)	93 (4.7)	83 (3.2)	4632 (3.2)	59 (5.2)	72 (4.2)
Paternal age at child's birth (years)						
<25	29,291 (7.0)	161 (8.1)	304 (11.7)	12,035 (8.4)	85 (7.4)	173 (10.1)
25–29	96,529 (22.9)	473 (23.9)	716 (27.5)	30,224 (21.1)	200 (17.5)	359 (21.0)
30–34	148,547 (35.3)	635 (32.1)	794 (30.5)	40,178 (28.0)	304 (26.6)	449 (26.2)
35–39	97,630 (23.2)	430 (21.7)	499 (19.1)	32,127 (22.4)	258 (22.6)	373 (21.8)
40+	48,908 (11.6)	282 (14.2)	293 (11.2)	28,950 (20.2)	296 (25.9)	357 (20.9)
Parental region of origin						
Sweden	420,905 (100.0)	1981 (100.0)	2606 (100.0)			
Other European countries				36,000 (25.1)	218 (19.1)	297 (17.4)
Middle East and North Africa				61,000 (42.5)	439 (38.4)	863 (50.4)
Sub-Saharan Africa				20,030 (14.0)	258 (22.6)	296 (17.3)
Central and South Asia				9709 (6.8)	88 (7.7)	105 (6.1)
Latin America and the Caribbean				10,666 (7.4)	114 (10.0)	120 (7.0)
East Asia and Pacific				5529 (3.9)	26 (2.3)	28 (1.6)
North America				580 (0.4)	0 (0.0)	2 (0.1)

(Continues)

TABLE 1 (Continued)

	No. (%)					
	Children with both Swedish parents			**Children with both parents born abroad**		
	Total *n* = 420,905	**ID with autism *n* = 1981**	**ID without autism *n* = 2606**	**Total *n* = 143,514**	**ID with autism *n* = 1143**	**ID without autism *n* = 1711**
Timing of child's birth in relation to maternal migration (paternal in sub-cohort with only father born abroad)						
≥5 years before migration				17,979 (12.5)	58 (5.1)	241 (14.1)
0–4 years before migration				16,782 (11.7)	116 (10.1)	190 (11.1)
In the year after migration				12,816 (8.9)	135 (11.8)	152 (8.9)
1–4 years after migration				35,657 (24.8)	348 (30.4)	403 (23.6)
5–9 years after migration				27,229 (19.0)	230 (20.1)	316 (18.5)
10–14 years after migration				15,520 (10.8)	134 (11.7)	197 (11.5)
15–19 years after migration				9280 (6.5)	70 (6.1)	122 (7.1)
≥20 years after migration				8110 (5.7)	52 (4.5)	87 (5.1)
Missing				141 (0.1)	0 (0.0)	3 (0.2)
Paternal reason for migration (maternal in sub-cohort with only mother born abroad)						
Refugee				28,997 (20.2)	242 (21.2)	352 (20.6)
Family reunion of refugee				8115 (5.7)	68 (5.9)	114 (6.7)
Other family reunion				29,855 (20.8)	253 (22.1)	331 (19.3)
Humanitarian reason				25,634 (17.9)	242 (21.2)	377 (22.0)
Work and study				12,858 (9.0)	45 (3.9)	56 (3.3)
Other				700 (0.5)	4 (0.3)	6 (0.4)
Missing				37,355 (26.0)	289 (25.3)	475 (27.8)
	No. (%)					
	Children with mother born abroad and father born in Sweden			**Children with father born abroad and mother born in Sweden**		
	Total *n* = 49,695	**ID with autism *n* = 300**	**ID without autism *n* = 299**	**Total *n* = 55,984**	**ID with autism *n* = 357**	**ID without autism *n* = 460**
Child sex						
Male	25,660 (51.6)	209 (69.7)	154 (51.5)	28,427 (50.8)	238 (66.7)	251 (54.6)
Female	24,035 (48.4)	91 (30.3)	145 (48.5)	27,557 (49.2)	119 (33.3)	209 (45.4)

(Continues)

TABLE 1 (Continued)

	No. (%)					
	Children with mother born abroad and father born in Sweden			Children with father born abroad and mother born in Sweden		
	Total n = 49,695	ID with autism n = 300	ID without autism n = 299	Total n = 55,984	ID with autism n = 357	ID without autism n = 460
Child birth year						
1984–1990	9836 (19.8)	52 (17.3)	76 (25.4)	11,102 (19.8)	70 (19.6)	121 (26.3)
1991–1997	11,242 (22.6)	117 (39.0)	94 (31.4)	13,379 (23.9)	130 (36.4)	158 (34.3)
1998–2004	12,354 (24.9)	71 (23.7)	71 (23.7)	14,157 (25.3)	103 (28.9)	109 (23.7)
2005–2011	16,263 (32.7)	60 (20.0)	58 (19.4)	17,346 (31.0)	54 (15.1)	72 (15.7)
Maternal age at child's birth (years)						
<25	6368 (12.8)	37 (12.3)	62 (20.7)	10,693 (19.1)	93 (26.1)	142 (30.9)
25–29	13,561 (27.3)	75 (25.0)	68 (22.7)	16,013 (28.6)	90 (25.2)	140 (30.4)
30–34	17,415 (35.0)	95 (31.7)	90 (30.1)	17,394 (31.1)	101 (28.3)	99 (21.5)
35–39	10,117 (20.4)	66 (22.0)	58 (19.4)	9597 (17.1)	60 (16.8)	50 (10.9)
40+	2234 (4.5)	27 (9.0)	21 (7.0)	2287 (4.1)	13 (3.6)	29 (6.3)
Paternal age at child's birth (years)						
<25	3074 (6.2)	18 (6.0)	28 (9.4)	5307 (9.5)	42 (11.8)	81 (17.6)
25–29	9193 (18.5)	52 (17.3)	64 (21.4)	13,486 (24.1)	99 (27.7)	120 (26.1)
30–34	14,923 (30.0)	80 (26.7)	85 (28.4)	17,404 (31.1)	99 (27.7)	122 (26.5)
35–39	12,050 (24.2)	71 (23.7)	56 (18.7)	11,945 (21.3)	61 (17.1)	77 (16.7)
40+	10,455 (21.0)	79 (26.3)	66 (22.1)	7842 (14.0)	56 (15.7)	60 (13.0)
Parental region of origin						
Other European countries	27,386 (55.1)	179 (59.7)	161 (53.8)	28,997 (51.8)	166 (46.5)	227 (49.3)
Middle East and North Africa	3558 (7.2)	19 (6.3)	31 (10.4)	10,617 (19.0)	90 (25.2)	120 (26.1)
Sub-Saharan Africa	1806 (3.6)	11 (3.7)	14 (4.7)	3322 (5.9)	26 (7.3)	32 (7.0)
Central and South Asia	1269 (2.6)	6 (2.0)	6 (2.0)	1074 (1.9)	6 (1.7)	9 (2.0)
Latin America and the Caribbean	5515 (11.1)	37 (12.3)	32 (10.7)	6853 (12.2)	40 (11.2)	43 (9.3)
East Asia and Pacific	8079 (16.3)	36 (12.0)	44 (14.7)	2289 (4.1)	7 (2.0)	16 (3.5)
North America	2082 (4.2)	12 (4.0)	11 (3.7)	2832 (5.1)	22 (6.2)	13 (2.8)
Timing of child's birth in relation to maternal migration (Paternal in sub-cohort with only father born abroad)						
≥5 years before migration	404 (0.8)	1 (0.3)	4 (1.3)	615 (1.1)	6 (1.7)	5 (1.1)
0–4 years before migration	1986 (4.0)	12 (4.0)	14 (4.7)	3254 (5.8)	27 (7.6)	29 (6.3)

(Continues)

TABLE 1 (Continued)

	No. (%)					
	Children with mother born abroad and father born in Sweden			Children with father born abroad and mother born in Sweden		
	Total $n = 49{,}695$	ID with autism $n = 300$	ID without autism $n = 299$	Total $n = 55{,}984$	ID with autism $n = 357$	ID without autism $n = 460$
In the year after migration	2929 (5.9)	12 (4.0)	18 (6.0)	3227 (5.8)	12 (3.4)	29 (6.3)
1–4 years after migration	9312 (18.7)	69 (23.0)	52 (17.4)	9951 (17.8)	64 (17.9)	107 (23.3)
5–9 years after migration	9408 (18.9)	51 (17.0)	53 (17.7)	9770 (17.5)	61 (17.1)	56 (12.2)
10–14 years after migration	6093 (12.3)	48 (16.0)	34 (11.4)	7061 (12.6)	49 (13.7)	49 (10.7)
15–19 years after migration	5028 (10.1)	28 (9.3)	34 (11.4)	6122 (10.9)	49 (13.7)	73 (15.9)
≥20 years after migration	14,177 (28.5)	77 (25.7)	85 (28.4)	15,437 (27.6)	86 (24.1)	109 (23.7)
Missing	358 (0.7)	2 (0.7)	5 (1.7)	547 (1.0)	3 (0.8)	3 (0.7)
Paternal reason for migration (maternal in sub-cohort with only mother born abroad)						
Refugee	874 (1.8)	8 (2.7)	7 (2.3)	2,028 (3.6)	14 (3.9)	23 (5.0)
Family reunion of refugee	443 (0.9)	2 (0.7)	2 (0.7)	604 (1.1)	3 (0.8)	4 (0.9)
Other family reunion	17,906 (36.0)	118 (39.3)	115 (38.5)	20,143 (36.0)	126 (35.3)	157 (34.1)
Humanitarian reason	985 (2.0)	8 (2.7)	3 (1.0)	1812 (3.2)	19 (5.3)	10 (2.2)
Work and study	1412 (2.8)	9 (3.0)	3 (1.0)	3106 (5.5)	14 (3.9)	13 (2.8)
Other	292 (0.6)	2 (0.7)	0 (0.0)	459 (0.8)	2 (0.6)	2 (0.4)
Missing	27,783 (55.9)	153 (51.0)	169 (56.5)	27,832 (49.7)	179 (50.1)	251 (54.6)

Abbreviation: ID, intellectual disability.

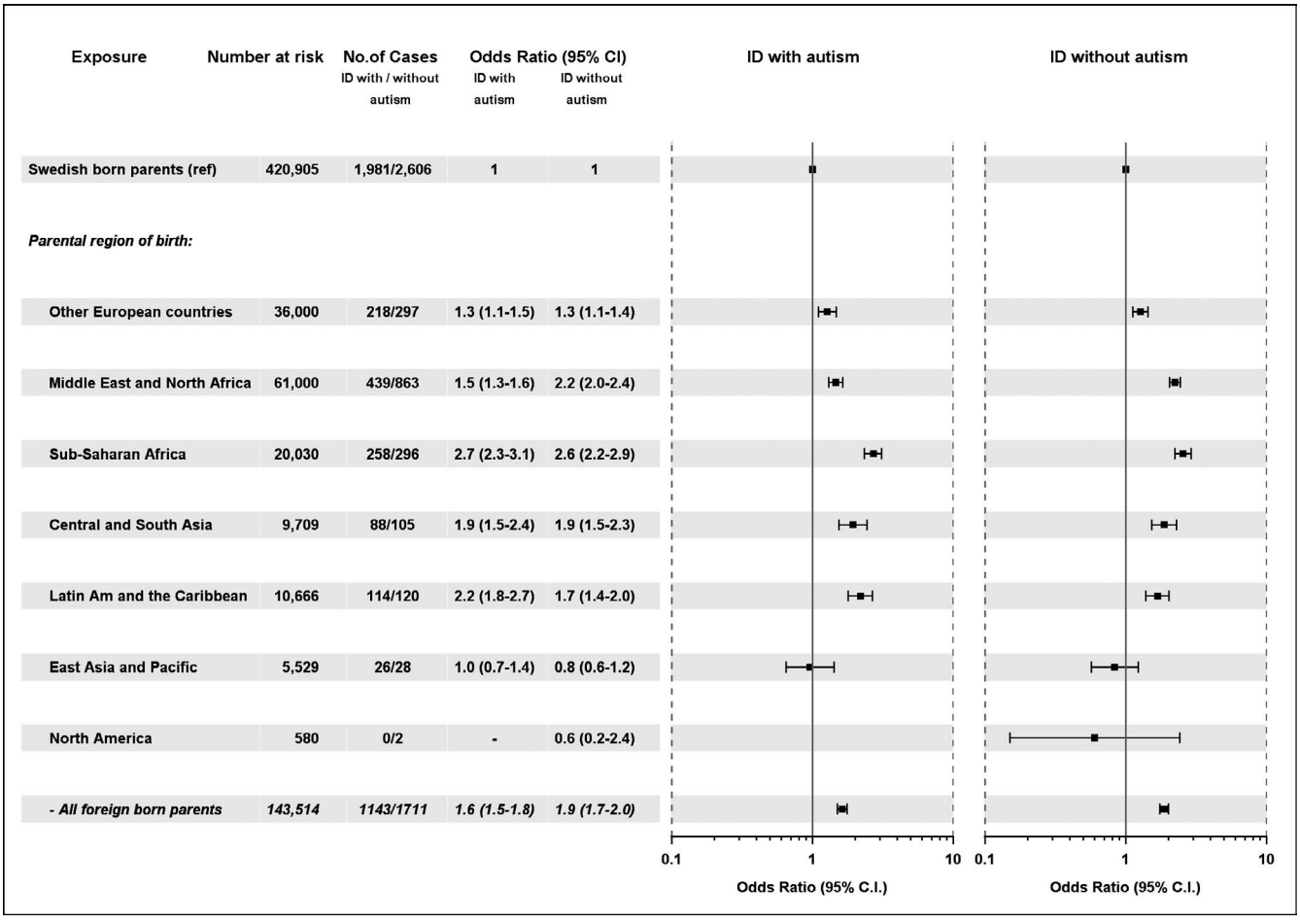


FIGURE 1 Adjusted odds ratio[a] for intellectual disability with and without autism in children with both parents born abroad as compared with children with both parents born in Sweden, in relation to parental region of origin. a. Adjusted for sex, birth year, and maternal and paternal age at child's birth. CI, confidence interval; ID, intellectual disability

originating from the Middle East and North Africa, while 55% and 52% of children with one parent born in Sweden and a mother or a father, respectively, born abroad had parental origins in other European countries. Furthermore, almost a third of mothers or fathers of children with one parent born abroad migrated more than 20 years before the child's birth, in contrast to 6% in mothers of children with both parents born abroad. A list of most frequent countries of parental former citizenship comprising each region in this study is summarized in Table S2. In addition, characteristics of the excluded population are reviewed in Table S3.

Figure 1 and Table 2 shows the ORs for ID with and without autism in relation to parental migration status and parental region of origin, as compared with children with both parents born in Sweden. Children with both parents born abroad had an increased risk of ID with autism (OR = 1.6, CI 1.5–1.8) and ID without autism (OR = 1.9, CI 1.7–2.0; Figure 1). The associations were similar between ID with and without autism for each region of parental origin, with more pronounced associations for parental origins in the Middle East, North Africa, Sub-Saharan Africa, Central and South Asia and Latin America. Among children with one parent born abroad and one parent born in Sweden, there was an association for ID with autism regardless of whether the father or mother was born abroad (OR = 1.4, CI 1.2–1.5 and OR = 1.3, CI 1.1–1.5, respectively; Table 2). However, for ID without autism, paternal, but not maternal, migration was associated with an increased risk (OR = 1.3, CI 1.2–1.5 and OR = 1.0, CI 0.9–1.2, respectively). The associations were pronounced with parental origin in the Middle East, North Africa and Sub-Sahara Africa. In the additional analysis including only children of migrant parents, those with a mother born abroad and a father born in Sweden had an unchanged risk of ID with autism (OR = 1.0, CI 0.9–1.2) and a decreased risk of ID without autism (OR = 0.8, CI 0.7–0.9) compared with children with a father born abroad and a mother born in Sweden, adjusted by child's sex and birth year, maternal and paternal age at child's birth, parental region of origin and timing of child's birth in relation to maternal migration.

Timing of child's birth in relation to maternal migration was examined among 143,373 individuals with both parents born abroad after excluding children without data on date for

TABLE 2 Adjusted odds ratio for intellectual disability with and without autism in children with a parent born abroad and a parent born in Sweden as compared with children with both parents born in Sweden, in relation to parental region of origin

		ID with autism		ID without autism	
	Number at risk	Number of cases	OR[a] (95% CI)	Number of cases	OR[a] (95% CI)
Swedish-born parents	420,905	1981	1.0	2606	1.0
Mother born abroad and father born in Sweden	49,695	300	1.3 (1.1–1.5)	299	1.0 (0.9–1.2)
Maternal region of birth					
Other European countries	27,386	179	1.3 (1.1–1.6)	161	0.9 (0.8–1.1)
Middle East and North Africa	3558	19	1.4 (0.9–2.1)	31	1.7 (1.2–2.6)
Sub-Saharan Africa	1806	11	1.4 (0.7–2.5)	14	1.4 (0.8–2.4)
Central and South Asia	1269	6	1.2 (0.6–2.8)	6	0.9 (0.4–2.1)
Latin America and the Caribbean	5515	37	1.5 (1.1–2.1)	32	1.0 (0.7–1.5)
East Asia and Pacific	8079	36	1.0 (0.7–1.4)	44	1.0 (0.7–1.4)
North America	2082	12	1.2 (0.7–2.1)	11	0.9 (0.5–1.8)
Father born abroad and mother born in Sweden	55,984	357	1.4 (1.2–1.5)	460	1.3 (1.2–1.5)
Paternal region of birth					
Other European countries	28,997	166	1.2 (1.0–1.4)	227	1.2 (1.1–1.4)
Middle East and North Africa	10,617	90	1.9 (1.5–2.4)	120	1.9 (1.6–2.3)
Sub-Saharan Africa	3322	26	1.8 (1.2–2.6)	32	1.7 (1.2–2.4)
Central and South Asia	1074	6	1.3 (0.6–2.9)	9	1.5 (0.8–2.9)
Latin America and the Caribbean	6853	40	1.3 (0.9–1.8)	43	1.0 (0.8–1.4)
East Asia and Pacific	2289	7	0.7 (0.3–1.5)	16	1.3 (0.8–2.1)
North America	2832	22	1.6 (1.05–2.5)	13	0.8 (0.4–1.3)

Abbreviations: OR, odds ratio; CI, confidence interval; ID, intellectual disability.

[a]Adjusted for sex, birth year and maternal and paternal age at child's birth.

maternal migration ($n = 141$; Figure S1). The results showed a non-linear relationship between timing of child's birth in relation to maternal migration and ID with autism, such that the risk seemed to reduce when the child's birth occurred before maternal migration and later than four years after maternal migration (Figure 2). Especially, children born earlier than four years before maternal migration had a 70% lower risk of ID with autism (OR = 0.3, CI 0.2–0.4) compared with children born in the year after maternal migration. No such pattern was observed for ID without autism. In the additional analysis comparing with children with Swedish-born parents, migrants' children born abroad before maternal migration had an increased risk of ID without autism (OR = 1.6, CI 1.4–1.8), but not of ID with autism (OR = 0.8, CI 0.7–1.0), while migrants' children born in Sweden after maternal migration had increased risks of both ID with autism (OR = 1.9, CI 1.7–2.0) and ID without autism (OR = 2.0, CI 1.8–2.1), adjusted for child's sex and birth year and maternal and paternal age at child's birth (Figure S2).

Furthermore, we conducted sibling analyses using a cohort of 861 individuals with ID with autism and 1547 unaffected siblings and a cohort of 1341 individuals with ID without autism and 2679 unaffected siblings, after excluding individuals without siblings ($n = 31,029$) and children in families without a child having ID with autism ($n = 109,936$) or ID without autism ($n = 108,324$; Figure S1). The matched sibling analyses broadly showed similar results as the one in Figure 2, although the confidence intervals were wider because of smaller sample sizes (Table S4). However, children born after maternal migration had a seemingly reduced risk of ID without autism compared with children born in the year of maternal migration, similar to the association with ID with autism.

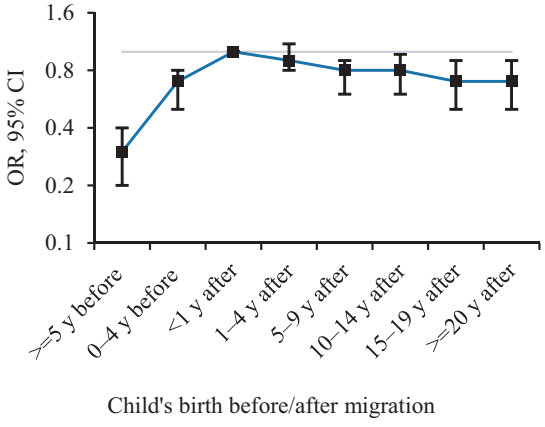
In the sample of children where both parents were born abroad and data on parental reason for migration was available ($n = 106,159$), we found that children whose parents had migrated for the purpose of working or studying in Sweden had lower risks of ID with autism (OR = 0.7, CI 0.5–0.9) and ID without autism (OR = 0.6, CI 0.4–0.8) compared with children with refugee parents (Table 3).

4 | DISCUSSION

We investigated the role of (i) parental migration, (ii) parental region of origin, (iii) timing of child's birth in relation to maternal migration and (iv) parental reason for migration with

ID with autism

Timing of child's birth	Number at risk	Number of cases	OR (95% CI)
>=5 years before migration	17,979	58	0.3 (0.2-0.4)
0–4 years before migration	16,782	116	0.7 (0.5-0.8)
in the year after migration	12,816	135	1.0
1–4 years after migration	35,657	348	0.9 (0.8-1.1)
5–9 years after migration	27,229	230	0.8 (0.6-0.9)
10–14 years after migration	15,520	134	0.8 (0.6-0.97)
15–19 years after migration	9,280	70	0.7 (0.5-0.9)
>=20 years after migration	8,110	52	0.7 (0.5-0.9)



ID without autism

Timing of child's birth	Number at risk	Number of cases	OR (95% CI)
>=5 years before migration	17,979	241	0.9 (0.7-1.1)
0–4 years before migration	16,782	190	0.9 (0.7-1.2)
in the year after migration	12,816	152	1.0
1–4 years after migration	35,657	403	0.9 (0.8-1.1)
5–9 years after migration	27,229	316	0.9 (0.7-1.1)
10–14 years after migration	15,520	197	1.0 (0.8-1.2)
15–19 years after migration	9,280	122	1.1 (0.9-1.4)
>=20 years after migration	8,110	87	1.1 (0.8-1.4)

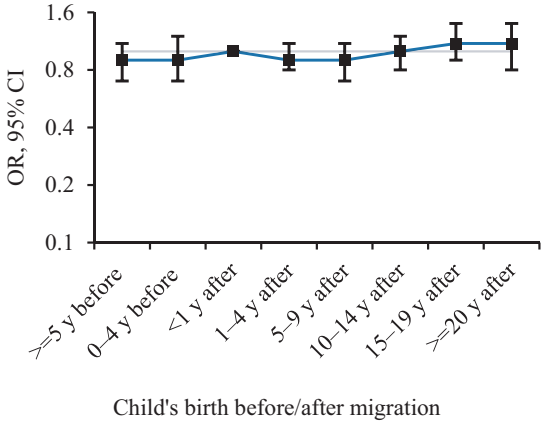


FIGURE 2 Adjusted odds ratio[a,b] for intellectual disability with and without autism among children with both parents born abroad, by timing of child's birth in relation to maternal migration. a. Adjusted for sex, birth year, maternal and paternal age at child's birth and parental region of origin. b. Reference group is children born in the year after maternal migration. CI, confidence interval; ID, intellectual disability; OR, odds ratio; y, years

TABLE 3 Odds ratio for intellectual disability with and without autism in children with both parents born abroad, by parental reason for migration

		ID with autism			ID without autism		
Parental reason for migration	**Number at risk**	**Number of cases**	**OR (95% CI)**	**aOR[a] (95% CI)**	**Number of cases**	**OR (95% CI)**	**aOR[a] (95% CI)**
Refugee	28,997	242	1.0	1.0	352	1.0	1.0
Family reunion of refugee	8115	68	1.0 (0.8–1.3)	1.1 (0.8–1.5)	114	1.2 (0.9–1.4)	1.2 (1.0–1.5)
Other family reunion	29,855	253	1.0 (0.8–1.2)	1.1 (0.9–1.4)	331	0.9 (0.8–1.1)	1.2 (1.0–1.4)
Humanitarian reason	25,634	242	1.1 (0.9–1.4)	1.1 (0.9–1.4)	377	1.2 (1.04–1.4)	1.3 (1.1–1.5)
Work and study	12,858	45	0.4 (0.3–0.6)	0.7 (0.5–0.9)	56	0.4 (0.3–0.5)	0.6 (0.4–0.8)
Other	700	4	0.7 (0.3–1.8)	0.9 (0.3–2.3)	6	0.7 (0.3–1.6)	0.9 (0.4–1.9)

(a)OR, (adjusted) odds ratio; CI, confidence interval; ID, intellectual disability.

[a]Adjusted for sex, birth year, maternal and paternal age at child's birth, parental region of origin and timing of child's birth in relation to maternal migration.

offspring risks of ID with and without autism in a large total population sample. We found that children with both migrant parents had increased risk of both ID with and without autism compared with children with Swedish-born parents. Among these children with both migrant parents, it was protective of ID with autism, but not of ID without autism, when the child's

birth occurred before and later than four years after maternal migration, which was largely replicated in the sibling comparison. Furthermore, the associations with both ID with and without autism were more pronounced when the parents had migrated from the Middle East, North Africa, Sub-Saharan Africa, Central and South Asia or Latin America and for reasons other than work or study among these children. Having one migrant parent meant a slightly increased risk of both conditions if the father was a migrant, while maternal migration status was associated with ID with autism but not ID without autism, compared with children with Swedish-born parents.

4.1 | Parental migration status

Results showing similar associations for both ID with and without autism in children with both parents born abroad suggest that there may be a general association between parental migration and a risk of ID or cognitive impairment. Our results for ID without autism are inconsistent with the two previous studies from the USA and Australia, showing a decreased or unchanged risk of ID without autism in children of migrant parents.[6,7] This discrepancy may reflect differences between health systems in access to diagnostic services among migrant groups,[6,22] small sample sizes, differences in origins of migrants or differential exposures to environmental factors among migrants.

Among children with one parent born abroad, maternal and paternal migration was similarly associated with ID with autism in our data. This is line with a Dutch study,[15] but in disagreement with studies from the Nordic countries indicating, albeit based on small numbers, that maternal, but not paternal, migration is associated with childhood autism.[12–14] In addition, our data showed that paternal, but not maternal, migration was associated with ID without autism. These results speak against in utero exposures related to maternal migration as the only explanation of the increased risks of ID with and without autism. However, a careful interpretation is needed, because the results may possibly be explained by other factors than parental migration-related factors, for example selection of individuals who marry with a person born abroad.

4.2 | Parental region of origin

We observed higher risks of ID with and without autism among children of migrant parents from the Middle East, North Africa, Sub-Saharan Africa, Central and South Asia and Latin America. These regions include larger share of low- and middle-income countries according to the classifications of World Bank.[23] This finding is in line with many previous studies.[3–5,8,12] There is some evidence that the prevalence of ID may be higher in low- and middle- than in high-income countries.[24] The risk increases among children of migrants maybe because of risk factors associated with the place of parental origin and remaining over time, for example deprivation, malnutrition, genetic variations and consanguinity. In addition, factors in the country of destination that may disproportionately affect migrants from low- and middle-income settings might be implicated, for example discrimination, stress, poor health literacy and lower utilization of healthcare including prenatal screening.[25,26]

4.3 | Timing of child's birth in relation to maternal migration

Among children with both migrant parents, those born before maternal migration had a decreased risk of ID with autism, but not of ID without autism, compared with children born near in time after maternal migration. There are three possible interpretations of the risk difference between the outcomes. Firstly, the lower risk of ID with autism may be because of selective migration where families with a child born abroad with ID with autism might not migrate, presumably because of additional pressures or challenges those families face. However, it is unlikely that families with a child with ID without autism migrate but not those with a child with ID with autism. Secondly, the difference may depend on assessment bias. In Sweden, autism and ID are normally diagnosed by clinical experts using diagnostic instruments including interviews with parents and teachers, and observation of the child. For families not speaking Swedish, professional interpreters are used for parent interviews, and child observations are focused on non-verbal behaviours. This may lead to an assessment bias in children of migrants[27] because of misunderstanding or misinterpretation of cultural norms in relation to child development. However, this would not explain why ID with autism and not ID without autism should be subjected to such assessment bias. Thirdly, the results may suggest that the aetiology of ID with autism is different from that of ID without autism. Some previous findings that the risk factor profiles differ between ID with and without autism support this notion.[7] Indeed, our results propose that factors in the travel and early post-migration phases of migration and acting in utero, such as prenatal maternal migration stress and infection, may be relevant in the aetiology of ID with autism but not ID without autism.[28,29] Further confirmative studies are, however, needed to examine the association.

4.4 | Parental reason for migration

To the best of our knowledge, this is the first study investigating parental reason for migration in relation to autism and ID. Parental reason for migration did not influence the risks of ID with or without autism except for the slightly decreased

risks in children with parents migrated for work or study. The risk decrease not only might depend on selective migration where the healthier population with an ability to work or study migrates, but may also suggest that migration in less adverse or better socioeconomic circumstances is associated with the lower risk of offspring ID with and without autism.

4.5 | Strengths and limitations

Our study has several strengths. Firstly, the large total population sample ensure a low risk of selection bias and random error. Secondly, the comprehensive approach contributes to the understanding of the complex association between migration and ID with and without autism. Thirdly, the analyses including only children with migrant parent(s) allowed to additionally adjust for potential confounders that are migrant-specific variables. Fourthly, the use of both standard adjustment and sibling-comparison analysis accounted for unobserved familial confounders, such as genetic risk and parental health behaviours. The observed associations with timing of child's birth in relation to maternal migration in the standard logistic models were largely replicated in the sibling-comparison models, which suggests that there was minimal shared familial confounding.

Some limitations should be noted. Firstly, the registers lacked detailed information on, for example circumstances before arrival in Sweden. Secondly, there was likely misclassification in the date of maternal migration, especially among refugees who may have arrived as asylum seekers before the date a resident permit is granted. This misclassification is likely to have been non-differential in relation to the outcomes, which may have diluted associations with timing of child's birth in relation to maternal migration. To mitigate against this, we adjusted the date of registration with the Swedish Tax Agency of these groups based on the self-reports of migration date collected by the Swedish Migration Agency. Thirdly, there may be some outcome misclassification. Although ID with autism diagnoses been validated in our cohort,[16] it is possible that the validity of the tools used to diagnose autism or ID may have different properties in different migrant groups leading to misclassification. Fourthly, the possibility of selection bias because of the exclusion of population cannot be excluded. For example, some specific groups of children such as asylum seekers, undocumented migrants, adopted children, unaccompanied migrant children, children of single parent and a part of newly arrived migrants were excluded because of a lack of data. Although the impact of the exclusion on the results is difficult to estimate, it is likely that selection bias was minimal in the most of analyses as the excluded population consisted only around 10% of the total population. However, for the analysis for parental reason for migration, 26% of the population was excluded, which could have affected the results. Fifthly, migration is a heterogeneous phenomenon and caution must be exercised before generalizing our results in a broader context. Our data are likely representative of Sweden and other Nordic countries, but further studies are needed to evaluate the association in the different countries of destination.

4.6 | Future studies

This study suggested several future areas for research. Firstly, more studies on the association between migration and ID is needed to draw any conclusion of the association. Especially, studies examining the severity of ID are urgently needed, as previous studies indicated that factors influencing severe ID differ from those influencing mild ID,[30] and there were observations of risk differences between these severities of ID among migrant's children.[6–8] Other subcategories of ID such as the association with a known medical or genetic condition is also of interest. Secondly, further research is needed in order to investigate the underlying factors explaining the increased risk of ID with and without autism in children with migrant parents. This study suggested some potential such factors including timing of child's birth in relation to maternal migration and parental reason for migration. In addition, our results indicated that there may be differences in the underlying factors between ID with and without autism, suggesting that the association needs to be examined separately for these conditions. Thirdly, there is a need for studies from different countries of destination on the association. Evaluating how migration from a same country of origin to different country of destination impact the risks of the conditions would give a clue of the importance of post-migration factors in a country of destination.

To Conclude, we found that parental migration is associated with ID regardless of co-occurrence of autism, although underlying factors may differ between the conditions. Our results suggested that these associations are partly explained by environmental factors during pregnancy related to circumstances around migration for ID with autism, and by factors linked to parental origin in low- and middle-income countries for ID in general, although other factors such as assessment bias and selection may also play a role. While these associations and factors need to be studied further, recipient countries should consider policies that lead to increased health literacy and access to antenatal care in migrants, to reduce the burden of the conditions.

ACKNOWLEDGEMENTS

This study was supported by the NIHR Biomedical Research Centre at University Hospitals Bristol, Weston NHS Foundation Trust, and the University of Bristol. The views expressed are those of the author(s) and not necessarily those of the NIHR or the UK Department of Health and Social Care.

CONFLICT OF INTEREST

None.

ETHICAL APPROVAL

The study was approved by the regional ethical review board for Karolinska Institutet (DNR 2010/1185-31/5 and 2016/987-32).

PEER REVIEW

The peer review history for this article is available at https://publons.com/publon/10.1111/acps.13350.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available because of privacy or ethical restrictions.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

How to cite this article: Morinaga M, Hollander A-C, Heuvelman H, et al. Migration and risk of intellectual disability with and without autism: A population-based cohort study. Acta Psychiatr Scand. 2021;00:1–14. https://doi.org/10.1111/acps.13350