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Socioeconomic conditions and type 1 diabetes in childhood in North Rhine–Westphalia, Germany

J.-B. du Prel · A. Icks · M. Grabert · R. W. Holl · G. Giani · J. Rosenbauer

Abstract

Aims/hypothesis The aim of the study was to investigate the relationships between childhood type 1 diabetes and socioeconomic conditions, which might provide clues to the aetiology of the disease.

Materials and methods In an ecological study, we investigated the relationships between socioeconomic conditions and the incidence of type 1 diabetes incidence among children aged 0–14 years in North Rhine–Westphalia (NRW), Germany, between 1996 and 2000 at the level of the 33 districts. Incidence data were obtained from the population-based NRW diabetes register and regional socioeconomic data from official statistics. Associations were assessed by Poisson regression models and Bayesian conditionally autoregressive regression models (CAR).

Results In simple Poisson regression, population density, proportion of non-German nationals in the population, measures of income, education and professional training, and deprivation scores were significantly associated with diabetes risk ($p<0.01$). An increase of about one interquartile range (IQR) in population density, proportion of non-German nationals or household income was associated with a 9–12% decrease in diabetes incidence. A rise of about one IQR in income ratio, measures of education and professional training, or in deprivation score (high values correspond to high deprivation) was associated with an 8–12% incidence increase. There was a significantly 'linear' increasing incidence trend across five deprivation classes (relative risk: 1.06; 95% CI: 1.03–1.09). All associations were confirmed when overdispersion and spatial autocorrelation were accounted for in Poisson and CAR models.

Conclusions/interpretations The results raise the possibility that the risk for type 1 diabetes is higher for children living in socially deprived and less densely populated areas. Subsequent investigations are necessary to verify the observed ecological relations at the individual level and to identify the causal factors behind the socioeconomic indicators.

Keywords Aetiology · Children · Ecological study · Incidence · Socioeconomic conditions · Type 1 diabetes

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Abbreviations

CAR model	conditionally autoregressive regression model
DPV	diabetes software for prospective disease documentation
ESPED	Erhebungseinheit für seltene pädiatrische Erkrankungen in Deutschland (German paediatric surveillance system)
EURODIAB ACE	European Diabetes: Aetiology of childhood diabetes on an epidemiological basis

IQR   interquartile range
NRW   North Rhine–Westphalia

Introduction

The incidence of type 1 diabetes mellitus in children is increasing worldwide, with wide variation among countries, particularly in those in Europe [1, 2]. In Germany, the annual rise in incidence has been estimated to be 3.6% [3], slightly above the average increase in Europe (3.2%) and the world (3.0%) [1, 2].

Despite decades of intensive research, the aetiology of type 1 diabetes is not fully understood. The low concordance rate in monozygotic twins, the rising incidence in most countries over a short period and the adaptation of the diabetes incidence rate among Asian migrants to the incidence of the indigenous British population point to an important role of environmental factors in the pathogenesis of the disease [4]. Current aetiological models propose gene–environment interactions, presuming that certain environmental exposures lead to the initiation of a T-cell-mediated autoimmune process in genetically susceptible individuals, which results in the destruction of the pancreatic islet cells [4]. External factors suggested to play a role in this autoimmune process are viral infections, pre-, peri- and postnatal influences, nutritional factors, psycho–social influences and stressful life events [4, 5].

The effects of socioeconomic conditions on children's health are generally accepted [6]. In Germany, as in other European countries, the growing social inequality among children is a serious problem [6]. Epidemiological studies on the association between social status and type 1 diabetes in children have reported conflicting results, finding positive [7–17], inverse [18–25] or no associations [26–28]. Likewise, the results of studies on the relation with population density and with urban versus rural areas are contradictory [10, 13, 14, 17, 19, 29, 30]. Conflicting results might be due to differences in study design, in the degree of aggregation of data in ecological studies, in assessment of socioeconomic status and in confounding factors. However, the aetiological effect of socioeconomic factors on type 1 diabetes autoimmunity might truly differ by population and geographical setting, possibly due to differences in genetic background and gene–environment interactions.

The aim of this ecological study was to investigate the relationships between socioeconomic conditions and the incidence of type 1 diabetes in a large at-risk population in Germany. Results of this exploratory data analysis could be the basis for further confirmatory investigations.

Subjects and methods

Study design, study region and study population This ecological study was based on the geographical level of 33 census tracts of the federal state of North Rhine–Westphalia (NRW) located in western Germany. Regional incidences of type 1 diabetes in children aged up to 14 years in the years 1996–2000 were correlated with socioeconomic conditions between 1991 and 2001 at census tract level. NRW is the most heavily populated German federal state with an area of 34,081 km². The average total population between 1996 and 2000 was about 18 million. About one-quarter of all children under 15 years of age in Germany live in NRW. During the study period, the average number of children up to 14 years of age was 2,931,927.

Data collection, diabetic cases and socioeconomic indicators In 1993, the German Diabetes Centre started a prospective population-based childhood type 1 diabetes register covering incident diabetic cases under 15 years of age. Since the register is part of the European Diabetes: Aetiology of childhood diabetes on an epidemiological basis (EURODIAB ACE) research network, new cases are recorded according to the EURODIAB ACE protocol [1, 3]. Until 1995, the register was confined to southern parts of the administrative region of Düsseldorf within NRW. In 1996, the catchment area of the register was extended to the total of NRW, and since 2002 new cases up to the age of 34 years have been registered. The primary data source for incident cases of diabetes is a well-established active hospital-based surveillance system for rare childhood diseases in Germany that is operated on the basis of monthly report cards and is known as Erhebungseinheit für seltene pädiatrische Erkrankungen in Deutschland (ESPED, German paediatric surveillance system) [31]. Amongst others, ESPED also serves as data source for a nationwide register on type 1 diabetes covering children under 5 years of age [32]. Within NRW, ESPED covers all paediatric as well as internal departments. When a child with newly diagnosed diabetes is registered by ESPED, the German Diabetes Centre is informed and sends questionnaires for the treating physician to the reporting institutions. Registration of cases is completed by two secondary data sources: an annual practice survey among paediatricians, general practitioners and internists performed by the German Diabetes Centre, and the computer-based diabetes software for prospective disease documentation (DPV) of the Department of Epidemiology at the University of Ulm [33]. The DPV was originally set up for quality management in paediatric diabetes care. It is a nationwide database for diabetes research and now comprises more than 100 centres, all of which are members of the German Working Group for Paediatric Diabetology.

The NRW diabetes register provided regional estimates of the type 1 diabetes incidence. In total, 2,499 children with type 1 diabetes in the 0–14-year-old age range were registered from 1996 to 2000 and included in this analysis. Of these, 1,282 (51.3%) were male. Distribution of registered children by age was as follows: 0–2 years, 253 (10.1%); 3–5 years, 431 (17.2%); 6–8 years, 555 (22.2%); 9–11 years, 675 (27.0%); and 12–14 years, 585 (23.4%). Cases were assigned to the 33 census tracts according to the postal code of residence at onset of diabetes. Registration of cases by data sources is presented in Table 1. Completeness of ascertainment for total NRW was estimated to be 96.6% (95% CI: 96.1–97.1%) by a three-sources capture–recapture method applying a log-linear model [34]. Across census tracts, the completeness of ascertainment ranged between 92.6 and 100%.

Demographic and socioeconomic data at census tract level were provided by the national and federal state statistical boards. Data on population, population density, proportion of welfare recipients and non-German nationals (defined by nationality according to criteria of official statistics), unemployment rate and total living space were taken from annually updated official statistics covering the total population. Data on population income and household income, education, professional training and proportion of single-parent families were taken from census tract files. The German microcensus is an annual survey of a representative 1% sample of all German households [35]. Definitions of socioeconomic indicators and the calendar years for which respective data were available are given in Table 2.

In order to accentuate the regional social gradient, for each central social indicator (population income, education, professional training) an additional socioeconomic indicator was defined as ratio of the most to the least deprived proportion of the population (Table 2). High values for these indicators correspond to areas of high deprivation. In addition, an unweighted additive score of deprivation was derived from these ratios as overall proxy for regional socioeconomic conditions. Census tracts were ranked according to deciles of each of these indicators (range of scores: 1–10), high scores being correlated to high deprivation. The deprivation score (range: 3–30) was calculated by summing up the three individual scores. By classifying the deprivation score into quintiles, a deprivation class (range: I–V, with class V representing the most deprived areas) was assigned to each census tract.

Statistical methods For all socioeconomic variables a weighted average was calculated from the available calendar year-specific values to give one respective figure for each census tract. Thus, the basis for the analysis was a dataset with 33 observation units, one for each census tract, with socioeconomic variables, number of cases and population at risk in the age between 0 and 14 years. To account for possible different age- and sex-distributions between census tracts this basic data set was subdivided by sex and five 3-year age groups (0–2, 3–5, 6–8, 9–11 and 12–14 years) while replicating the socioeconomic variables for the census tracts. The resulting data set for analysis comprised 330 observations, with ten sex-by-age strata for each of the 33 census tracts.

The incidence of type 1 diabetes was estimated by assuming a Poisson distribution for cases of newly diagnosed diabetes. Descriptive statistics (median, interquartile range [IQR], minimum, maximum) were calculated to characterise regional distributions of the incidence of type 1 diabetes and socioeconomic indicators. Spearman's rank-order correlation coefficient was used to test bivariate monotonic correlations between socioeconomic indicators. In addition, a scatterplot matrix was generated to visualise associations between the social variables. Associations between the incidence of type 1 diabetes and socioeconomic conditions were analysed by Poisson regression models adjusting for sex and age. Corresponding relative risk estimates of type 1 diabetes related to sociodemographic indicators with 95% CIs are presented in terms of 'round increases' in the social indicators corresponding approximately to the IQRs. Chi squared tests were used to test for significance. Multiple Poisson regression analyses were performed to adjust for confounding among the sociodemographic and socioeconomic variables found to be significant in 'simple' Poisson regression. Apart from models including only two social indicators, more elaborate models were applied. Allowing for the high correlations between social indicators and the relatively small number of census tracts, these final multiple models included only one sociodemographic variable (population density or proportion of non-German nationals) and one indicator of income (income ratio or average household income per person) and education (education ratio or vocational training ratio); one of the variables unemployment rate and quota of welfare recipients was included at the same time. As the central parameters of socioeconomic status (income, education, professional training) were highly correlated, real associations between these variables and type 1 diabetes might have remained undetected in multiple regression analysis. We therefore analysed the deprivation score and the

Table 1 Number of registered cases by data source

ESPED	Medical practices/DPV			
	Yes/yes	Yes/no	No/yes	No/no
Yes	645	410	665	349
No	57	335	38	–

Table 2 Socioeconomic variables based on official statistics 1991–2001

Socioeconomic indicator and period where applicable	Definition[a] (unit of measure)	Median, interquartile range (minimum, maximum)
Total population[b] 1996–2000	Total census tract population (1,000 persons)	547.30, 167.45 (287.32, 961.98)
Census tract area[b]	Census tract area (km^2)	733.72, 1201.82 (104.84, 3286.10)
Population density[b] 1995–2000	Number of people per km^2 (persons per km^2)	777.57, 1733.39 (178.30, 2915.20)
Non-German nationals[b] 1995–2000	Non-German nationals in census tract population (%)	11.11, 4.26 (6.37, 19.52)
Income ratio[c] 1991–2001	Percentage of persons with <€511.29 income:percentage of persons with income ≥€1,533.88 income	0.88, 0.23 (0.58, 1.16)
Household income[c] 1991–2001	Household income per no. of persons per household (€/person)	811.48, 66.87 (713.87, 960.91)
Education ratio[c] 1991, 1993, 1995–2001	Percentage of working persons with secondary education:percentage of working persons with A-level education	3.11, 1.14 (0.88, 5.12)
Professional training ratio[c] 1991, 1993, 1995–2001	Percentage of working persons with apprenticeship:percentage of working persons with university degree	6.38, 2.45 (1.65, 11.58)
Living space[b] 1996–2000	Living space per no. of persons (m^2 per person)	37.25, 2.49 (33.61, 39.36)
Single-parent family[c] 1991–2001	Single-parent families among all families (%)	7.35, 0.66 (6.91, 10.07)
Unemployment rate[b] 1996–2000	Persons without a job among all persons capable of work (%)	11.43, 4.08 (7.80, 17.45)
Welfare recipients[b] 1996, 1997, 2000	Welfare recipients in census tract population (%)	3.61, 1.26 (2.18, 6.56)
Deprivation score	Additive score derived from the ratios for population income, education and professional training	17, 11 (4, 29)

[a] For each indicator a weighted average of calendar year-specific values was calculated at census tract level
[b] Data from annually updated official statistics covering the total population
[c] Data from census tract files

deprivation class indicator, as defined above, as explanatory variables in simple Poisson models. To test for trend across the deprivation classes the respective categorical indicator was included as continuous term in the Poisson model. We further investigated a possible interaction between age and deprivation class as well as differences between age-specific trends across deprivation classes in Poisson models. Consistently, using equal weights (0.5) for both sexes, directly sex-standardised incidence rates were estimated for the 25 age-by-deprivation-class strata.

To account for possible overdispersion of incidence rates in Poisson regression, estimates of standard errors of the regression parameters were multiplied by a scale factor (square root of [residual deviance/degrees of freedom]; dscale-option in the SAS procedure 'genmod') [36] and then used to estimate overdispersion-corrected confidence intervals for relative risks. To account for possible spatial autocorrelation beyond spatial heterogeneity (unstructured overdispersion), we applied Bayesian conditionally autoregressive regression models (CAR models) using the first-order adjacency pattern of census tracts [37–39]. WinBUGS software [37] was used to obtain point and credible interval estimates for the posterior distribution of regression parameters and relative risks. For each CAR-model we used two Markov chains for estimation. After a run-in phase until convergence of chains looked reasonable (assessed by visual inspection of trace plots and the Gelman-Rubin convergence statistic), 30,000 additional

samples were generated for each chain and used for estimation.

The statistical significance level was set to 5%. Correspondingly, confidence (credible) intervals were estimated at the level of 95%.

Statistical analyses were performed with SAS for Windows (Release 8.1; SAS Institute, Cary, NC, USA) or WinBUGS Version 1.4.

Results

Incidence of type 1 diabetes and socioeconomic indicators The overall incidence of type 1 diabetes among children aged 0–14 years in NRW between 1996 and 2000 was estimated to be 17.1 per 100,000 person–years (95% CI, 16.4–17.7). The median regional incidence during this period was 17.0 per 100,000 person–years (IQR 3.2). There was a roughly twofold difference in incidence rate between the area with the highest and that with the lowest incidence (23.1 vs 12.6 per 100,000 person–years).

The sociodemographic and socioeconomic variables also showed marked differences between census tracts (Table 2). Population density and the deprivation score showed the broadest variation between census tracts (assessed as ratio of IQR and median). Smallest variations were observed for household income, living space and quotas of single-parent

families, while the other social indicators showed intermediate differences between census tracts.

As expected, the various sociodemographic and socioeconomic variables were highly correlated (Electronic supplementary material [ESM] Fig. 1). There was a marked positive association between population density and proportion of non-German nationals; both sociodemographic indicators were positively associated with household income, unemployment and receipt of welfare benefits and inversely associated with living space. Indicators of income, education, professional training and the deprivation score were highly correlated in pairs. Furthermore, education ratio and vocational training ratio showed negative associations with living conditions (living space, single-

parent family). Living space was negatively associated with rate of unemployment and receipt of welfare benefits. Both latter conditions showed a high positive correlation.

Associations between type 1 diabetes incidence and socioeconomic indicators In simple Poisson regression analysis, all socioeconomic and sociodemographic indicators were closely associated with the incidence of type 1 diabetes, except for living space and single-parent family (Table 3). The strongest relations were observed for population density, indicators of income and the deprivation score. Adjusted for sex and age, increases in population density or average household income per person by approximately one IQR (1,700 persons/km^2 or €70,

Table 3 Poisson regression analyses: socioeconomic variables and type 1 diabetes incidence in children <15 years, 1996–2000, NRW

Socioeconomic indicator (unit of measure where applicable); period	Simple Poisson regression[a]		Multiple Poisson regression[b]		Multiple Poisson regression[b]	
	Relative risk (95% CI)	p value	Relative risk (95% CI)	p value	Relative risk (95% CI)	p value
Population density[c] (1,000 citizens per km^2); 1995–2000	0.878 (0.813–0.948)	<0.001	–	–	0.961 (0.834–1.106)	0.576
Non–German nationals[d] (%); 1995–2000	0.912 (0.871–0.955)	<0.001	0.978 (0.917–1.042)	0.483	–	–
Income ratio[e]; 1991–2001	1.122 (1.071–1.176)	<0.001	1.095 (1.033–1.161)	0.002	–	–
Household income per person[f] (€ per person); 1991–2001	0.889 (0.843–0.936)	<0.001	–	–	0.895 (0.812–0.987)	0.027
Education ratio[g]; 1991, 1993, 1995–2001	1.079 (1.028–1.132)	0.002	1.018 (0.958–1.082)	0.558	–	–
Professional training ratio[h]; 1991, 1993, 1995–2001	1.083 (1.026–1.143)	0.004	–	–	0.988 (0.903–1.080)	0.773
Living space per person[i] (m^2 per person); 1996–2000	1.045 (0.981–1.114)	0.173	–	–	–	–
Single-parent families[j] (%); 1991–2001	0.981 (0.944–1.020)	0.333	–	–	–	–
Unemployment rate[k] (%); 1996–2000	0.913 (0.858–0.970)	0.003	0.938 (0.866–1.015)	0.111	–	–
Welfare recipients[l] (%); 1996, 1997, 2000	0.950 (0.908–0.994)	0.026	–	–	0.986 (0.917–1.060)	0.698
Deprivation score[m]; 1991–2001	1.112 (1.056–1.172)	<0.001	–	–	–	–

[a] Models including sex, age and each socioeconomic indicator separately
[b] Model including sex, age and all socioeconomic indicators with risk estimates presented in this column
[c] Relative risk (RR) per increase of 1,700 persons per km^2
[d] RR per increase of 4%
[e] RR per increase of 0.2
[f] RR per increase of €70
[g] RR per increase of 1.1
[h] RR per increase of 2.5
[i] RR per increase of 2.5 m^2 per person
[j] RR per increase of 0.7%
[k] RR per increase of 4%
[l] RR per increase of 1.3%
[m] RR per increase of 10

respectively) were associated with an 11 to 12% decrease in diabetes risk. A respective increase in income ratio by 0.2 or deprivation score by 10 (high values correspond to low income and high deprivation) was associated with an 11 to 12% rise in diabetes incidence in children under 15 years old. Proportion of non-German nationals, unemployment rate and other central indicators of socioeconomic status (education, professional training) showed somewhat weaker associations with diabetes risk. An increase of about one IQR (4%) in proportion of non-German nationals and unemployment rate was associated with a 9% decrease in diabetes incidence. The relative risks associated with a respective increase in educational ratio by 1.1 or in vocational training ratio by 2.5 were estimated to be about 1.08. The rate of welfare recipients had only a minor effect on the incidence of type 1 diabetes.

Results of multiple Poisson regression Population density had no independent effect on type 1 diabetes incidence after adjustment for the proportion of non-German nationals in the local population ($p > 0.7$). Likewise, the effects of unemployment rate and receipt of welfare benefits disappeared when adjusting for one of these sociodemographic variables ($p > 0.2$). Education ratio and professional training ratio had no independent influence on diabetes risk when adjustment was made for one of the income variables ($p > 0.2$). In contrast, the effect of household income on diabetes incidence only disappeared when adjusting for income ratio ($p > 0.4$).

In accordance with the results of the simple analyses, the marked associations between both variables of income and diabetes incidence held in the more elaborate multiple regression models (Table 3). The relative risks for the other socioeconomic indicators were attenuated and became no longer significant.

The effect of the deprivation score, as a composite index of socioeconomic conditions, on the type 1 diabetes incidence held after adjustment for the sociodemographic indicators (population density, proportion of non-German nationals). An increase in the deprivation score of ten was associated with a 1.08-fold increase (95% CI, 1.02–1.15) in diabetes incidence.

Association between and type 1 diabetes incidence and deprivation class by age Sex-adjusted incidence rates suggested that diabetes risks related to deprivation classes varied between age groups (Fig. 1). In particular, the estimated age-specific risk trends across deprivation classes appeared to be more distinct in young children of 0–8 years. Corresponding relative risk estimates from Poisson models are presented in Table 1 of the ESM. According to a test for trend of the age-specific trends (age-specific slopes in Poisson model) the effect of social deprivation on type 1
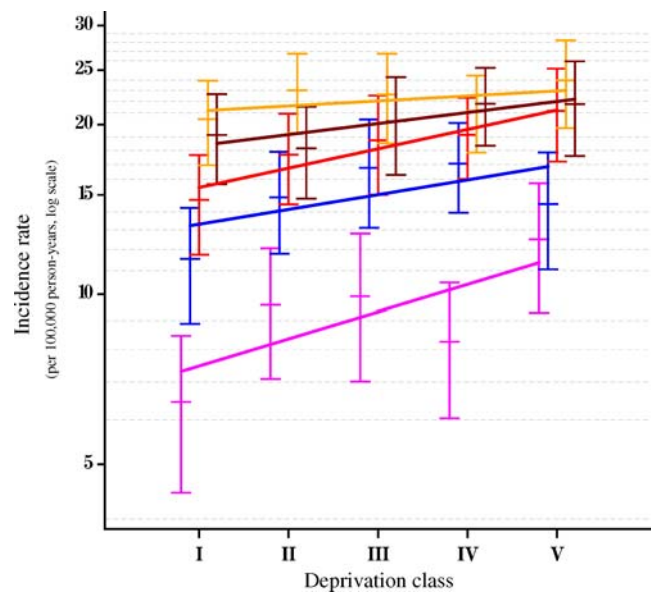

Fig. 1 Directly sex-standardised incidence rates by age and deprivation class and age-specific trends across deprivation classes estimated by Poisson regression. Colour key for age groups: *pink*, 0–2 years; *blue*, 3–5 years; *red*, 6–8 years; *orange*, 9–11 years; *dark brown*, 12–14 years

diabetes risk tended to diminish continuously with increasing age ($p = 0.153$). The trend across deprivation classes was estimated to decrease for consecutive age groups (relating to an increase of 3 years in age) by a factor 0.984 (95% CI: 0.963–1.006).

Independently of age, diabetes risk of children aged 0–14 years old was estimated to be 30% (95% CI: 14–48%) higher in the most deprived areas compared with the least deprived areas. There was an overall markedly 'linear' increasing trend in the risk for type 1 diabetes with increasing social deprivation (ESM Table 1).

Overdispersion and spatial autocorrelation Incidence rates showed no serious overdispersion or spatial autocorrelation. Consistently, overdispersion-corrected risk estimates from Poisson regression and estimates from CAR models complied very well with the estimates from ordinary Poisson models (ESM Tables 1 and 2). In part, 95% CIs from CAR models were somewhat wider than respective confidence intervals from Poisson regression, but without affecting the interpretation of results.

Discussion

The results of this ecological study in NRW, Germany, indicate that the incidence of type 1 diabetes in childhood is higher in geographical areas with socioeconomic deprivation, lower population density and a lower proportion of

non-German nationals in the local population. The associations between indicators of income and diabetes incidence were confirmed in multiple regression analysis. There was a markedly increasing trend of diabetes risk with increasing socioeconomic deprivation, assessed by a composite deprivation class index derived from income, education and professional training. This is of special interest given the strong correlations between these variables. Importantly, the effect of social deprivation on the type 1 diabetes risk was indicated to diminish with increasing age.

The incidence of type 1 diabetes was estimated from one of the largest incidence registries in Europe, with high ascertainment and only minor variation among geographical areas. Thus, the regional incidence estimates based on 2,499 cases can be assumed not to be biased. Further, regional socioeconomic conditions were assessed from a broad spectrum of socioeconomic indicators taken from annually updated official statistics for the total population or from a standardised, continuous household sample survey (the German Microcensus). Thus, in contrast to many other ecological studies based on census data covering only a short period [9, 10, 12, 17, 19, 21, 26, 27], our socioeconomic data covered a reasonable time span.

'Ecological fallacy' might have played a role in the observed associations. Another source of bias might be the asymmetrical distribution of social classes within regional observation units. Regarding the large number of children in each observation unit this source of bias is unlikely. Possible bias due to different area-level risk populations was adjusted for in the Poisson regression analysis. In addition, results were confirmed when accounting for spatial heterogeneity (overdispersion) and autocorrelation in Poisson and CAR models.

Socioeconomic risk factors for diseases act at the group level by the interaction of individuals. These effects are not covered by studies at the individual level ('individualistic fallacy') [40]. For this the ecological study design can be advantageous. In particular, measures from small areas might be better indicators of social conditions than individual measures [41]. With regard to this, however, our ecological study is possibly limited by the relatively high level of aggregation in the data.

The risk of cross-level bias due to misclassification and the risk of confounding might increase with rising level of aggregation. But larger areas present much less diversity [42]. In small area studies, low numbers of events in observation units might be a problem [42]. The higher aggregation level in this ecological study ensures both valid incidence estimates of the rare disease type 1 diabetes, and stable estimates of area-level socioeconomic indicators.

Several previous studies have shown an inverse relation between type 1 diabetes and population density [10, 13, 17, 19]. Of these, only those conducted in Scotland and

Yorkshire, UK, were small-area studies. In contrast, other studies showed higher incidences of diabetes in more densely populated (mostly urban) areas [29]. Other studies found no relation between population density and type 1 diabetes [13, 14, 30]. In the two studies conducted on a large scale [13, 14], a close inverse association was observed between population density and type 1 diabetes incidence, in accordance with our results and the so-called 'hygiene hypothesis' [43]. Our observed associations might, however, have been attributable to confounding due to the proportion of non-German nationals in the local population, because no effect of population density was detectable after adjustment for this factor. The observation of a lower incidence of type 1 diabetes in areas with a higher proportion of non-German nationals is consistent with the fact that the ethnic origin of more than three-quarters of children of non-German origin under 15 years of age in NRW is Mediterranean (Greece, Italy, Turkey, former Yugoslavia) or Polish. In these countries, the risk for type 1 diabetes is known to be lower than in NRW [1, 2].

Several studies have shown a positive relationship between type 1 diabetes and socioeconomic status [7–17]. While small-area ecological data were used in some of these studies [9, 10, 12, 17], only four indicated an association between socioeconomic status and type 1 diabetes at the individual level. One of these was a prospective cohort study [8], which was clearly underpowered, having a loss to follow-up of nearly one-third and covering only 18 cases of type 1 diabetes. Two case-control studies in the UK and one in the USA were larger and were based on socioeconomic data from questionnaires and interviews [11, 15, 16]. However, the results of the study in Scotland, where no association was observed, were inconsistent with those in Northern Ireland [16]. In at least one study in the UK, possible selection bias was discussed, and a high incidence of diabetes was found among the children of unemployed fathers in northern England and Wales [11]. Other studies showed no relation between social status and type 1 diabetes [26–28].

In simple regression, we found an inverse association between the rates of unemployment and welfare recipients and type 1 diabetes risk, contrasting with our results relating to the other socioeconomic indicators. However, the effects of unemployment and receipt of welfare benefits might be due to confounding, because they disappeared when adjusting for population density or proportion of non-German nationals. In addition, no relevant associations were observed with living space per person or proportion of single-parent families; but both indicators showed only little regional variation across census tracts.

Several studies have indicated an association between lower socioeconomic status and a higher incidence of type 1 diabetes [18–25], in accordance with our prevailing

results. One of these studies included a small-area analysis, and several case-control studies have indicated an inverse correlation between socioeconomic status and type 1 diabetes at the individual level [20, 22, 25]. Although case-control studies are the preferred design for investigating risk factors for rare diseases, differential selection bias cannot be excluded completely in these studies. Families of higher social status, in particular those of unaffected controls, tend to participate more frequently in such studies than families of low social status. Overmatching might have played a role in two studies [20, 22], as control subjects were taken from the same counties or were classmates of cases in one study. Despite these potential sources of bias, it is remarkable that the results of these large case-control studies are consistent with our findings.

The observed relationship between low socioeconomic status and high risk for type 1 diabetes might be due to differences in lifestyle or nutrition. In particular, the duration of breast-feeding is usually longer in mothers of higher social classes and associated with a reduced risk of type 1 diabetes [11, 20, 22]. Social differences in hygiene and the risk of getting infected with a diabetogenic microorganism triggering autoimmunity might be another explanation [4].

In summary, we hypothesise, on the basis of our results, that the risk for type 1 diabetes is higher among children living in socially deprived, less densely populated geographical areas and areas with a low proportion of non-German nationals. Well-performed case-control studies or, preferably, very large cohort studies are required to prove our hypotheses and to clarify the conflicting results of earlier studies. Subsequent identification of causal risk factors for type 1 diabetes could provide clues for prevention and therapy. In view of the considerable individual and social burden of the disease, such efforts would be worthwhile.

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