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Associations of area deprivation and urban/rural traits with the incidence of type 1 diabetes: analysis at the municipality level in North Rhine-Westphalia, Germany

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What's new?

- Socio-economic and environmental variables are suggested to influence the risk of type 1 diabetes.
- For the first time, an Index of Multiple Deprivation and urban/rural traits were associated with the geographical variation in type 1 diabetes incidence in children and adolescents at the municipality level in Germany.
- Children and adolescents aged 0–19 years living in more remote, less densely populated or less deprived areas were at a higher risk of developing type 1 diabetes.
- Urban/rural traits were stronger predictors of type 1 diabetes risk than indicators of area deprivation.

Abstract

Aim To analyse the associations of area deprivation and urban/rural traits with the incidence of type 1 diabetes in the German federal state of North Rhine-Westphalia.

Methods Data of incident type 1 diabetes cases in children and adolescents aged <20 years between 2007 and 2014 were extracted from a population-based diabetes register. Population data, indicators of area deprivation and urban/rural traits at the municipality level (396 entities) were obtained from official statistics. Area deprivation was assessed in five groups based on quintiles of an index of multiple deprivation and its seven deprivation domains. Poisson regression accounting for spatial dependence was applied to investigate associations of area deprivation and urban/rural traits with type 1 diabetes incidence.

Results Between 2007 and 2014, 6143 incident cases were reported (99% completeness); the crude incidence was 22.3 cases per 100 000 person-years. The incidence decreased with increasing employment and environmental deprivation (relative risk of the most vs. the least deprived municipalities: 0.905 [95% CI: 0.813, 1.007] and 0.839 [0.752, 0.937], respectively) but was not associated with the composite deprivation index. The incidence was higher in more peripheral, rural, smaller and less densely populated municipalities, and the strongest association was estimated for the location trait (relative risk of peripheral/very peripheral compared with very central location: 1.231 [1.044, 1.452]).

Conclusions The results suggest that the type 1 diabetes risk is higher in more remote, more rural, less densely populated and less deprived areas. Urban/rural traits were stronger predictors of type 1 diabetes risk than area deprivation indicators.

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<H1>Introduction

Type 1 diabetes is an autoimmune disease that develops in genetically susceptible individuals and is triggered by environmental factors [1]. The incidence of type 1 diabetes in children has shown an increasing trend worldwide, with annual increases of 4.0% in Asia, 3.2% in Europe, 5.3% in North America [2] and 3.4% in Germany [3]. Several studies have reported regional differences in the incidence of type 1 diabetes. Thus far, the high regional variability in type 1 diabetes incidence among and particularly within countries remains unexplained [4,5] but has been attributed to environmental influences and socio-economic conditions [5-8]. Some studies have investigated the relationships between type 1 diabetes incidence, deprivation and the degree of urbanization in several countries at different area levels (Northern Ireland

[5], USA [7], Finland [9], Austria [10] and the UK [11]) but reported contradictory results. While some studies observed an inverse relationship between the risk of type 1 diabetes and deprivation levels [7,8,11,12], other studies found a positive relationship [13], and some studies did not confirm a relationship [14]. Similarly, studies investigating associations with the population density and level of urbanization reported inconsistent results [8-12,15].

A previous study conducted in the German federal state of North Rhine-Westphalia (NRW) showed that the type 1 diabetes risk is higher among children living in more socially deprived or less densely populated areas [6]. This study was confined to the age group of 0–14 years, the period between 1996 and 2000, and the district level. However, to date, the associations between area deprivation and type 1 diabetes have not been evaluated at the municipality level, which is the lowest administrative level in Germany.

The German Index of Multiple Deprivation was implemented as a measure of area deprivation based on an established British method [16] and was validated in several studies showing associations between area deprivation and type 2 diabetes and other health-related factors [17]. Furthermore, the German Index of Multiple Deprivation was previously used to jointly analyse the associations of area- and individual-level socio-economic conditions with quality of life and glycaemic control in adolescents with early-onset type 1 diabetes [18]. However, the German Index of Multiple Deprivation has not been applied to assess the impact of area deprivation on the type 1 diabetes risk in Germany.

Therefore, the aims of the current study were to analyse the geographical variation in type 1 diabetes incidence in children and adolescents at the municipality level in

NRW, Germany, and to investigate its associations with area deprivation and urban/rural traits.

<H1>Methods

<H2>Study population

This study was carried out in NRW, which is the most populous German federal state located in Western Germany, comprising an area of 34 081 km^2, with a population of ~ 17.6 million people in 2014 (22% of the total population of Germany). The administrative structure (districts and municipalities) of NRW is shown in Figure S1. Data regarding incident type 1 diabetes cases were selected from the NRW diabetes register, which has been maintained by the German Diabetes Centre since 1996 [2,3]. The NRW register had been approved by the responsible data protection agency of NRW. The register ascertains incident cases by three data sources, a hospital-based active surveillance system, annual practice surveys and the nationwide Diabetes Prospective Follow-up register [19]. Children and adolescents with type 1 diabetes onset of <20 years from 2007 to 2014 were included. The completeness of the case ascertainment was estimated to be 98.7% (95% CI: 98.5%, 98.8%) by applying a main effects log-linear model [20] to the cross-classification table of the cases registered by the three data sources (Table S1). The cases were assigned to the 396 municipalities of NRW by the postal codes of individuals' residences at diabetes onset. The population data were obtained from the Statistical State Office of NRW [21].

<H2>Area deprivation

To quantify area deprivation, we used the North Rhine-Westphalian Index of Multiple Deprivation for 2010 (NRW-IMD-2010), which is a regional version of the German Index of Multiple Deprivation-2010 [22]. Like the German Index of Multiple Deprivation-2010, the NRW-IMD-2010 combines official information from seven deprivation domains from 2010 (income, employment, education, municipal revenue, social capital, environment and security) to quantify different dimensions of material and social deprivation [22]. Further details of the deprivation indicators are provided in Table S2. All municipalities of NRW were categorized into five groups with increasing deprivation (termed quintile groups Q1 to Q5 and coded 1 to 5 for analysis) according to the quintiles of the NRW-IMD-2010 and its seven deprivation domains.

<H2>Urban/rural traits

The urban/rural traits were obtained from the Federal Institute for Research on Building, Urban Affairs and Spatial Development [S4,S5] or EUROSTAT [S6]. The details of the urban/rural indicators (location, settlement structure, city/town type and degree of urbanization) are provided in Table S3.

<H2>Statistical analysis

The crude incidence rates were estimated according to the person-years method assuming a Poisson distribution of the cases. Indirectly standardized incidence ratios were estimated as the ratio of the observed and sex- and age-standardized expected number of incident cases at the municipal level to account for differences in the sex and age distribution across the municipalities (Table 1).

<INSERT TABLE 1>

The spatial distributions of the standardized incidence ratios, the NRW-IMD-2010 and its deprivation domains, and urban/rural traits, were analysed descriptively (median, interquartile range, minimum, first and third quartiles, maximum) and plotted on quintile-based choropleth maps [23] using ArcGIS 10.4.1 software (ESRI, Redlands, CA, USA). Spearman's rank correlation coefficient was used to assess the bivariate correlations between the quintile groups of the NRW-IMD-2010 and its deprivation domains and urban/rural traits.

The municipality level crude type 1 diabetes incidence and standardized incidence ratios showed a weak spatial autocorrelation (Moran's I [24]: 0.069 [95% CI: 0.010, 0.128] and 0.068 [0.009, 0.127], respectively), indicating spatial dependence. To account for this spatial dependence, the associations between the type 1 diabetes incidence/standardized incidence ratios and the NRW-IMD-2010, its deprivation domains and urban/rural traits were assessed by Gaussian intrinsic conditional autoregressive (ICAR) Poisson regression models that included a spatially correlated and normally distributed random intercept term [S8]. The details of the ICAR Poisson model are provided in the supporting information. Briefly, the logarithm of the number of observed incident cases was modelled as a linear term of the covariates (NRW-IMD-2010, deprivation domains and urban/rural traits) and a spatially correlated random intercept. The logarithm of the expected incident cases was used as an offset variable.

First, each covariate was analysed separately as a categorical variable in an ICAR Poisson model. To identify trends across categories, each covariate was additionally analysed as a linear ordinal variable. The deprivation domains and urban/rural traits were further analysed by a multivariable ICAR Poisson regression model to account for possible confounding. A stepwise forward selection approach was used to successively include all of the seven deprivation domain indicators and the four urban/rural traits as categorical variables in the model according to the corrected Akaike information criterion [25]. From the resulting 11 models, the model with the overall best data fit according to the corrected Akaike information criterion was chosen as the final model to estimate the adjusted associations. The final model was additionally fitted with covariates as linear ordinal terms.

The results of the ICAR Poisson regression analyses are presented as relative risk (RR) with the respective 95% confidence intervals (CIs). Furthermore, indirectly standardized incidence rates were estimated by multiplying the model-derived adjusted standardized incidence ratios (estimated as least square means assuming the random effect to be zero) by the crude overall incidence in NRW. For each ICAR model, the spatial variance parameter was estimated. Approximate F-tests were used to test for significance. In addition to the raw *P*-values, *P*-values adjusted for multiple testing according to the Benjamini–Hochberg procedure controlling for the false discovery rate [26] were calculated. The statistical significance level of the two-sided tests was set at 0.05. All statistical analyses were performed with SAS® version 9.4 (SAS Institute, Cary, NC, USA) and Stata® version 14.2 (estimation of Moran's I) software (StataCorp, College Station, TX, USA).

<H1>Results

Between 2007 and 2014, 6143 incident type 1 diabetes cases in children and adolescents aged 0–19 years were registered in NRW. Fifty-four percent of the cases were in males, and the mean age at onset (SD) was 9.7 (4.5) years, while the median (first quartile, third quartile) was 9.9 (6.3, 13.2) years. The crude overall incidence (95% CI) was estimated to be 22.3 (21.7, 22.8) per 100 000 person-years. Table 1 shows the age- and sex-specific incidence rates. The highest incidence was observed among boys aged 10–14 years and girls aged 5–9 years. Among youths aged 15–19 years, the incidence was considerably higher in boys than in girls.

<H2>Spatial distribution of type 1 diabetes incidence, area deprivation and urban/rural traits

At the municipality level, the median crude type 1 diabetes incidence was 22.7 (range 0–55.7) per 100 000 person-years, and the median standardized incidence ratio was 1.0 (range 0–2.5). Further descriptive parameters of the incidence, the distribution of the NRW-IMD-2010 and its deprivation domains, and urban/rural traits across the municipalities are given in Tables S4 and S5. In some cases, the indicators of deprivation and urban/rural traits were highly correlated (Table S5).

The spatial distribution of the incidence and the quintile groups of the NRW-IMD-2010 and its deprivation domains, as well as the urban/rural traits at the municipality level, are shown in Figs 1 and S2. A visual comparison of the spatial distributions indicates a lower incidence in more deprived areas, at least in the employment and environmental deprivation domains. Furthermore, the incidence was higher in more peripherally located, more rural, smaller, and less densely populated municipalities.

<INSERT FIGURE 1>

<H2>Simple ICAR Poisson regression models

<H3>Area deprivation

Type 1 diabetes incidence slightly decreased with increasing deprivation as assessed by the NRW-IMD-2010. However, this association was not statistically significant, as indicated by the related RRs and standardized incidences (Table 2). The trend model indicated a 1.2% (-1.0%, 3.3%) decrease in the incidence per one-level increase in deprivation.

<INSERT TABLE 2>

The standardized incidences and respective RRs were consistently lower in areas with higher employment and levels of environmental deprivation. The incidence was 9.5% (-0.7%, 18.7%) lower in areas with the highest (Q5) compared with the lowest unemployment rate (Q1),and 16.1% (6.3%, 24.8%) lower in areas with the highest (Q5) compared with the lowest levels of environmental deprivation (Q1). The trend models showed a significant decrease in the incidence by 2.5% (0.3%, 4.7%) and 3.5% (1.3%, 5.6%) per one-level increase in employment and environmental deprivation, respectively, even after adjusting for multiple testing (Table 2).

The income, education, municipal revenue, social capital and security deprivation domains showed weak and less consistent, non-significant associations with type 1 diabetes incidence across the deprivation quintile groups (Table S6).

<H3>Urban/rural traits

All of the investigated urban/rural indicators were significantly associated with type 1 diabetes incidence in all trend models, even after adjusting for multiple testing (Table 2). The RRs and standardized incidences increased with increasing peripheral location, increasing rural settlement structure, decreasing population size and decreasing degree of urbanization of the municipalities. The trend models showed an incidence increase of 14.3% (8.0%, 20.9%), 7.6% (2.1%, 13.3%), 5.1% (1.0%, 9.3%) and 7.4% (2.1%, 13.0%) per increasing level of peripheral location and rural settlement structure and decreasing municipality size and degree of urbanization, respectively.

<H2>Multivariable ICAR Poisson regression models

The selection approach identified the multivariable ICAR Poisson model, which included employment deprivation and the urban/rural traits ‘location’ and ‘degree of urbanization’, as the best data-fitting model, as assessed by the corrected Akaike information criterion (data not shown). According to this model, the indicators of location, degree of urbanization and employment deprivation showed statistically significant associations with type 1 diabetes risk, even after adjusting for multiple testing (Table 3). The RR estimates of the levels of employment deprivation and location showed nearly the same patterns as the estimates from the simple ICAR models, but the RR estimates shifted towards 1, indicating somewhat weaker associations. Type 1 diabetes incidence was lower in municipalities with higher levels of employment deprivation (corresponding to higher unemployment) and higher in more peripherally located and less densely populated areas. The trend model of the location trait indicated an increase in the incidence by 12.6% (5.8%, 19.9%) per increasing level of peripheral location.

<INSERT TABLE 3>

In all ICAR Poisson regression models, the spatial variance parameter σ_{spat}^2 was estimated to be positive, confirming the approach considering the spatial autocorrelation in the spatial analyses. The point estimates from the models with a single indicator of deprivation or a single urban/rural trait (Tables 1 and S6) ranged between 0.050 and 0.071 and between 0.042 and 0.058, respectively. The multivariable ICAR Poisson regression models with categorical or linear ordinal covariates (Table 3) yielded somewhat lower estimates of 0.030 and 0.039, respectively.

<H1>Discussion

The results of this study indicate that the incidence of type 1 diabetes during childhood and adolescence tends to be higher in less deprived, more remote, rural, and less densely populated areas. Urban/rural traits appear to be more strongly associated with incidence than indicators of deprivation.

There was a decreasing trend of type 1 diabetes incidence with increasing area deprivation when deprivation was assessed through employment (unemployment rate) and environmental deprivation. However, the incidence was somewhat higher in areas with higher levels of income and education deprivation, whereas the composite deprivation index, NRW-IMD-2010, showed no association with incidence. This finding may be conditional on the observed opposing effects of the single deprivation domains, because the deprivation domains of employment, environment and security were inversely related to the incidence, while those of income, education municipal revenue and social capital showed positive associations.

Our results regarding area deprivation are consistent with the results reported in some European studies showing a higher incidence of type 1 diabetes in areas with lower levels of deprivation [5,7,8,11,12,15]. In addition, studies conducted in the UK and Canada showed that childhood-onset type 1 diabetes is more common in families with higher individual-level socio-economic status [4,27]. Thus, the observed associations between the area-level socio-economic status and type 1 diabetes incidence could be attributed to spatial patterns in the population composition of individual-level socio-economic status, which is related to differences in lifestyle and exposure to infections [6,8,28,29].

Our results seem to conflict with the findings of a previous study at the district level in NRW that reported a higher type 1 diabetes incidence in childhood between 1996 and 2000 in areas with a higher socio-economic deprivation score [6]. However, this deprivation score was an additive score of three deprivation indicators (income, education and professional training), which were all positively associated with incidence. By contrast, the NRW-IMD-2010 aggregated information from deprivation domains that were positively or inversely associated with the incidence of type 1 diabetes; thus, as previously mentioned, the effects of the single domains nearly cancelled each other out when aggregated. Notably, the results indicating a lower incidence in areas with high unemployment and a higher incidence in areas with higher income and education deprivation were consistent with the results of the previous study [6]. Thus, the current study actually confirms associations between socio-economic conditions and type 1 diabetes risk at the municipality level that have previously been observed at the district level.

Studies conducted in New Zealand and Australia found no evidence of an association between type 1 diabetes incidence and population density [14,30], which is contradictory to the present findings. However, in accordance with our results, a higher incidence of type 1 diabetes was reported in the least compared with the most disadvantaged socio-economic quintile group in the Australian study [30]. Furthermore, a significantly higher incidence was observed in urban communities in New Zealand [14], which is contradictory to the present results. Our results of the association between type 1 diabetes incidence and urban/rural traits are consistent with the findings of a previous German study [6] and findings from small-area analyses in other countries (Northern Ireland, Finland, Austria and the UK), which also reported a higher type 1 diabetes incidence in rural, sparsely populated and remote areas [5,8-11,15]. Consistent with previous reports [4,8,28], in the current study, the urban/rural traits, particularly the location indicator, were more strongly associated with type 1 diabetes risk than were the measures of socio-economic deprivation, according to the RR estimates and the model fit assessed by the corrected Akaike information criterion (data not shown).

The higher type 1 diabetes rates in sparsely populated areas could possibly be explained by the hypothesis that young children living in remote and sparsely populated areas experience reduced exposure to communicable infections during infancy and early childhood, which are believed to provide the necessary stimuli for regular development of the immune system [5,6,8,29].

The above-mentioned contradictory results related to both area deprivation and population density-related indicators (urban/rural traits) are difficult to explain. One factor to consider is the use of different area-level units and analytical scales, such as those based on different political or geographical subdivisions. In addition, the indicators and categories of deprivation and urban/rural traits are defined differently across studies.

Our study has several strengths and limitations. One weakness is the ecological design, which might be subject to ecological bias and cannot provide causal associations. Furthermore, the identification of the deprivation and urban/rural indicators that are most relevant for type 1 diabetes risk is complicated by the high correlations between various indicators (Table S5). An additional drawback is the use of people's residential addresses at the time of diagnosis for the assignment to municipalities, which may not be relevant for exposures occurring earlier in life if the child subsequently moved to the current residence. However, a major strength of our study is the use of incidence data with a very high degree of completeness in mainly small-area geographical units (municipalities). Additionally, the analysis of the urban/rural classification was performed using several variables to confirm the results. An additional strength is the application of the ICAR Poisson regression model explicitly considering the spatial autocorrelation of type 1 diabetes incidence.

In conclusion, the results suggest that type 1 diabetes risk is differentially distributed in NRW in Germany. Children and adolescents living in less deprived, more remote or less densely populated areas were at a higher risk of developing type 1 diabetes. Information regarding the small-area variation in type 1 diabetes incidence may help identify the underlying causal factors of the disease in future research.

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<H2>Competing interests

The authors declare that they have no conflicts of interest relevant to this article.

<H2>Ethical statement

<H1>References

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<H1>Supporting Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Table S1 Number of registered cases by data source.

Table S2 Deprivation domains and indicators of the North Rhine-Westphalian Index of Multiple Deprivation from 2010 (NRW-IMD 2010).

Table S3 Urban/rural traits.

Table S4 Distribution of the type 1 diabetes incidence (2007–2014) and deprivation domains across municipalities in North Rhine-Westphalia, Germany.

Table S5 Spearman's correlation coefficients between the quintile groups of the deprivation domains and urban/rural traits.

Table S6 Association between the type 1 diabetes incidence and the indicators of deprivation: results from simple Gaussian intrinsic conditional autoregressive (ICAR) Poisson regression models.

Figure S1 Municipalities of the Federal State of North Rhine-Westphalia (NRW), Germany.

Figure S2 Spatial distribution of the type 1 diabetes incidence and indicators of deprivation at the municipality level in NRW, Germany.

Gaussian Intrinsic Conditional Autoregressive Poisson Model.

<Tables>

Table 1 The incidence of type 1 diabetes in North Rhine-Westphalia, Germany, by sex and age between 2007 and 2014

Sex	**Age group (years)**	**Cases**	**Incidence (95% CI)[a]**
Boys	0–4	566	18.5 (17.0, 20.0)
	5–9	981	29.8 (27.9, 31.7)
	10–14	1245	33.6 (31.8, 35.5)
	15–19	515	12.6 (11.6, 13.8)
Girls	0–4	530	18.2 (16.7, 19.8)
	5–9	1015	32.4 (30.5, 34.5)
	10–14	985	28.0 (26.3, 29.8)
	15–19	306	7.9 (7.0, 8.8)

[a]per 100 000 person-years; 95% CI: 95% confidence interval

Table 2 The association between type 1 diabetes incidence and indicators of deprivation and urban/rural traits: results from simple Gaussian intrinsic conditional autoregressive (ICAR) Poisson regression models

Indicator of deprivation or urban/rural trait[a]	**Number of municipalities**	**Standardized incidence (95% CI)**[b]	**Relative risk (95% CI)**[b]	***P***[b]
NRW-IMD-2010				0.781 [c], 0.781 [f]
Q1 (1)	79	23.4 (21.6, 25.3)	1	
Q2 (2)	80	23.3 (21.5, 25.2)	0.997 (0.892, 1.114)	
Q3 (3)	78	22.2 (20.6, 23.9)	0.950 (0.852, 1.060)	
Q4 (4)	80	22.6 (21.1, 24.2)	0.968 (0.872, 1.075)	
Q5 (5)	79	22.2 (21.0, 23.5)	0.952 (0.863, 1.049)	
Trend		-	0.988 (0.967, 1.010)[d]	0.268[d,e], 0.444[d,f]
Employment deprivation				0.027 [c], 0.057 [e]
Q1 (1)	79	24.8 (22.6, 27.3)	1	
Q2 (2)	79	23.9 (22.0, 26.0)	0.965 (0.852, 1.094)	
Q3 (3)	80	23.0 (21.3, 24.8)	0.927 (0.822, 1.045)	
Q4 (4)	79	20.8 (19.4, 22.3)	0.839 (0.746, 0.944)	
Q5 (5)	79	22.4 (21.4, 23.6)	0.905 (0.813, 1.007)	
Trend		-	0.975 (0.953, 0.997)[d]	0.024[d,e], 0.047[d,f]
Environmental deprivation				0.029[c], 0.057[f]
Q1 (1)	79	25.8 (23.4, 28.5)	1	
Q2 (2)	79	23.3 (21.3, 25.4)	0.902 (0.792, 1.029)	
Q3 (3)	80	23.2 (21.5, 25.0)	0.899 (0.794, 1.018)	
Q4 (4)	79	22.7 (21.2, 24.3)	0.878 (0.779, 0.990)	
Q5 (5)	79	21.6 (20.7, 22.7)	0.839 (0.752, 0.937)	
Trend		-	0.965 (0.944, 0.987)[d]	0.002[d,e], 0.012[d,f]
Location				<0.001[c], <0.001[f]
Very central (1)	236	21.7 (20.9, 22.5)	1	
Central (2)	133	25.3 (23.8, 26.9)	1.168 (1.089, 1.253)	
Peripheral/very peripheral (3)[g]	27	26.7 (22.7, 31.4)	1.231 (1.044, 1.452)	
Trend		-	1.143 (1.080, 1.209)[d]	<0.001[d,e], <0.001[d,f]
Settlement structure				0.011[c], 0.055[f]
Predominantly urban (1)	219	22.0 (21.3, 22.8)	1	
Partially urban (2)	111	24.6 (22.9, 26.3)	1.115 (1.033, 1.205)	
Rural (3)	66	24.3 (21.5, 27.5)	1.105 (0.971, 1.257)	
Trend		-	1.076 (1.021, 1.133)[d]	0.007[d,e], 0.020[d,f]
City/town type				0.020[c], 0.057[f]
Large city (2)	28	20.9 (19.7, 22.1)	1	
Mid-sized city (2)	178	23.2 (22.3, 24.2)	1.112 (1.035, 1.194)	
Large town (3)	133	23.4 (21.8, 25.2)	1.123 (1.023, 1.232)	
Small town/rural community (4)[g]	57	23.5 (20.4, 27.2)	1.127 (0.964, 1.318)	
Trend		-	1.051 (1.010, 1.093)[d]	0.014[d,e], 0.034[d,f]
Degree of urbanization				0.014[c], 0.055[f]
Densely populated (1)	34	21.1 (20.0, 22.3)	1	
Intermediately populated (2)	274	23.2 (22.3, 24.1)	1.098 (1.026, 1.175)	
Sparsely populated (3)	88	23.9 (21.7, 26.2)	1.130 (1.013, 1.261)	
Trend		-	1.074 (1.021, 1.130)[d]	0.006[d,e], 0.020[d,f]

[a]Figures in parentheses represent the integer-valued coding of indicator categories for regression analysis.
[b]Estimated from separate models including a single indicator of deprivation or a single urban/rural trait as a categorical variable (if not stated otherwise); standardized incidences are given per 100 000 person-years.
[c]*P*-value from the approximate F-test for testing the hypothesis of no differences between the categories of the respective indicator.
[d]Estimated from separate models including a single indicator of deprivation or a single urban/rural trait as a linear ordinal variable.
[e]*P*-value from the approximate F-test for testing the hypothesis of no trend across the categories of the respective indicator.

[f] *P*-values according to [c] or [e], but adjusted for multiple testing according to the Benjamini-Hochberg procedure controlling for the false discovery rate [26]. The adjustment considered the NRW-IMD-2010 and all of the seven deprivation domain indicators and the four urban/rural traits listed in Tables 2 and S6, but was performed separately for indicators modelled as categorical or linear ordinal variables.
[g] The very peripheral and the peripheral location categories as well as the rural community and small town categories were combined in the analysis due to low numbers.
NRW-IMD-2010, North Rhine-Westphalian Index of Multiple Deprivation for 2010.
Q1-Q5: lowest to highest deprivation quintile groups.

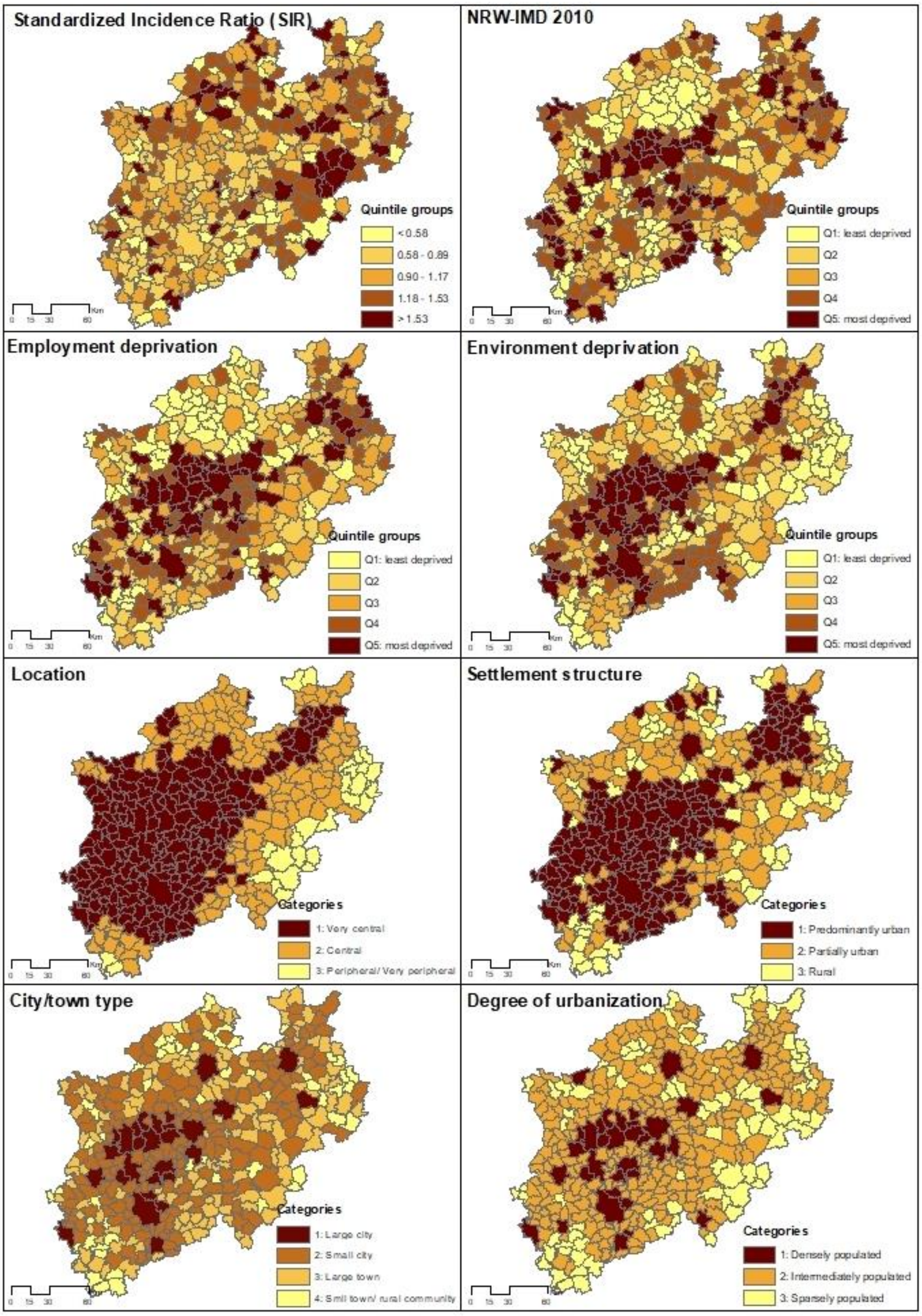
Table 3 The association between type 1 diabetes incidence and indicators of deprivation and urban/rural traits: results from the multivariable Gaussian intrinsic conditional autoregressive (ICAR) Poisson regression model

Indicator of deprivation or urban/rural trait[a]	**Number of municipalities**	**Standardized incidence (95% CI)**[b]	**Relative risk (95% CI)**[b]	***P***[b]
Employment deprivation				0.039[c], 0.039[f]
Q1 (1)	79	24.6 (22.4, 27.0)	1	
Q2 (2)	79	23.7 (21.9, 25.7)	0.966 (0.854, 1.093)	
Q3 (3)	80	23.3 (21.6, 25.0)	0.947 (0.841, 1.067)	
Q4 (4)	79	21.3 (19.8, 22.8)	0.866 (0.769, 0.975)	
Q5 (5)	79	24.2 (22.7, 25.8)	0.985 (0.876, 1.107)	
Trend		-	0.992 (0.966, 1.018)[d]	0.534[d,e], 0.634[d,f]
Location				<0.001[c], <0.001[f]
Very central (1)	236	21.9 (21.0, 22.9)	1	
Central (2)	133	25.3 (23.8, 26.9)	1.153 (1.069, 1.244)	
Peripheral/very peripheral (3)[g]	27	27.5 (23.3, 32.5)	1.255 (1.051, 1.498)	
Trend		-	1.126 (1.058, 1.199)[d]	<0.001[d,e], <0.001[d,f]
Degree of urbanization				0.029[c], 0.039[f]
Densely populated (1)	34	21.9 (20.3, 23.5)	1	
Intermediately populated (2)	274	23.9 (23.0, 24.9)	1.096 (1.015, 1.183)	
Sparsely populated (3)	88	22.2 (20.1, 24.6)	1.017 (0.888, 1.183)	
Trend			1.016 (0.953, 1.082)[d]	0.634[d,e], 0.634[d,f]

[a]Figures in parentheses represent the integer-valued coding of indicator categories for regression analysis.
[b]Estimated from a model jointly including all listed indicators as categorical variables (if not stated otherwise); standardized incidences are given per 100 000 person-years.
[c]*P*-value from the approximate F-test for testing the hypothesis of no differences between the categories of the respective indicator.
[d]Estimated from a model jointly including all listed indicators as linear ordinal variables.
[e]*P*-value from the approximate F-test for testing the hypothesis of no trend across the categories of the respective indicator.
[f]*P*-values according to [c] or [e], but adjusted for multiple testing according to the Benjamini-Hochberg procedure controlling for the false discovery rate [26]. The adjustment considered all listed indicators, but was performed separately for indicators modelled as categorical or linear ordinal variables.
[g]The very peripheral and the peripheral location categories were combined in the analysis due to low numbers.
Q1-Q5: lowest to highest deprivation quintile groups

<Figure legend>

FIGURE 1 Spatial distribution of type 1 diabetes incidence, indicators of deprivation and urban/rural traits at the municipality-level in North Rhine-Westphalia, Germany



Cartography: © Katty Castillo-Reinado, German Diabetes Centre, 2019
Data source: GeoBasis-DE / German Federal Agency for Cartography and Geodesy (VG250, UTM32, 2018) [S4]
NRW-IMD-2010: North Rhine-Westphalian Index of Multiple Deprivation for 2010