



Area Deprivation and Regional Disparities in Treatment and Outcome Quality of 29,284 Pediatric Patients With Type 1 Diabetes in Germany: A Cross-sectional Multicenter DPV Analysis

<https://doi.org/10.2337/dc18-0724>

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OBJECTIVE

This study analyzed whether area deprivation is associated with disparities in health care of pediatric type 1 diabetes in Germany.

RESEARCH DESIGN AND METHODS

We selected patients <20 years of age with type 1 diabetes and German residence documented in the “diabetes patient follow-up” (Diabetes-Patienten-Verlaufsdocumentation [DPV]) registry for 2015/16. Area deprivation was assessed by quintiles of the “German Index of Multiple Deprivation” (GIMD 2010) at the district level and was assigned to patients. To investigate associations between GIMD 2010 and indicators of diabetes care, we used multivariable regression models (linear, logistic, and Poisson) adjusting for sex, age, migration background, diabetes duration, and German federal state.

RESULTS

We analyzed data from 29,284 patients. From the least to the most deprived quintile, use of continuous glucose monitoring systems (CGMS) decreased from 6.3 to 3.4% and use of long-acting insulin analogs from 80.8 to 64.3%, whereas use of rapid-acting insulin analogs increased from 74.7 to 79.0%; average HbA_{1c} increased from 7.84 to 8.07% (62–65 mmol/mol), and the prevalence of overweight from 11.8 to 15.5%, but the rate of severe hypoglycemia decreased from 12.1 to 6.9 events/100 patient-years. Associations with other parameters showed a more complex pattern (use of continuous subcutaneous insulin infusion [CSII]) or were not significant.

CONCLUSIONS

Area deprivation was associated not only with key outcomes in pediatric type 1 diabetes but also with treatment modalities. Our results show, in particular, that the access to CGMS and CSII could be improved in the most deprived regions in Germany.

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Received 3 April 2018 and accepted 12 September 2018.

This article contains Supplementary Data online at <http://care.diabetesjournals.org/lookup/suppl/doi:10.2337/dc18-0724/-/DC1>.

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Despite considerable advances in the management of pediatric type 1 diabetes over the last two decades, major geographic variations in metabolic control and diabetes-related complications have persisted between countries around the world (1). Treatment and outcome quality of patients with type 1 diabetes also vary within countries. In Brazil, large discrepancies were found in clinical care across different regions (2). In Germany, significant disparities in the use of insulin pumps and rapid-acting or long-acting analogs, HbA_{1c} levels, the prevalence of overweight, and the rate of severe hypoglycemia have been reported between the federal states (3). However, regional variations in treatment and outcome quality of care of patients with type 1 diabetes are not completely explained.

Relative material and social deprivation (i.e., the lack of resources for people compared with the societies to which they belong) show significant area-level disparities associated with health (4). Therefore, indices of multiple deprivation (IMD) have been used increasingly since 2000 to assess area deprivation, not only for epidemiological research but also for public health policy (5). According to Noble et al. (6), area deprivation refers not merely to the proportion of deprived people in an area but also to an “area effect” and to the negative consequences of “the lack of facilities in that area.” Correspondingly, indices of multiple deprivation provide multidimensional information on living conditions at the regional level.

Concerning type 2 diabetes, a notable number of studies have shown that area deprivation is associated with worse indicators of outcome quality, such as BMI, HbA_{1c}, lipid profile, and short-term or long-term diabetes-related complications (7,8). However, evidence is weaker with regard to type 1 diabetes (9–13). Moreover, to date, studies on type 1 diabetes focused on associations between area deprivation and metabolic control but not medical treatment (9–13).

Nevertheless, regional socioeconomic disparities may be a major determinant of the use of insulin pump therapy (continuous subcutaneous insulin infusion [CSII]), continuous glucose monitoring systems (CGMS), and insulin analogs. In Germany, CSII is reimbursed by the

statutory health insurance (covering ~90% of the population) if poor glycemic control persists despite intensified conventional insulin treatment (14). Patients and diabetologists have to apply to the health insurance company for reimbursement by providing a comprehensive documentation of the blood glucose levels and insulin therapy over the last 3 months. Exigent documentation and uncertainty of reimbursement may discourage some families in socioeconomic disadvantaged areas. Application for reimbursement of real-time CGM by statutory health insurance is also necessary and only possible since 2016. For patients covered by private health insurance (~10% of the population), reimbursement depends on specifications in the insurance contract. Different proportions of patients with private versus statutory health insurance between areas in Germany could also lead to regional variation in diabetes treatment (15).

The objective of our study was therefore to analyze whether area deprivation is associated with regional disparities in the treatment and outcome quality of pediatric patients with type 1 diabetes in Germany.

RESEARCH DESIGN AND METHODS

Study Population

We used data from the multicenter “diabetes patient follow-up” registry (Diabetes-Patienten-Verlaufsdokumentation [DPV]). Currently, 459 diabetes care centers, mainly in Germany ($n = 416$) and Austria ($n = 40$), participate in the DPV initiative and prospectively document demographic and clinical data on treatment and outcome quality. Twice a year, centers transmit locally collected and anonymized data to the University of Ulm, Germany, for central analysis and quality assurance (16). Inconsistent or implausible data are reported back to centers for verification or correction. Data collection and analysis of anonymized data from the DPV registry were approved by the Medical Faculty Ethics Committee of the University of Ulm, Germany, and by the local review boards of participating centers.

As of March 2017, 484,365 patients with any type of diabetes were documented in the DPV database. We included only patients younger than 20 years of age with type 1 diabetes

and German residence documented in the DPV for 2015 and 2016. The definition of type 1 diabetes in the DPV database is based on a physician’s diagnosis according to the international guidelines (17) and can be revised based on the course of the disease. For each patient, we aggregated clinical data for the years 2015 and 2016 as median, percentage, or rate per 1 or 100 patient-years (PYs) for continuous, categorical, and event variables, respectively.

Area Deprivation

Area deprivation was assessed using the German Index of Multiple Deprivation from 2010 (GIMD 2010). This index was developed by Maier et al. (18,19) and is a validated measure of area deprivation for Germany (5,8,19,20). The GIMD includes seven domains of deprivation with different weighting: income (25%), employment (25%), education (15%), municipal/district revenue (15%), social capital (10%), environment (5%), and security (5%) (18,19). The GIMD 2010 was generated for all 412 districts of Germany (boundaries at 31 December 2010). Districts were categorized into deprivation quintiles, with quintile 1 (Q1) representing the least deprived and quintile 5 (Q5) the most deprived districts. We used the five-digit postal code of the patient’s residence to assign the district of residence. The postal code of residence was not available for 2.6% of the patients ($n = 766$), so we used the postal code of the treating diabetes center as proxy.

Indicators of Diabetes Care

Indicators of medical treatment in our analysis were use of insulin pump therapy (CSII), use of CGMS, frequency of self-monitoring of blood glucose (SMBG), use of rapid-acting insulin analogs and use of long-acting insulin analogs in patients on injection therapy, and participation in diabetes education programs. CGMS includes real-time CGM and CGM with intermittent scanning, also called “flash glucose monitoring.” Diabetes education was documented if a teaching session lasted for at least 45 min and if the patient and/or members of his or her family or other caregivers participated (21).

Indicators of outcome quality were BMI, presence of overweight or obesity, HbA_{1c}, rates of severe hypoglycemia (with or without coma) and of severe hypoglycemia with coma, rates of

diabetic ketoacidosis (DKA) and of severe DKA, and number of hospital days per person and year (/PY). BMI values, expressed as weight in kilograms/squared height in meters (kg/m^2), were transformed to a BMI SD score (BMI SDS) using national reference data from the German Health Interview and Examination Survey for Children and Adolescents (KIGGS) (22). A BMI above the 90th or 97th percentile of this reference population was defined as overweight (including obesity) or obesity, respectively (22), according to the German national guideline (Arbeitsgemeinschaft Adipositas im Kindes- und Jugendalter [AGA]) (23) and the European Childhood Obesity Group (ECOG) guideline (24). HbA_{1c} was standardized to the Diabetes Control and Complications Trial (DCCT) reference of 4.05–6.05% (21–43 mmol/mol), applying the “multiple-of-the-mean” transformation method to adjust for differences between local laboratories (25). Severe hypoglycemia (with or without coma) was defined as self-reported unconsciousness, convulsion, or being unable to take glucose without third-party assistance (26) or, in preschool children, as an altered mental status and an inability to assist in hypoglycemia treatment (27). DKA was defined as $\text{pH} < 7.3$ and/or requirement of hospital treatment; severe DKA was defined as $\text{pH} < 7.1$. DKA at diabetes onset was not considered in this analysis.

Statistical Analysis

We present descriptive data as median (lower–upper quartile), percentage, or rate per 1 or 100 PYs for continuous, categorical, and event variables respectively.

To illustrate the regional distribution of CSII, HbA_{1c} , prevalence of overweight, rate of severe hypoglycemia, and rate of DKA at district level in Germany, we created quintile-based choropleth maps (Fig. 1B–F). Choropleth maps display areas that are shaded or patterned in relation to the level of the variable of interest. They are frequently used to visualize the geographical distribution of health outcomes (28) and also in the field of diabetes research (29). For this purpose, we derived district-specific adjusted mean estimates (least square means) for each of these outcomes from multivariable regression models (linear, logistic, or Poisson considering overdispersion) with district as the categorical

independent variable, adjusting for sex, age group (< 6 years, 6 to < 12 years, 12 to < 20 years), migration background (defined as at least one parent or the child born outside Germany), and diabetes duration (< 2 years, ≥ 2 years). Adjusted mean estimates for districts were then categorized into outcome quintiles.

To investigate the association between the GIMD 2010 quintiles and indicators of diabetes care, we performed multivariable regression models (linear, logistic, or Poisson considering overdispersion) with GIMD 2010 quintiles as the categorical independent variable and adjusting for sex, age group, migration background, and diabetes duration. In a second step, we also adjusted for German federal state in regression models to investigate whether the effects of area deprivation were independent of the federal structure of Germany. All analyses were repeated stratified by sex to examine possible differences in the associations of GIMD 2010 with indicators of care between girls and boys.

The number of cases used in the analysis of each variable is indicated in the tables and figures. Results of regression analyses are presented as adjusted mean estimates (least square means) with 95% CIs. *P* values were adjusted for multiple testing using the false discovery rate controlling Benjamini-Hochberg procedure (30). The level of significance of two-sided tests was set at $P < 0.01$. Statistical analysis was performed using SAS 9.4 software (SAS Institute, Cary, NC). Choropleth maps were created using QGIS 2.14 open source software.

RESULTS

The study population comprised 29,284 children and adolescents with type 1 diabetes (selection presented in Supplementary Fig. 1). Of all subjects included, 45.6% used CSII, 6.3% used CGMS, and 46.8% had participated in a diabetes education program. Median HbA_{1c} was 7.62% (60 mmol/mol; interquartile range 6.94–8.50% [52–69 mmol/mol]). The rate was 10.2 events/100 PYs for severe hypoglycemia and 1.8 events/100 PYs for DKA. Data showed that 13.4% of the patients were overweight (including obesity) and 3.5% were obese. The number of hospital days was 4.9/PY. Demographic data of the study population stratified by GIMD

2010 quintiles are given in Table 1. Results of regression models for CSII, HbA_{1c} , prevalence of overweight, rate of severe hypoglycemia, and rate of DKA are illustrated graphically (Fig. 2); results for other outcomes are presented in Table 2.

Medical Treatment

Visual comparison of the regional distributions of CSII and GIMD 2010 (Fig. 1) indicated that CSII was used less frequently in the least deprived districts. Regression analyses with and without adjusting for federal state confirmed this impression (CSII use was 41.7% in Q1 and 42.4–48.0% in other quintiles, in the model adjusting for federal state), but showed further that use of CSII decreased from Q2 to Q5 (Fig. 2A). Regression analyses, with and without adjusting for federal state, showed that CGMS was used less frequently in districts with higher deprivation (3.4% in Q5 vs. 6.3% in Q1 in the model adjusting for federal state) (Table 2). Rapid-acting insulin analogs among patients on injection therapy tended to be used more frequently with increasing area deprivation according to the model not considering federal states. However, differences between deprivation quintiles became smaller after adjusting for federal state (79.0% in Q5 vs. 74.7% in Q1). In the model without federal states, the pattern of association between long-acting insulin analogs and area deprivation appeared to be more complex (highest use in Q1 and Q5, lowest use in Q2 and Q3). After adjustment for federal state, long-acting insulin analogs tended to be used less frequently with increasing area deprivation (64.3% in Q5 vs. 80.8% in Q1 and Q3). In all models, associations with frequency of SMBG were not significant. With increasing area deprivation, patients and their families participated more often in diabetes education programs, but these associations were no longer significant after additional adjustment for federal state.

Outcome Quality

Visual comparison of the regional distributions of HbA_{1c} and GIMD 2010 (Fig. 1) indicated that HbA_{1c} was higher in the most deprived districts. Regression analyses with and without adjusting for federal state confirmed this finding. Average HbA_{1c} increased almost linearly

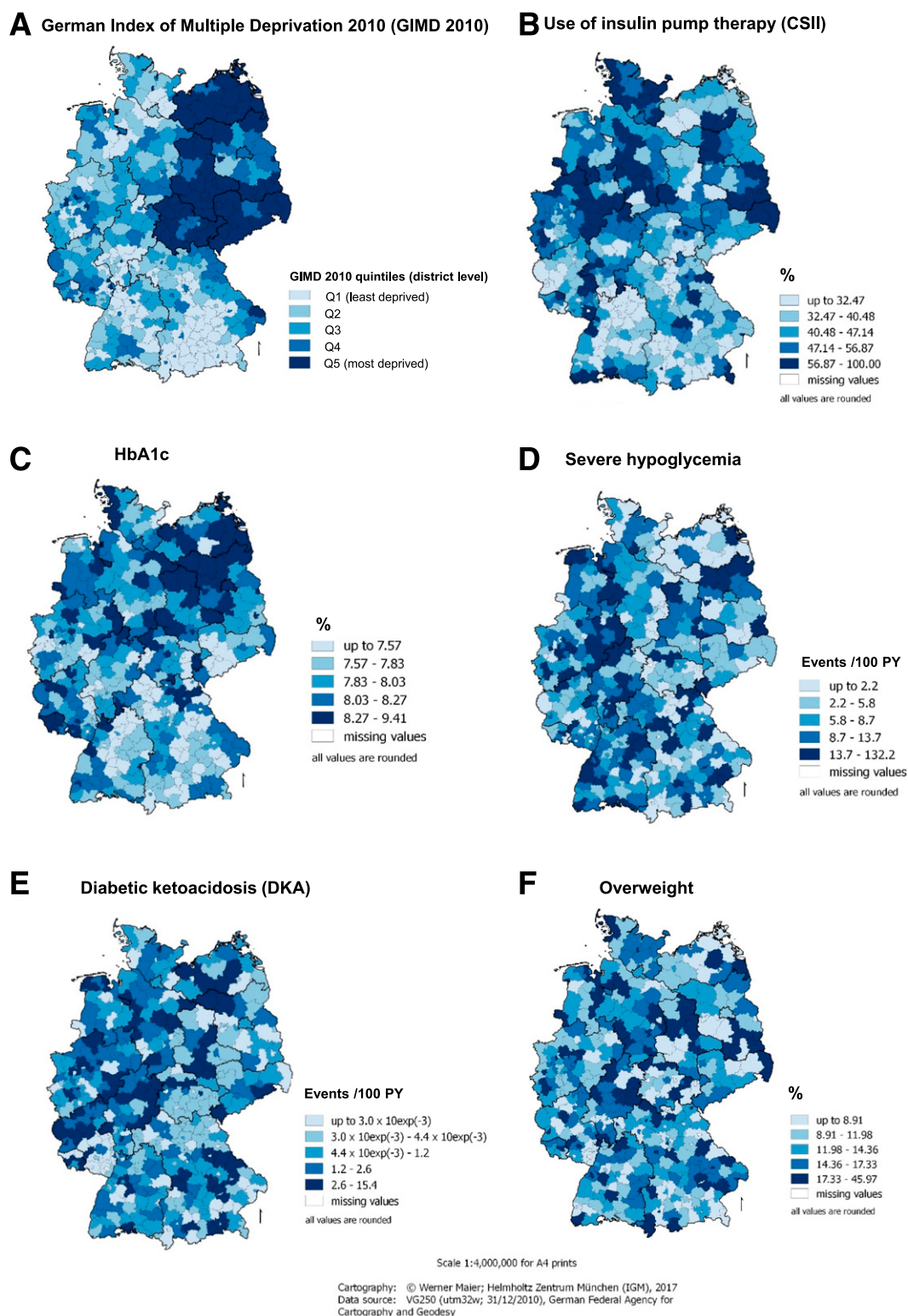


Figure 1—Quintile-based distribution of the GIMD 2010 (A) and of selected indicators of type 1 diabetes care at district level (B–F). B–F: Adjusted mean estimates (least square means) from regression models (linear, logistic, and Poisson), adjusting for sex, age group, migration, and diabetes duration, with district as the categorical independent variable, categorized into outcome quintiles. (A high-quality color representation of this figure is available in the online issue.)

from the least to the most deprived districts (from 7.84% [62 mmol/mol] in Q1% to 8.07% [65 mmol/mol] in Q5, after adjusting for federal state)

(Fig. 2B). In contrast to HbA_{1c}, the rate of severe hypoglycemia (with or without coma) decreased in all models with higher area deprivation (from

12.1 events/100 PYs to 6.9 events/100 PYs in the model adjusted for federal state) (Fig. 2C), whereas the rate of severe hypoglycemia with coma did

Table 1—Characteristics of the study population by GIMD 2010 quintiles

	All patients <i>n</i> = 29,284	Q1 <i>n</i> = 7,109	Q2 <i>n</i> = 7,541	Q3 <i>n</i> = 5,353	Q4 <i>n</i> = 5,804	Q5 <i>n</i> = 3,477
Girls, %	47.2	46.7	48.1	48.2	46.2	46.6
Age, years*	13.4 (9.8–16.2)	13.5 (9.9–16.3)	13.4 (9.9–16.2)	13.3 (9.8–16.2)	13.3 (9.7–16.2)	13.1 (9.7–16.0)
Age at onset, years*	7.7 (4.4–11.1)	7.8 (4.4–11.2)	7.6 (4.4–11.1)	7.8 (4.4–11.1)	7.6 (4.4–11.1)	7.7 (4.5–11.1)
Diabetes duration, years*	4.0 (1.3–7.5)	4.0 (1.4–7.5)	4.1 (1.4–7.6)	4.0 (1.3–7.5)	3.9 (1.2–7.5)	3.7 (1.2–7.3)
Migration background, %	21.6	21.1	23.7	22.5	23.9	13.3
East German residence (new federal states), %	15.9	0.0	0.4	3.1	30.5	77.3

Unadjusted data. *Data are median (lower–upper quartile).

not vary significantly with area deprivation level (Table 2). Positive associations between area deprivation and DKA (Fig. 2D) or severe DKA (pH <7.1) (Table 2) were not significant. The prevalence of overweight (including obesity) increased steadily with area deprivation, and this association was stronger when additionally adjusting for federal state (from 11.8% in Q1 to 15.5% in Q5) (Fig. 2E). The pattern of association was similar for BMI SDS (Table 2). The increase in obesity prevalence was not significant. The number of hospital days (rate/PY) increased with higher area deprivation in the model not adjusting for federal state, but this association was no longer significant after controlling for federal state (Table 2).

Analysis by Sex

Considering the model adjusting for federal state, stratified by sex, the results were similar in boys and girls except for a slightly but significantly less frequent SMBG only in boys in Q5 compared with other deprivation quintiles (Supplementary Table 2).

CONCLUSIONS

We found that area deprivation was associated with the use of CSII, CGMS, rapid-acting or long-acting insulin analogs, HbA_{1c} levels, the rate of severe hypoglycemia, BMI SDS, and the prevalence of overweight, independently of the federal states. Associations of other factors with area deprivation were not significant regardless of the model considered or no longer significant after adjustment for federal state.

Our analysis showed a significantly less frequent use of CSII in the least deprived districts (Q1) compared with others (Q2–Q5). In Germany, CSII is reimbursed on a case-by-case basis, if

certain medical criteria have been met (leading to approval by the health insurance company), for instance, if intensified conventional insulin therapy is not sufficient to achieve goals for glycemic control (14). We found the lowest HbA_{1c} levels in the least deprived districts (Q1) where pump use was also less frequent. It is possible that HbA_{1c} goals in these districts (Q1) are more often achieved with intensified conventional insulin therapy compared with more deprived districts, so that medical criteria for reimbursement of CSII are less frequently met. Further, in districts in deprivation quintiles Q2 to Q5, CSII was used less frequently with increasing area deprivation. This pattern may be associated with the uncertainty of reimbursement of the insulin pump, which may constitute an obstacle for some families in more deprived regions. Associations between socioeconomic factors and the use of CSII have been rarely investigated. However, some studies have indicated that individuals in higher socioeconomic groups injected insulin more frequently and were also more likely to use insulin pumps (13).

We found that CGMS was used less in more deprived districts. Associations between area deprivation or individual socioeconomic status (SES) and CGMS have not been investigated yet. Since June 2016 only, real-time CGM but not intermittent scanning CGM has been reimbursed by statutory health insurance in Germany. Absence of reimbursement until this date may have led to avoidance of CGMS use, particularly in more deprived regions.

Use of rapid-acting insulin analogs was positively associated with area deprivation, whereas long-acting insulin analogs were used less frequently with increasing area deprivation, after adjustment

for federal state. Here, many factors may interact in a complex manner. Possible explanations include differences in patients' health insurance (private vs. statutory) or regionally different local discount agreements with pharmaceutical companies (15).

With regard to indicators of outcome quality, our results concerning the association between area deprivation and HbA_{1c} are in line with the findings from previous studies. Several reports on patients with type 1 diabetes have shown significant associations between higher area deprivation and poorer metabolic control in children (9) and adults (11).

We also found a positive association between area deprivation and overweight or BMI SDS, and these findings are also consistent with previous reports in the general population (8,31). For example, significant associations between area deprivation and obesity have been reported in adults in Germany, after controlling for education (8). A strong association between area deprivation and weight status was also confirmed in British children: children living in more deprived locations had both greater waist circumference and greater body mass, even after controlling for confounders (age, sex, stature, hip circumference) (31).

In contrast to previous reports (32), we found a negative association between area deprivation and the rate of severe hypoglycemia (with or without coma). Recent studies have demonstrated that the evidence for an association between low HbA_{1c} and hypoglycemia risk in type 1 diabetes no longer exists (33). However, we cannot exclude the possibility that in our setting, the lower rate of severe hypoglycemia in the most deprived districts is associated with higher

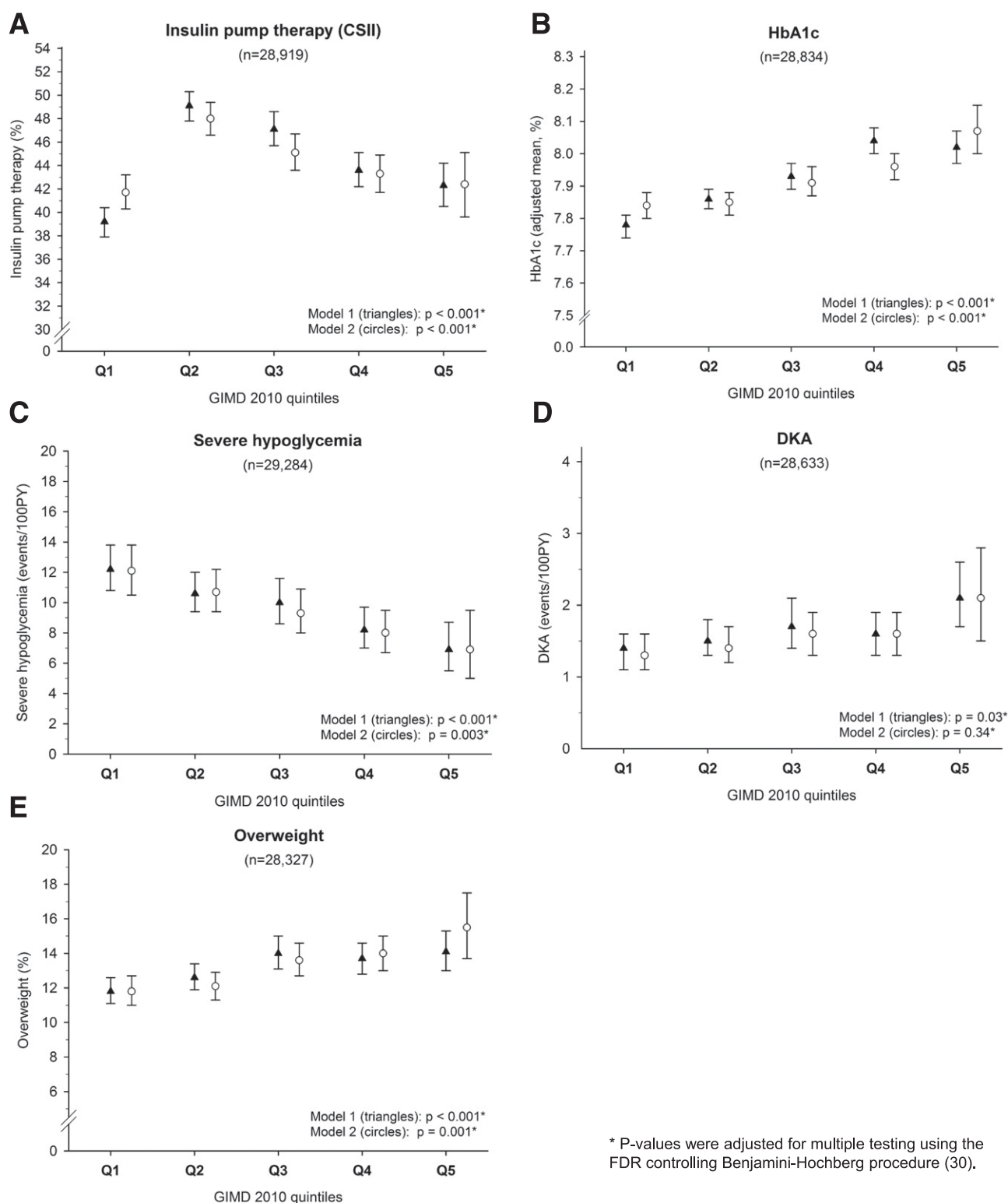


Figure 2—Multiple adjusted mean estimates of indicators of type 1 diabetes care—CSII (A), HbA_{1c} (B), severe hypoglycemia (C), DKA (D), and overweight (E)—by GIMD 2010 quintiles. Model 1 (triangles): Adjusted mean estimates (least square means) from regression models (linear, logistic, and Poisson), with GIMD 2010 quintiles as the categorical independent variable, adjusting for sex, age group, migration, and diabetes duration. Model 2 (circles): Adjusted mean estimates (least square means) from regression models (linear, logistic, and Poisson), with GIMD 2010 quintiles as the categorical independent variable, adjusting for sex, age group, migration, diabetes duration, and federal state.

HbA_{1c}, which is related to higher area deprivation in our study. Another hypothesis could be that parents of children

with type 1 diabetes living in more deprived areas tend to underreport severe hypoglycemia (minimization of

the medical relevance or social desirability bias) compared with parents of children living in less deprived districts. In

Table 2—Multiple adjusted mean estimates (95% CI) of indicators of type 1 diabetes care by GIMD 2010 quintiles

Outcome	<i>n</i>	Model	Q1	Q2	Q3	Q4	Q5	<i>P</i> value*
Treatment								
CGMS, %	29,284	1	7.3 (6.7–7.9)	5.6 (5.2–6.2)	5.6 (5.1–6.3)	4.8 (4.3–5.4)	4.5 (3.9–5.2)	<0.001
		2	6.3 (5.7–7.0)	5.6 (5.1–6.2)	5.7 (5.1–6.4)	5.3 (4.7–6.0)	3.4 (2.7–4.3)	0.002
Rapid-acting insulin analogs, %	15,719**	1	66.8 (65.3–68.3)	70.4 (68.8–71.9)	66.7 (64.8–68.5)	78.0 (76.5–79.5)	87.8 (86.2–89.2)	<0.001
		2	74.7 (73.1–76.2)	75.9 (74.3–77.4)	70.9 (68.9–72.7)	76.7 (74.9–78.3)	79.0 (75.8–81.8)	<0.001
Long-acting insulin analogs, %	15,719**	1	77.8 (76.5–79.2)	71.5 (69.9–73.0)	75.2 (73.4–76.8)	72.5 (70.8–74.1)	81.2 (79.4–82.9)	<0.001
		2	80.8 (79.4–82.2)	77.3 (75.8–78.8)	80.8 (79.3–82.3)	72.4 (70.5–74.3)	64.3 (60.4–68.0)	<0.001
SMBG	27,335	1	5.8 (5.7–5.8)	5.7 (5.7–5.8)	5.8 (5.7–5.8)	5.7 (5.7–5.8)	5.6 (5.6–5.7)	0.02
		2	5.7 (5.7–5.8)	5.7 (5.7–5.8)	5.7 (5.7–5.8)	5.8 (5.8–5.9)	5.7 (5.6–5.8)	0.03
Diabetes education program, %	29,284	1	44.2 (43.0–45.4)	46.8 (45.7–48.0)	46.1 (44.8–47.5)	47.7 (46.4–49.0)	51.7 (50.0–53.5)	<0.001
		2	46.0 (44.6–47.4)	48.2 (47.0–49.5)	46.6 (45.1–48.1)	46.6 (45.1–48.1)	46.0 (43.4–48.7)	0.18
Outcome quality								
Severe hypoglycemia with coma, events/100 PYs	29,284	1	1.8 (1.5–2.2)	2.1 (1.8–2.5)	2.5 (2.1–3.0)	2.0 (1.7–2.4)	1.6 (1.3–2.2)	0.06
		2	1.9 (1.6–2.3)	1.9 (1.6–2.3)	2.2 (1.8–2.7)	1.9 (1.5–2.3)	1.8 (1.2–2.6)	0.76
Severe DKA (pH <7.1), events/100 PYs	28,965	1	0.2 (0.1–0.3)	0.2 (0.1–0.3)	0.3 (0.2–0.4)	0.2 (0.2–0.4)	0.4 (0.3–0.7)	0.04
		2	0.2 (0.1–0.3)	0.1 (0.1–0.3)	0.2 (0.1–0.5)	0.2 (0.1–0.5)	0.3 (0.1–0.8)	0.48
BMI SDS	28,327	1	0.28 (0.26–0.30)	0.33 (0.31–0.35)	0.35 (0.33–0.37)	0.33 (0.31–0.35)	0.36 (0.33–0.39)	<0.001
		2	0.26 (0.24–0.29)	0.29 (0.27–0.32)	0.33 (0.31–0.36)	0.35 (0.33–0.38)	0.46 (0.41–0.50)	<0.001
Obesity, %	28,327	1	3.2 (2.8–3.6)	3.0 (2.6–3.4)	3.7 (3.2–4.2)	3.6 (3.2–4.2)	3.8 (3.2–4.5)	0.07
		2	3.2 (2.8–3.7)	2.8 (2.5–3.3)	3.6 (3.1–4.2)	3.7 (3.2–4.3)	3.9 (3.0–5.0)	0.10
Number of hospital days/1 PY	29,284	1	3.9 (3.3–4.6)	4.5 (3.9–5.3)	4.5 (3.8–5.4)	4.7 (4.0–5.6)	6.8 (5.7–8.2)	<0.001
		2	4.2 (3.5–5.0)	4.7 (4.0–5.5)	4.5 (3.8–5.5)	4.7 (3.9–5.6)	5.1 (3.8–7.0)	0.85

Model 1: Adjusted mean estimates (least square means) with respective 95% CI derived from logistic regression analysis (for outcomes use of CGMS, use of rapid-acting insulin analogs, use of long-acting insulin analogs, participation in diabetes education program, prevalence of obesity), linear regression analysis (for outcomes SMBG, BMI SDS), or Poisson regression analysis considering overdispersion (for outcomes rate of severe hypoglycemia with coma, rate of severe DKA (pH <7.1), number of hospital days). All regression models were performed with GIMD 2010 quintiles as the categorical independent variable and adjusting for sex, age group, migration background, and diabetes duration. Model 2: Estimates from regression models additionally adjusted for German federal state. *P value of test of no difference in outcome distribution across GIMD quintiles. P values were adjusted for multiple testing using the false discovery rate controlling Benjamini-Hochberg procedure (30). ** Only patients without CSII.

fact, contrary to DKA, which requires a visit to the diabetes care center, severe hypoglycemia can be treated by patients or parents themselves and may easily be forgotten until the next medical visit. In accordance with this explanation, no association was observed between area deprivation and severe hypoglycemia with coma, where underreporting is less likely.

In our results, higher area deprivation tended to be associated with higher risk of hospital admission for DKA, and this is consistent with previous findings (34).

Overall, many factors may contribute to the differences in treatment and outcome quality in pediatric patients with type 1 diabetes within Germany. The GIMD 2010 partly reflects East–West inequalities in Germany: districts in less deprived quintiles were mostly located in the western part, whereas districts in the most deprived quintiles were mostly located in the eastern part of the

country (Table 1 and Fig. 1A). Although the living conditions in former East and West Germany have slowly converged since German reunification (35), economic performance is still lower and the proportion of people affected by poverty and unemployment remains higher in the eastern part of the country (36). The health status of children and adolescents has become more similar, but some important differences in health behavior still remain. In particular, compared with peers living in the western part of the country, more adolescents in the eastern part regularly drink alcohol or smoke, and fewer children are members of a sports club (37). However, our study indicates that half of the analyzed diabetes-related outcomes (use of CSII, CGMS, or insulin analogs, HbA_{1c}, rate of severe hypoglycemia, BMI SDS, and prevalence of overweight) were significantly associated with area deprivation independently of the federal state and,

thus, independently of East–West disparities.

The major strength of this study is its very large sample size with patients from a large number of diabetes care centers throughout the country. We used a nationwide diabetes follow-up registry covering more than 85% of the pediatric subjects with type 1 diabetes in Germany, so that the results can be considered as representative of this population. Moreover, detailed information on the patients' demographic and clinical characteristics was available, which allows comprehensive control of potential confounders.

One limitation of this study is that analyses could not consider individual-level SES. In DPV, education level is incompletely documented, and household income is not available. Studies on patients with type 2 diabetes have demonstrated that the effect of area deprivation remains significant after

controlling for individual SES (8,19). Maier et al. (19) argue that individual SES and area deprivation may “act through different pathways.” For instance, a strong net of social safety, as well as dedicated resources through social spending to “stable housing, educational opportunities, nutrition and transportation,” is considered to play a decisive role in enhancing the quality of care, especially for populations with lower income, lower educational level, or minority status (38).

Another weakness is the heterogeneity of German districts: they are administrative units that vary considerably in area and population size (from ~35,000 up to more than 1 million inhabitants). We assume that the analysis could be less sensitive in larger districts than in smaller ones. However, the influence of extreme values in single domains of the GIMD is limited because a ranking transformation was used in the algorithm for the index calculation. Furthermore, because pediatric diabetes health care in Germany is organized at the district level, heterogeneity within districts may play a less important role.

Further shortcomings of this study are that complete data were not available for each patient, and variability in the measurements of clinical characteristics cannot be completely excluded because of the multicenter design. However, we standardized locally measured HbA_{1c} values to the DCCT standard. Furthermore, because of the cross-sectional design, this study does not allow us to draw any causal interpretation. Finally, the nature of the database does not allow in-depth analysis of all possibly important determinants (e.g., individual socioeconomic data), and the nature of the German diabetes care system limits generalizability of the findings.

In conclusion, we showed that in pediatric patients with type 1 diabetes in Germany, area deprivation was significantly associated with many indicators of treatment and outcome quality, independently of the federal state. In particular, our findings suggest that a focus on equal access to diabetes treatment, such as CGMS and CSII, is important because treatment is a directly modifiable factor. Moreover, diabetes technology may improve metabolic control regardless of educational level (39). Consequently, a better access to diabetes technology in the most deprived areas may improve the

quality of care of pediatric type 1 diabetes, even in high-income countries.

Acknowledgments. Special thanks to A. Hungele and R. Ranz for support and the development of the DPV documentation software, and K. Fink and E. Bollow for the DPV data management (Institute of Epidemiology and Medical Biometry, ZIBMT, University of Ulm, respectively). Special thanks also to R.W. Holl from the Institute of Epidemiology and Medical Biometry, ZIBMT, University of Ulm, for data management, initiation of the DPV collaboration, and being the principal investigator of the DPV registry. The authors thank G.G. Greiner, from the Institute of Health Economics and Health Care Management, Helmholtz Zentrum München, for his assistance in creating the maps. Furthermore, the authors thank all participating centers in the DPV initiative, especially the centers contributing data to this investigation and their patients. A detailed list of the centers contributing data to this analysis can be found in the online supplementary material (Supplementary Appendix 3).

Funding. The DPV registry and this analysis are supported by the German Center for Diabetes Research (DZD). Further financial support for the DPV registry was provided by the German Diabetes Association (DDG) and by the European Foundation for the Study of Diabetes (EFSD). The DPV registry receives funding from the Innovative Medicines Initiative 2 Joint Undertaking (INNODIA) under grant agreement 115797, supported by the European Commission's Horizon 2020 Research and Innovation Program and the European Federation of Pharmaceutical Industries and Associations, JDRF, and The Leona M. and Harry B. Helmsley Charitable Trust.

Quality of Interest. No potential conflicts of interest relevant to this article were reported.

Author Contributions. M.A. wrote the manuscript and created the figures. M.A., S.L., B.B., J.R., and W.M. designed the study. S.L., J.R., and W.M. analyzed the study data and reviewed and edited the manuscript. B.B., P.K., U.K.-K., P.M.H., K.P., J.H., R.B., J.R., and W.M. contributed to the discussion and reviewed and edited the manuscript. W.M. created the maps. S.L. 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.

Prior Presentation. Parts of this study were presented in abstract form at the 43rd Annual Conference of the International Society for Pediatric and Adolescent Diabetes (ISPAD), Innsbruck, Austria, 18–21 October 2017, and at the European Congress of Epidemiology, Lyon, France, 4–6 July 2018.

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