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Maternal exposure to air pollution and type 1 diabetes – Accounting for genetic factors

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ABSTRACT

Background: Genetic and non-genetic factors probably act together to initiate and accelerate development of type 1 diabetes [T1D]. One suggested risk factor contributing to development of T1D is air pollution.
Objective: The aim of the study was to investigate whether maternal exposure during pregnancy to air pollution, measured as nitrogen oxides [NO_x] and ozone, in a low-dose exposure area was associated with the child developing T1D.
Method: In Scania (Skåne), the most southern county in Sweden, 84,039 infants were born during the period 1999–2005. By the end of April 2013, 324 of those children had been diagnosed with T1D. For each of those T1D children three control children were randomly selected and matched for HLA genotype and birth year. Individually modelled exposure data at residence during pregnancy were assessed for nitrogen oxides [NO_x], traffic density and ozone.
Results: Ozone as well as NO_x exposures were associated with T1D. When the highest exposure group was compared to the lowest group an odds ratios of 1.62 (95% confidence interval [CI] 0.99–2.65) was observed for ozone in the second trimester and 1.58 (95% CI 1.06–2.35) for NO_x in the third trimester.
Conclusion: This study indicates that living in an area with elevated levels of air pollution during pregnancy may be a risk factor for offspring T1D.

1. Introduction

Type 1 diabetes [T1D] is the result of autoimmune destruction of insulin-producing pancreatic islet beta cells. It is a serious condition where survival depends on daily insulin injections. The incidence of T1D in Sweden is the second highest in the world, surpassed only by Finland (Green and Patterson, 2001, Karvonen et al., 2000). The aetiology of T1D is only partly understood, but it is widely accepted that genetic and non-genetic factors act together to initiate and accelerate the development of T1D (Daneman, 2006; Lernmark, 1999). One hypothesis is that T1D results from the action of environmental factors on genetically predisposed individuals (Mehers and Gillespie, 2008).

There is more evidence for the genetic risk of the disease than the potentially contributing environmental factors (Regnéll and Lernmark, 2013). The Human Leukocyte Antigen [HLA] system is linked to the immune system and is located on chromosome 6p21. It is a highly variable region of the human genome, and HLA haplotypes can act in both a risk-enhancing and protective way. One or both of the susceptibility haplotypes with alleles at the DQA1 and DQB1 loci are present in 90–95% of young children developing T1D, whereas the protective haplotype is present in less than 0.1% of T1D cases (Regnéll and Lernmark, 2013; Mehers and Gillespie, 2008). The main mechanism of action of these molecules is their peptide-binding activity in antigen-presenting cells (Regnéll and Lernmark, 2013).

But only 6% of the individuals with the highest known genetic risk of developing T1D actually develop T1D, emphasising the importance of environmental triggers in disease development (Ilonen et al., 2002). Several perinatal environmental factors have been suggested to trigger the development of T1D, such as viral infections, intrauterine growth and diet, although none of them has been unequivocally confirmed (Regnéll and Lernmark, 2013). Studies from the US have given the first indications that air

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pollution may be a risk factor for T1D (Hathout et al., 2002, 2006). Hathout and colleagues found an association between early-life exposure to sulphate (SO_4^{2-}) and ozone (O_3), with increased risks of developing T1D (odds ratios [OR] of 2.89 and 1.65, respectively). Exposure to particles, measured as PM_{10}, was associated with the development of T1D before the age of 5 years with an OR of 3.32 (Hathout et al., 2002). To date, no further studies in this field, to the best of the authors' knowledge, have been performed

Evidence is scarce regarding sensitive exposure windows of the hypothesised association between environmental factors and the risks of developing T1D. It has been suggested that T1D is likely to originate from gene–environment interactions during foetal development (Howard et al., 2011). Recent evidence provides a convincing link between a suboptimal gestational environment and an increased risk of onset of metabolic diseases (Joss-Moore and Lane, 2009). Most cases (94%) of T1D can be predicted by detecting multiple islet autoantibodies in children below the age of five years, supporting the hypothesis that the autoimmune processes occur early in life (Regnéll and Lernmark, 2013; Mehers and Gillespie, 2008).

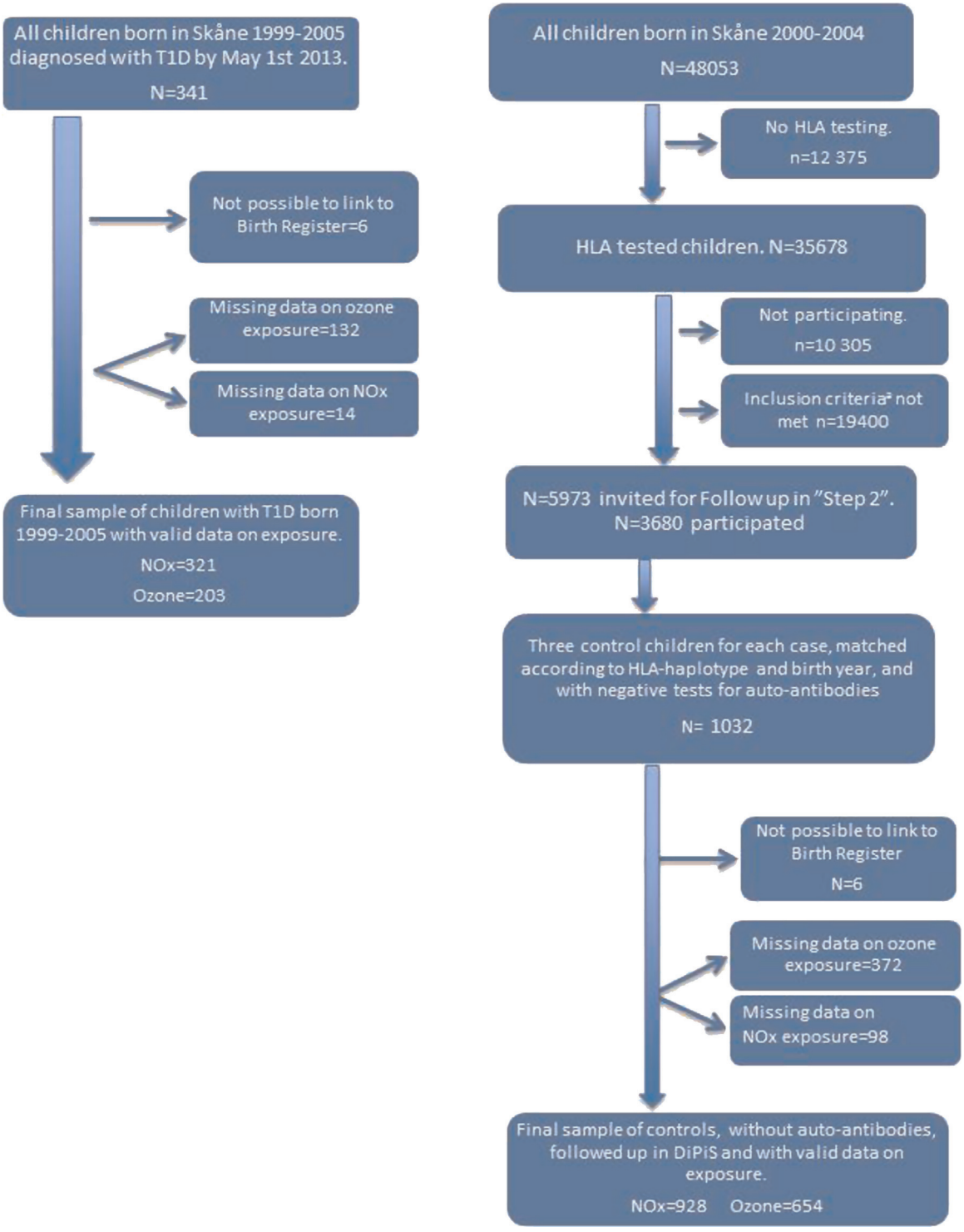

Fig. 1. Flowchart describing how cases and controls stipulates study population.