



# The Risk of Type 1 Diabetes Among Offspring of Immigrant Mothers in Relation to the Duration of Residency in Sweden

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## OBJECTIVE

The risk for type 1 diabetes mellitus (T1DM) is increased in the second compared with the first generation of immigrants in Sweden. We investigated the effect of the mother's duration of stay in Sweden on the risk of T1DM in the offspring.

## RESEARCH DESIGN AND METHODS

Using data from national registries, we identified all subjects with T1DM among 984,798 children born in Sweden (aged 0–18 years) between 1992 and 2009. Incidence rate ratios (IRRs) with 95% CI were estimated using Poisson regression.

## RESULTS

Offspring of mothers living in Sweden for up to 5 years had a 22% lower risk of T1DM (adjusted IRR 0.78, 95% CI 0.63–0.96) compared with offspring of mothers living in Sweden for 11 years or more. The risk increased with the mother's duration of stay in Sweden.

## CONCLUSIONS

Our findings support the hypothesis that immigration to Sweden is associated with exposure to new environmental factors that contribute to the development of T1DM in genetically susceptible individuals.

The incidence of type 1 diabetes mellitus (T1DM) varies greatly between countries and different ethnic groups (1). This is likely a reflection of differences in genetic susceptibility and environmental exposures between populations. Sweden has one of the highest reported incidences of T1DM in the world (2). In Sweden, offspring of immigrants from most parts of the world have a decreased risk of T1DM compared with native Swedes (3). However, the risk of T1DM is increased in offspring of immigrants from Eastern Africa (4). A number of environmental factors have been suggested to contribute to the development of T1DM in genetically susceptible individuals (5–8). Immigration, will by necessity lead to a change in certain environmental exposures. Investigation of the effect of exposure to a new environment on the risk for T1DM in different immigrant groups could hopefully add new information on the gene-environment interaction for the development of T1DM.

This nationwide cohort study analyzed the risk of T1DM in offspring of immigrants in relation to the number of years the mother had lived in Sweden before the baby was born. We hypothesized that the risk of T1DM in the offspring of immigrant mothers would increase with their duration of stay in Sweden.

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**RESEARCH DESIGN AND METHODS**

**Database**

We used data from a nationwide data set, The Migration and Health Cohort (9), which is the result of linkage of a variety of Swedish national health and demographic registers.

**Study Cohort**

The study base consisted of 1,263,358 individuals aged 0–18 years, born and living in Sweden any time between 1 January 1992 and 31 December 2004. After exclusions (Table 1), the final cohort comprised 984,798 eligible individuals.

**Follow-up**

The cohort members were followed from the date of birth between 1992 and 2004 until the date of diagnosis of T1DM according to the Swedish versions of the ICD (ICD-9: 250, 1987–1996 and ICD-10: E10, 1997 and onwards), emigration, death, or end of follow-up (31 December 2009), whichever occurred first.

**Statistical Analysis**

Using Poisson regression models, we calculated incidence rate ratios (IRRs) with 95% CI to estimate the risk of T1DM in the offspring, stratified by parental country of birth and maternal duration of residency in Sweden before the child’s birth. Parental country of birth was first defined as foreign born (both parents born abroad). We further categorized parents as of Nordic (parents born in Finland, Norway, Denmark, and Iceland) and East African (parents born in East African countries) origin.

The main exposure variable was maternal duration of stay in Sweden before the child’s birth, classified into 0–5 years, 6–10 years, and ≥11 years. Risk estimates were adjusted for maternal age at delivery, first trimester BMI, maternal smoking, parental education, parity, preeclampsia, birth weight, and sex and age of the child at follow-up.

The outcome of interest was defined as a diagnosis of T1DM in children aged 0–18 years, identified in the national patient registry according to the ninth and tenth Swedish versions of ICD (ICD-9 code 250 between 1987 and 1996, and ICD-10 code E10 from 1997 onwards).

All statistical analyses were performed with SAS 9.3 software (SAS Institute, Inc., Cary, NC).

**RESULTS**

During the study period between 1992 and 2009, 4,825 cases of T1DM were

**Table 1—IRR and 95% CI of T1DM among children and young adults (aged 0–18 years) born in Sweden between years 1992 and 2004 and followed until 2009 by maternal duration of residence in Sweden before the child’s birth and parental country of birth**

Parental migration status	IRR* (95% CI)			IRR** (95% CI)		
	0–5 years	6–10 years	≥11 years	0–5 years	6–10 years	≥11 years
Foreign born vs. Swedest	0.54 (0.47–0.63)	0.69 (0.56–0.84)	0.71 (0.61–0.83)	0.55 (0.48–0.64)	0.69 (0.57–0.85)	0.71 (0.62–0.83)
Foreign born††	0.77 (0.62–0.94)	0.98 (0.76–1.25)	1	0.78 (0.63–0.96)	0.96 (0.75–1.24)	1
East African vs. Swedest	1.03 (0.72–1.46)	1.39 (0.86–2.24)	2.34 (1.30–4.24)	1.00 (0.70–1.42)	1.32 (0.82–2.14)	2.27 (1.25–4.10)
East African††	0.36 (0.17–0.75)	0.48 (0.21–1.09)	1	0.39 (0.17–0.86)	0.49 (0.21–1.12)	1
Other Nordic vs. Swedent†	0.85 (0.54–1.33)	1.11 (0.69–1.78)	1.07 (0.87–1.32)	0.88 (0.56–1.38)	1.13 (0.70–1.81)	1.08 (0.88–1.33)
Other Nordic††	1.11 (0.43–2.86)	1.34 (0.44–4.04)	1	0.94 (0.34–2.55)	1.22 (0.40–3.75)	1

The study base comprised 1,263,358 individuals. Exclusions: infants delivered before 28th or after 43rd completed weeks of gestation, from multiple births, with any congenital malformation, individuals with missing data on gestational age, missing data on birth weight, infants with a birth weight ± 6 standard deviations from the mean, records with missing or extreme data on maternal height, weight, and age, and women with invalid immigration. The final cohort comprised 984,798 eligible individuals. \*Adjusted for child’s age at follow-up. \*\*Adjusted for maternal age, maternal BMI, smoking at enrollment, parental education, parity, preeclampsia, and child’s sex and age at follow-up. †Swedes as a reference. ††Longest duration of stay as a reference.

diagnosed among 984,798 Sweden-born children between 0 and 18 years of age; of these, 474 children were offspring of immigrant mothers. Offspring of mothers living in Sweden for up to 5 years had a 22% lower risk of T1DM (IRR 0.78, 95% CI 0.63–0.96; Table 1) compared with offspring of mothers living in Sweden for at least 11 years. The risk of T1DM in offspring of immigrants increased with increasing duration of the mother's stay in Sweden. Offspring of mothers from eastern Africa had the same risk pattern with increasing risks with longer duration of stay. Children born to eastern African mothers living in Sweden for more than 11 years had a doubled risk of T1DM compared with native Swedes (IRR 2.27, 95% CI 1.25–4.10; Table 1). Confining the analyses to only term offspring did not significantly change the risk estimates.

## CONCLUSIONS

This nationwide cohort study demonstrated that the risk of T1DM in the offspring of immigrants increased with the mother's duration of stay in Sweden. This was in accordance with our prespecified hypothesis.

One might speculate that the increased risk of T1DM in offspring of foreign-born mothers with longer duration of stay in Sweden is partly due to changes in environmental exposures and life style. A limitation with the current study is that we did not have information on possible environmental determinants of interest, including dietary habits, changes in BMI over time, physical activity, viral exposures, and psychological stress. Therefore, the potential effect of different exposures on the risk for T1DM could not be explored. Another possibility is that the effect of different exposures differs with genetic profile.

The cases of T1DM were identified by ICD codes. The ICD-9 did not allow separation of type 1 from type 2 diabetes. Thus, there is a risk of misclassification of type 2 as type 1 in cases diagnosed before 1997. However, in a previous study using the same data set, we performed a sensitivity analysis including only individuals living in Sweden between 1997 and 2008 and after the introduction of ICD-10 (3,4). The results were similar in this analysis and in those reported in the main analysis extending to the period before 1997.

Exposure to viral infections and early introduction of certain nutrients, such as cow's milk and gluten, may contribute to the development of T1DM in the genetically susceptible individual (5,10). Data also indicate that different exposures may interact and increase the risk for T1DM even further (11). In Sweden, the cold climate with increased time spent indoors may facilitate the spread of viral infections, and the consumption of milk products and gluten is high. The finding of increasing risks of T1DM in the offspring of immigrants with length of stay in Sweden may thus partly be a reflection of changes in dietary habits and increased exposure to viral infections.

Time spent in Sweden per se is accompanied by an increased risk of overweight and obesity (12,13). It has recently been described that certain HLA profiles are associated with an increased risk of obesity and with T1DM. This genetic profile is increasingly common in newly diagnosed children with T1DM in Sweden (14). Maternal overweight and obesity are also associated with high birth weight, a well-known risk factor for T1DM (15). Thus, it is possible that both maternal and offspring obesity may have contributed to the observed increment in risk. In conclusion, the risk of T1DM in offspring of immigrant mothers increases with duration of stay in Sweden and supports the hypothesis that immigration to Sweden is associated with exposure to a number of new environmental factors that contribute to the development of T1DM in genetically susceptible individuals.

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**Author Contributions.** H.I.H. designed the research, drafted the manuscript, analyzed data, and interpreted results. T.M. designed the research, interpreted the results, critically reviewed and edited the manuscript, and handled research data and funding. M.P. designed the research, interpreted the results, and critically reviewed and edited the manuscript. T.M. is the guarantor of this work and, as such, had

full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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