

# 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.

Journal:	Diabetes Care
Manuscript ID	DC18-0724
Manuscript Type:	Original Article: Epidemiology/Health Services Research
Date Submitted by the Author:	03-Apr-2018
Complete List of Authors:	Auzanneau, Marie; University of Ulm, Institute of Epidemiology and Medical Biometry, ZIBMT; German Center for Diabetes Research (DZD), Lanzinger, Stefanie; Universitat Ulm, Institute of Epidemiology and Medical Biometry, ZIBMT; German Center for Diabetes Research (DZD) Bohn, Barbara; University of Ulm, Institute of Epidemiology and Medical Biometry, ZIBMT; German Center for Diabetes Research (DZD) Kroschwald, Peter; Children's Hospital, Ruppiner Kliniken GmbH, Hochschulklinikum der Medizinischen Hochschule Brandenburg Kuhnle-Krahl, Ursula; Practice for Pediatric Endocrinology and Diabetology Holterhus, Paul Martin; University Hospital of Schleswig-Holstein, Campus Kiel/Christian-Albrechts University of Kiel, Division of Pediatric Endocrinology and Diabetes, Department of Pediatrics Placzek, Kerstin; University Hospital, Martin-Luther University, Pediatric and Adolescent Medicine Hamann, Johannes; St. Marien Hospital Landshut, Department of Pediatrics Bachran, Rainer; Pediatric Practice Rosenbauer, Joachim; German Diabetes Center, Leibniz Institute at Duesseldorf University, Institute of Biometrics & Epidemiology; German Center for Diabetes Research (DZD) Maier, Werner; Helmholtz Zentrum München, Institute of Health Economics and Health Care Management; German Center for Diabetes Research (DZD)
1	1

SCHOLARONE<sup>™</sup> Manuscripts

1	Title page
2	Area deprivation and regional disparities in treatment and outcome quality of
3	29,284 pediatric patients with type 1 diabetes in Germany: a cross-sectional
4	multicenter DPV analysis.
5	
6	Short-running-title:
7	Area deprivation and type 1 diabetes
8	
9	Marie Auzanneau MPH <sup>1, 10</sup> , Stefanie Lanzinger PhD <sup>1, 10</sup> , Barbara Bohn PhD <sup>1, 10</sup> ,
10	Peter Kroschwald MD <sup>2</sup> , Ursula Kuhnle-Krahl MD <sup>3</sup> , Paul Martin Holterhus MD <sup>4</sup> ,
11	Kerstin Placzek MD⁵, Johannes Hamann MD <sup>6</sup> , Rainer Bachran MD <sup>7</sup> , Joachim
12	Rosenbauer MD <sup>8, 10*</sup> , Werner Maier PhD <sup>9, 10*</sup> on behalf of the DPV Initiative
13	<sup>1</sup> Institute of Epidemiology and Medical Biometry, ZIBMT, University of Ulm, Ulm,
13 14	<sup>1</sup> Institute of Epidemiology and Medical Biometry, ZIBMT, University of Ulm, Ulm, Germany
14	Germany
14 15	Germany <sup>2</sup> Children's Hospital, Ruppiner Kliniken GmbH, Hochschulklinikum der Medizinischen
14 15 16	Germany <sup>2</sup> Children's Hospital, Ruppiner Kliniken GmbH, Hochschulklinikum der Medizinischen Hochschule Brandenburg, Neuruppin, Germany
14 15 16 17	Germany <sup>2</sup> Children's Hospital, Ruppiner Kliniken GmbH, Hochschulklinikum der Medizinischen Hochschule Brandenburg, Neuruppin, Germany <sup>3</sup> Practice for Pediatric Endocrinology and Diabetology, Gauting, Germany
14 15 16 17 18	Germany <sup>2</sup> Children's Hospital, Ruppiner Kliniken GmbH, Hochschulklinikum der Medizinischen Hochschule Brandenburg, Neuruppin, Germany <sup>3</sup> Practice for Pediatric Endocrinology and Diabetology, Gauting, Germany <sup>4</sup> Division of Pediatric Endocrinology and Diabetes, Department of Pediatrics,
14 15 16 17 18 19	Germany <sup>2</sup> Children's Hospital, Ruppiner Kliniken GmbH, Hochschulklinikum der Medizinischen Hochschule Brandenburg, Neuruppin, Germany <sup>3</sup> Practice for Pediatric Endocrinology and Diabetology, Gauting, Germany <sup>4</sup> Division of Pediatric Endocrinology and Diabetes, Department of Pediatrics, University Hospital of Schleswig-Holstein, Campus Kiel/Christian-Albrechts University
14 15 16 17 18 19 20	Germany <sup>2</sup> Children's Hospital, Ruppiner Kliniken GmbH, Hochschulklinikum der Medizinischen Hochschule Brandenburg, Neuruppin, Germany <sup>3</sup> Practice for Pediatric Endocrinology and Diabetology, Gauting, Germany <sup>4</sup> Division of Pediatric Endocrinology and Diabetes, Department of Pediatrics, University Hospital of Schleswig-Holstein, Campus Kiel/Christian-Albrechts University of Kiel, Kiel, Germany
14 15 16 17 18 19 20 21	Germany <sup>2</sup> Children's Hospital, Ruppiner Kliniken GmbH, Hochschulklinikum der Medizinischen Hochschule Brandenburg, Neuruppin, Germany <sup>3</sup> Practice for Pediatric Endocrinology and Diabetology, Gauting, Germany <sup>4</sup> Division of Pediatric Endocrinology and Diabetes, Department of Pediatrics, University Hospital of Schleswig-Holstein, Campus Kiel/Christian-Albrechts University of Kiel, Kiel, Germany <sup>5</sup> Pediatric and Adolescent Medicine, University Hospital, Martin-Luther University,

25	<sup>8</sup> Institute for Biometrics and Epidemiology, German Diabetes Center, Leibniz Center
26	for Diabetes Research at Heinrich Heine University, Düsseldorf, Germany
27	<sup>9</sup> Institute of Health Economics and Health Care Management, Helmholtz Zentrum
28	München, German Research Center for Environmental Health (GmbH), Neuherberg,
29	Germany
30	<sup>10</sup> German Center for Diabetes Research (DZD), Neuherberg, Germany
31	
32	
33	*Shared last authorship
34	
35	
36	
37	Corresponding author:
38	Marie Auzanneau, MPH
39	Institute of Epidemiology and Medical Biometry
40	ZIBMT
41	University of Ulm
42	Albert-Einstein-Allee 41
43	D-89081 Ulm
44	Germany
45	Tel.: +49/731/5025483
46	Fax.: +49/ 731/5025309
47	marie.auzanneau@uni-ulm.de
48	
49	
50	

51	
52	
53	Abstract (250 words)
54	
55	Objective
56	To analyze whether area deprivation is associated with disparities in pediatric
57	diabetes care in Germany.
58	
59	Research Design and Methods
60	We selected patients younger than 20 years of age with type 1 diabetes and German
61	residence documented in the "diabetes patient follow-up" (DPV) registry for the years
62	2015/16. Area deprivation was assessed by quintiles of the "German Index of
63	Multiple Deprivation" (GIMD 2010) at district level and was assigned to patients. To
64	investigate associations between GIMD 2010 and indicators of diabetes care, we
65	used multivariable regression models (linear, logistic, and Poisson) adjusting for sex,
66	age, migration background, diabetes duration, and German federal states.
67	
68	Results
69	We analyzed data from 29,284 patients. From the least to the most deprived quintile,
70	use of continuous glucose monitoring systems decreased from 6.3% to 3.4% and use
71	of long-acting insulin analogs decreased from 80.8% to 64.3%, whereas use of rapid-
72	acting insulin analogs increased from 74.7% to 79.0%; average HbA1c increased
73	from 7.84% to 8.07% (62 to 65 mmol/mol), and the prevalence of overweight from
74	11.8% to 15.5%, but the rate of severe hypoglycemia decreased from 12.1 to 6.9
75	events/100 patient-years. Associations with other parameters showed a more

complex pattern (use of insulin pump) or were not significant (e.g., rate of diabetic

77 ketoacidosis).

78

# 79 Conclusions

- 80 Area deprivation was associated with half the analyzed indicators. Investigation of
- potential mediating variables, such as accessibility of care, quality of housing and
- transportation, or density of urban green spaces, might allow a better understanding
- 83 of the underlying mechanisms of the observed associations.

84	
85	Main text (4,080 words, 2 tables and 2 figures)
86	Over the last two decades, the management of pediatric type 1 diabetes has
87	changed considerably, in particular with regard to increased use of insulin analogs,
88	basal-bolus regimens, and insulin pump therapy. However, major geographic
89	variations in metabolic control and diabetes-related complications have persisted
90	between countries around the world (1,2). Treatment and outcome quality of patients
91	with type 1 diabetes also vary within countries. In Brazil, large discrepancies were
92	found in clinical care across different regions (3). In Germany, significant disparities
93	in the use of insulin pumps and rapid-acting or long-acting analogs, HbA1c levels, the
94	prevalence of overweight, and the rate of severe hypoglycemia have been reported
95	between the federal states (4).
96	
97	Regional variations in treatment and outcome quality of patients with type 1 diabetes
98	care are not completely explained. Concerning type 2 diabetes, a notable number of
99	studies have shown that both area-level and individual socioeconomic factors are
100	associated with worse indicators of outcome quality, such as body mass index (BMI),
101	HbA1c, lipid profile, and short-term or long-term diabetes-related complications (5,6).
102	Concerning type 1 diabetes, the evidence of associations between area-level or
103	individual socioeconomic factors and diabetes-related outcomes is weaker (7–12).
104	Furthermore, individual socioeconomic indicators (income, education, and
105	occupation) have often been analyzed, whereas associations between area
	den die Bernend Constantischer Gescher der Sterne Berne B

106 deprivation and type 1 diabetes outcomes have been investigated in a few countries

107 only, as in the UK, Canada, New Zealand, and Australia (7–12).

108

109	Indices of Multiple Deprivation, which encompass several domains of deprivation
110	such as income, employment, environment, or security, are a useful tool to study
111	associations of area deprivation and health outcomes. First developed in the UK (13),
112	such indices have been used increasingly since the year 2000 for epidemiological
113	research and public policy (14). In Germany, Indices of Multiple Deprivation started to
114	be used in public health-related research in 2011 (15). Maier and colleagues adopted
115	the conceptual and technical approach used in the UK to develop Indices of Multiple
116	Deprivation for Germany (German Index of Multiple Deprivation, GIMD, and its
117	regional versions) (16,17). Associations were shown between the GIMDs and several
118	health outcomes, for example the prevalence of type 2 diabetes and obesity (6,18),
119	or with health service indicators such as hip and knee replacement (19).
120	
121	The objective of our study was to enalyze whether area deprivation, accorded by the

The objective of our study was to analyze whether area deprivation, assessed by the GIMD from the year 2010 (GIMD 2010), is associated with regional disparities in the treatment and outcome quality of pediatric patients with type 1 diabetes in Germany.

124

## **Research Design and Methods**

### 126 Study population

127 We used data from the multicenter "diabetes patient follow-up" registry (Diabetes-

128 **P**atienten-**V**erlaufsdokumentation, DPV). Currently, 459 diabetes care centers,

mainly in Germany (n=416) and Austria (n=40), participate in the DPV initiative and

- 130 prospectively document demographic and clinical data on treatment and outcome
- 131 quality. Twice a year, centers transmit locally collected and anonymized data to the
- 132 University of Ulm, Germany, for central analysis and quality assurance (20).
- 133 Inconsistent or implausible data are reported back to centers for verification or
- 134 correction. Data collection and analysis of anonymized data from the DPV registry

135

### **Diabetes** Care

were approved by the Ethics Committee of the Medical Faculty of the University of

136	Ulm, Germany, and by the local review boards of participating centers.
137	
138	As of March 2017, 484,365 patients with any type of diabetes were documented in
139	the DPV database. We included only patients younger than 20 years of age with type
140	1 diabetes and German residence documented in the DPV for the time period 2015
141	and 2016. For each patient, we aggregated clinical data for the years 2015 and 2016
142	as median, percentage, or rate per 1 or 100 patient-years (PY) for continuous,
143	categorical, and event variables respectively.
144	
145	Area deprivation
146	Area deprivation was assessed using the German Index of Multiple Deprivation from
147	the year 2010 (GIMD 2010). The GIMD includes seven domains of deprivation with
148	different weighting: income (25%), employment (25%), education (15%),
149	municipal/district revenue (15%), social capital (10%), environment (5%), and
150	security (5%) (16,17). The GIMD 2010 was generated for all 412 districts of Germany
151	(boundaries at 31 December 2010). Districts were categorized into deprivation
152	quintiles, with quintile 1 (Q1) representing the least deprived and quintile 5 (Q5) the
153	most deprived districts. We used the five-digit postal code of the patient's residence
154	to assign the district of residence. In case the postal code of residence was not
155	available, we used the postal code of the treating diabetes center as proxy.
156	
157	Indicators of diabetes care
158	Indicators of medical treatment in our analysis were: use of insulin pump therapy

- 159 (CSII), use of continuous glucose monitoring systems (CGMS), frequency of self-
- 160 monitoring of blood glucose (SMBG), use of rapid-acting or long-acting insulin

Page 8 of 38

analogs in patients on injection therapy, and participation in diabetes education
programs. CGMS includes real-time continuous glucose monitoring (rtCGM) and
continuous glucose monitoring with intermittent scanning (iscCGM; also called "flash
glucose monitoring", FGM). Diabetes education was documented if a teaching
session lasted for at least 45 min and if the patient and/or members of his/her family
or other caregivers participated (21).

167

168 Indicators of outcome quality were: body mass index (BMI), presence of overweight 169 or obesity, HbA1c, rates of severe hypoglycemia (with or without coma) and of 170 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 171 as weight in kilograms/squared height in meters (kg/m<sup>2</sup>), were transformed to a 172 standard deviation score (BMI SDS) using national reference data from the German 173 Health Interview and Examination Survey for Children and Adolescents (KIGGS) 174 (22). A BMI above the 90th or 97th percentile of this reference population was 175 176 defined as overweight (including obesity) or obesity respectively (22). HbA1c was 177 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 178 method in order to adjust for differences between local laboratories (23). Severe 179 180 hypoglycemia (with or without coma) was defined as self-reported unconsciousness, 181 convulsion, or being unable to take glucose without third-party assistance (24) or, in 182 preschool children, as an altered mental status and an inability to assist in hypoglycemia treatment (25). DKA was defined as pH< 7.3 and/or requirement of 183 hospital treatment; severe DKA was defined as pH< 7.1. DKA at diabetes onset was 184 not considered in this analysis. 185

186

## 187 Statistical analysis

We presented descriptive data as median (lower–upper quartile), percentage, or rate per 1 or 100 patient-years (PY) for continuous, categorical, and event variables respectively.

191

In order to illustrate the regional distribution of CSII, HbA1c, prevalence of 192 overweight, rate of severe hypoglycemia, and rate of DKA at district level in 193 194 Germany, we created quintile-based choropleth maps (Figure 1, B–F). For this 195 purpose, we derived district-specific adjusted mean estimates (least square means) 196 for each of these outcomes from multivariable regression models (linear, logistic, or 197 Poisson considering overdispersion) with district as the categorical independent variable, adjusting for sex, age group (<6 years, 6–<12 years, 12–<20 years), 198 199 migration background (defined as at least one parent or the child itself born outside Germany), and diabetes duration (<2 years,  $\geq$ 2 years). Adjusted mean estimates for 200 201 districts were then categorized into outcome quintiles. 202 203 To investigate the association between the GIMD 2010 quintiles and indicators of 204 diabetes care, we performed multivariable regression models (linear, logistic, or Poisson considering overdispersion) with GIMD 2010 guintiles as the categorical 205 206 independent variable and adjusting for sex, age group, migration background, and 207 diabetes duration. In a second step, we also adjusted for German federal states in 208 regression models to investigate whether the effects of area deprivation were independent of the federal structure of Germany. Results of regression analyses are 209 210 presented as adjusted mean estimates (least square means) with respective 95% confidence intervals (95% CI). Results for CSII, HbA1c, prevalence of overweight, 211

rate of severe hypoglycemia, and rate of DKA are illustrated graphically (Figure 2);

results for other outcomes are presented in Table 2. 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.

216

The number of cases used in the analysis of each variable is indicated in the tables

and figures. The level of significance of two-sided tests was set at p<0.01. Statistical

analysis was performed using the software SAS 9.4 (Statistical Analysis Software,

SAS Institute, Cary, NC, USA). Choropleth maps were created using the open source

software "QGIS", version 2.14.

222

# 223 **Results**

- The study population comprised 29,284 children and adolescents with type 1
- diabetes (selection presented in Supplemental figure S1). Of all subjects included,

45.6% used CSII, 6.3% CGMS, and 46.8% participated in a diabetes education

227 program. Median HbA1c was 7.62% (60 mmol/mol), IQR: 6.94-8.50% (52-69

228 mmol/mol). The rate of severe hypoglycemia was 10.2 events/100 PY, and of DKA

1.8 events/100 PY. Thirteen percent (13.4%) of the patients were overweight

(including obesity) and 3.5% obese. The number of hospital days was 4.9 /PY.

Demographic data of the study population stratified by GIMD 2010 quintiles are givenin Table 1.

233

## 234 Medical treatment

Visual comparison of the regional distributions of CSII and GIMD 2010 (Figure 1)

indicated that CSII was used less frequently in the least deprived districts.

- 237 Regression analyses with and without adjusting for federal states confirmed this
- finding (CSII use: 41.7% in Q1, 42.4–48.0% in other quintiles, in the model adjusting

239	for federal states), but showed further that use of CSII decreased from Q2 to Q5
240	(Figure 2 A). Regression analyses with and without adjusting for federal states
241	showed that CGMS was used less frequently in districts with higher deprivation (3.4%
242	in Q5 versus 6.3% in Q1 in the model adjusting for federal states) (Table 2). Rapid-
243	acting insulin analogs among patients on injection therapy tended to be used more
244	frequently with increasing area deprivation according to the model not considering
245	federal states. However, differences between deprivation quintiles became smaller
246	after adjusting for federal states (79.0% in Q5 versus 74.7% in Q1). In the model
247	without federal states, the pattern of association between long-acting insulin analogs
248	and area deprivation appeared to be more complex (highest use in Q1 and Q5,
249	lowest use in Q2 and Q3). After adjustment for federal states, long-acting insulin
250	analogs tended to be used less frequently with increasing area deprivation (64.3% in
251	Q5 versus 80.8% in Q1 and Q3). In all models, associations with frequency of SMBG
252	were not significant. With increasing area deprivation, patients and their family
253	participated more often in diabetes education programs, but these associations were
254	no longer significant after additional adjustment for federal states.

255

# 256 **Outcome quality**

257 Visual comparison of the regional distributions of HbA1c and GIMD 2010 (Figure 1) 258 indicated that HbA1c was higher in the most deprived districts. Regression analyses 259 with and without adjusting for federal states confirmed this finding. Average HbA1c increased almost linearly from the least to the most deprived districts (from 7.84% (62 260 mmol/mol) in Q1 to 8.07% (65 mmol/mol) in Q5, after adjusting for federal state) 261 (Figure 2 B). In contrast to HbA1c, the rate of severe hypoglycemia (with or without 262 coma) decreased in all models with higher area deprivation (from 12.1 events/100 PY 263 to 6.9 events/100 PY in the model adjusted for federal state) (Figure 2 C), whereas 264

265	the rate of severe hypoglycemia with coma did not vary significantly with area
266	deprivation level (Table 2). Positive associations between area deprivation and DKA
267	(Figure 2 D) or severe DKA (pH< 7.1) (Table 2) were not significant. The prevalence
268	of overweight (including obesity) with increasing deprivation increased steadily with
269	area deprivation, and this association was stronger when additionally adjusting for
270	federal states (from 11.8% in Q1 to 15.5% in Q5) (Figure 2 E). The pattern of
271	association was similar for BMI SDS (Table 2). The increase in obesity prevalence
272	was not significant. The number of hospital days (rate/PY) increased with higher area
273	deprivation in the model not adjusting for federal state, but this association was no
274	longer significant after controlling for federal states (Table 2).
275	
276	Analysis by sex
277	Considering the model adjusting for federal states, stratified by sex, most of the
278	results were similar in boys and girls (Supplemental table S2). However, the
279	association between area deprivation and the use of CGMS (less frequent use with
279 280	increasing area deprivation), as well as between area deprivation and the prevalence
280	increasing area deprivation), as well as between area deprivation and the prevalence
280 281	increasing area deprivation), as well as between area deprivation and the prevalence of overweight (higher prevalence with increasing area deprivation) was significant in
280 281 282	increasing area deprivation), as well as between area deprivation and the prevalence of overweight (higher prevalence with increasing area deprivation) was significant in boys, but not in girls. In addition, we found a slight but significantly less frequent
280 281 282 283	increasing area deprivation), as well as between area deprivation and the prevalence of overweight (higher prevalence with increasing area deprivation) was significant in boys, but not in girls. In addition, we found a slight but significantly less frequent
280 281 282 283 284	increasing area deprivation), as well as between area deprivation and the prevalence of overweight (higher prevalence with increasing area deprivation) was significant in boys, but not in girls. In addition, we found a slight but significantly less frequent SMBG only in boys in Q5 compared with other deprivation quintiles.
280 281 282 283 284 285	increasing area deprivation), as well as between area deprivation and the prevalence of overweight (higher prevalence with increasing area deprivation) was significant in boys, but not in girls. In addition, we found a slight but significantly less frequent SMBG only in boys in Q5 compared with other deprivation quintiles.
280 281 282 283 284 285 286	increasing area deprivation), as well as between area deprivation and the prevalence of overweight (higher prevalence with increasing area deprivation) was significant in boys, but not in girls. In addition, we found a slight but significantly less frequent SMBG only in boys in Q5 compared with other deprivation quintiles. <b>Conclusions</b> We found that area deprivation was associated with the use of CSII, CGMS, rapid-

- Associations of other factors with area deprivation were not significant regardless of
- the model considered or no longer significant after adjustment for federal states.

Association between area deprivation and SMBG was significant only in boys, but differences between quintiles were very small and not clinically relevant.

293

Our analysis showed a significantly less frequent use of CSII in the least deprived 294 295 districts (Q1) compared with others (Q2–Q5). Most of the least deprived districts (Q1) are located in Southern Germany (federal states of Bavaria and Baden-Württemberg) 296 where a previous study with data from the years 2012 and 2013 has already shown a 297 298 lower use of CSII (4). However, adjustment for federal states did not change the 299 observed pattern of association between area deprivation and CSII. Differences in 300 health insurance (private versus statutory), in discount agreements with 301 pharmaceutical companies or in marketing, as well as patient preferences (e.g., 302 technique affinity) may lead to this finding. Furthermore, in Germany, CSII is 303 reimbursed on a case-by-case basis, if certain medical criteria have been met 304 (approval by the health insurance company), for instance if intensified conventional 305 insulin therapy is not sufficient to achieve goals for glycemic control (26). We found the lowest HbA1c levels in the least deprived districts (Q1) where pump use was also 306 307 less frequent. It is possible that, in these districts (Q1), HbA1c goals are more often achieved with intensified conventional insulin therapy compared with more deprived 308 districts. Further, in districts in deprivation guintiles Q2 to Q5, CSII was used less 309 310 frequently with increasing area deprivation. This pattern may be associated with the 311 uncertainty of reimbursement of the insulin pump, which may constitute an obstacle 312 for some families in more deprived regions. To the best of our knowledge, there is no 313 study investigating associations between area deprivation or individual 314 socioeconomic status (SES) and CSII in patients with type 1 diabetes. However, some studies have indicated that individuals in higher socioeconomic groups injected 315 insulin more frequently each day and were also more likely to use insulin pumps (7). 316

We found that CGMS was used less in more deprived districts. Associations between area deprivation or individual SES and CGMS have not been investigated yet. Since June 2016 only, rtCGM, but not iscCGM, 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. The difference in significance of associations between girls and boys may result from the different numbers of cases in each category.

326 Use of rapid-acting insulin analogs was positively associated with area deprivation. 327 We know that rapid-acting insulin analogs are used more frequently in Eastern 328 Germany, where a significant number of deprived districts are located (4). After controlling for federal states, this pattern of association between area deprivation and 329 the use of rapid-acting insulin analogs was attenuated but remained significant. In 330 331 contrast, long-acting insulin analogs were used less frequently with increasing area 332 deprivation, after adjustment for federal state. Many factors may interact in a complex 333 manner. Possible explanations include, among other things, differences in patients' health insurance (private versus statutory) or regionally different local discount 334 agreements with pharmaceutical companies (27,28). 335

336

317

With regard to indicators of outcome quality, our results concerning the association between area deprivation and HbA1c 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 (8,11,12) and adults (9).

342

Page 15 of 38

#### **Diabetes** Care

343 We also found a positive association between area deprivation and overweight or 344 BMI SDS, and these findings are also consistent with previous reports in the general 345 population (6,29). For example, significant associations between area deprivation and obesity have been reported in adults in Germany, after controlling for education 346 347 (6). A strong association between area deprivation and weight status was also confirmed in British children: children living in more deprived locations had both 348 greater waist circumference and greater body mass, even after controlling for 349 350 confounders (age, sex, stature, hip circumference) (29). Similar to our findings, 351 differences between girls and boys in the relationship between social factors and 352 overweight have been reported previously, in particular in Swedish children: social 353 inequality at individual level was related to overweight only in boys younger than 13 354 years of age (30). However, we cannot exclude the possibility that, in our study, the 355 difference in the significance of associations between girls and boys is caused by the 356 different numbers of cases in each category. Finally, given that area deprivation is 357 associated with higher BMI, and that higher BMI itself is associated with higher HbA1c (31), overweight (also resulting from less physical activity) might be an 358 359 intermediate factor in the causal pathway between area deprivation and HbA1c. In 360 addition, it is possible that area deprivation affects glycemic control independently of 361 body weight.

362

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 HbA1c 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 HbA1c, which is related to higher

369	area deprivation in our study. Another hypothesis could be that parents of children
370	with type 1 diabetes living in more deprived areas tend to underreport severe
371	hypoglycemia more often (minimization of the medical relevance or social desirability
372	bias) compared with parents of children living in less deprived districts. In fact,
373	contrary to DKA, which requires a visit to the diabetes care center, severe
374	hypoglycemia can be treated by patients or parents themselves, and may easily be
375	forgotten until the next medical visit. In accordance with this explanation, no
376	association was observed between area deprivation and severe hypoglycemia with
377	coma, where underreporting is less likely.
378	
379	In our results, higher area deprivation tended to be associated with higher risk of
380	hospital admission for DKA, and this is consistent with previous findings (34).
381	
382	Overall, many factors may contribute to the differences in treatment and outcome
383	quality in pediatric patients with type 1 diabetes within Germany. The GIMD 2010
384	partly reflects East-West inequalities in Germany: districts in less deprived quintiles
385	were mostly located in the western part, whereas districts in the most deprived
386	quintiles were mostly located in the eastern part of the country (Table 1 and Figure 1

387 A). Although the living conditions in former Eastern and Western 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 compared with the western part of the country (36). The health

391 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 Eastern Germany 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, HbA1c, rate of severe hypoglycemia, BMI SDS, and
prevalence of overweight) were significantly associated with area deprivation
independently of the federal states and, thus, independently of East–West disparities.
The major strength of this study is the use of a nationwide diabetes follow-up registry

400 The major strength of this study is the use of a nation wide diabetes follow-up registry
401 covering more than 85% of the pediatric subjects with type 1 diabetes in Germany, so
402 that the results can be considered as representative of this population. Moreover,
403 detailed information on the patients' demographic and clinical characteristics were
404 available, which allows comprehensive control of potential confounders.

405

406 One limitation of this study is that analyses could not consider individual-level SES. In 407 DPV, education level is incompletely documented and household income is not available. Studies on patients with type 2 diabetes have demonstrated that the effect 408 409 of area deprivation remains significant after controlling for individual SES (6,18). Maier and colleagues argue that individual SES and area deprivation may "act 410 through different pathways" (18). Several mechanisms probably act together. For 411 instance, a strong net of social safety, as well as dedicated resources through social 412 413 spending to "stable housing, educational opportunities, nutrition and transportation" is considered to play a decisive role in enhancing the quality of care, especially for 414 415 populations with lower income, lower educational level, or minority status (38). 416 Accessibility of health services, urban green spaces (39), sports facilities, or density of fast food outlets are also potential intermediate variables that could help to gain a 417 418 better understanding of the association between area deprivation and health (14). 419 Thus, these parameters should be investigated in further research.

420	
421	Another weakness is the heterogeneity of German districts: they are administrative
422	units that vary considerably in area and population size (from about 35,000 up to
423	more than one million inhabitants). We assume that the analysis could be less
424	sensitive in larger districts than in smaller ones. However, application of the GIMD at
425	district level fits the structure of pediatric diabetes care in Germany.
426	
427	Further shortcomings of this study are that complete data were not available for each
428	patient and, on account of the multicenter design, variability in the measurements of
429	clinical characteristics cannot be completely excluded. However, we standardized
430	locally measured HbA1c values to the DCCT standard. Finally, because of the cross-
431	sectional design, this study does not allow us to draw any causal interpretation.
432	
433	In conclusion, we showed that, in pediatric patients with type 1 diabetes in Germany,
434	area deprivation was significantly associated with many indicators of treatment and
435	outcome quality, independently of the federal states. The underlying mechanisms are
436	still unclear. Controlling for individual factors (SES, type of patients' health insurance)
437	and investigating potential intermediate variables, such as accessibility of diabetes
438	care facilities, quality of housing and transportation, as well as the density of urban
439	green spaces, would allow a better understanding of the observed associations.
440	
441	Acknowledgments
442	Author Contributions. 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/edited the manuscript. M.A.
- 444 wrote the manuscript and created the figures. W.M. created the maps. P.K., U.K.-K.,

445	P.M.H., K.P., J.H., R.B., B.B., J.R., and W.M. contributed to the discussion and
446	reviewed/edited the manuscript. B.B. is the guarantor of this work and, as such, had
447	full access to all the data in the study and takes responsibility for the integrity of the
448	data and the accuracy of the data analysis.
449	Special thanks to A. Hungele and R. Ranz for support and the development of the
450	DPV documentation software, and K. Fink and E. Bollow for the DPV data
451	management (Institute of Epidemiology and Medical Biometry, ZIBMT, University of
452	Ulm respectively). Also to R.W. Holl (MD, PhD) from the Institute of Epidemiology
453	and Medical Biometry, ZIBMT, University of Ulm, for data management, initiation of
454	the DPV collaboration, and being the principal investigator of the DPV registry. We
455	thank G.G. Greiner from the Institute of Health Economics and Health Care
456	Management, Helmholtz Zentrum München, for his assistance in creating the maps.
457	Furthermore, we thank all participating centers in the DPV initiative, especially the
458	centers contributing data to this investigation and their patients. A detailed list of the
459	centers contributing data to this analysis can be found in the online supplemental
460	material (Supplemental Appendix S3).

Funding. The DPV registry and this analysis are supported by the German Center 461 462 for Diabetes Research (DZD). Further financial support for the DPV registry was provided by the German Diabetes Association (DDG) and by the European 463 Foundation for the Study of Diabetes (EFSD). The DPV registry receives funding 464 from the Innovative Medicines Initiative 2 Joint Undertaking INNODIA under grant 465 agreement 115797, supported by the European Commission's Horizon 2020 466 research and innovation program and European Federation of Pharmaceutical 467 Industries and Associations, JDRF, and The Leona M. and Harry B. Helmsley 468 Charitable Trust. 469

470	
471	Conflict of interest. The authors report no conflicts of interest.
472	
473	
474	
475	
476	
477	
478	
479	

CONFIDENTIAL-For Peer Review Only

## 480 <u>References</u>

(1) Walsh MG, Zgibor J, Songer T, Borch-Johnsen K, Orchard TJ, DiaComp
Investigators. The socioeconomic correlates of global complication prevalence in type
1 diabetes (T1D): a multinational comparison. Diabetes Res Clin Pract 2005
Nov;70(2):143–150.

(2) de Beaufort CE, Swift PG, Skinner CT, Aanstoot HJ, Aman J, Cameron F, et al.
Continuing stability of center differences in pediatric diabetes care: do advances in
diabetes treatment improve outcome? The Hvidoere Study Group on Childhood
Diabetes. Diabetes Care 2007 Sep;30(9):2245–2250.

(3) Gomes MB, Cobas RA, Matheus AS, Tannus LR, Negrato CA, Rodacki M, et al.
Regional differences in clinical care among patients with type 1 diabetes in Brazil:
Brazilian Type 1 Diabetes Study Group. Diabetol Metab Syndr 2012 Oct 29;4(1):44–
5996–4-44.

(4) Bohn B, Rosenbauer J, Icks A, Vogel C, Beyer P, Rutschle H, et al. Regional
disparities in diabetes care for pediatric patients with type 1 diabetes. A crosssectional DPV multicenter analysis of 24,928 German children and adolescents. Exp
Clin Endocrinol Diabetes 2016 Feb;124(2):111–119.

497 (5) Grintsova O, Maier W, Mielck A. Inequalities in health care among patients with
498 type 2 diabetes by individual socio-economic status (SES) and regional deprivation: a
499 systematic literature review. Int J Equity Health 2014 Jun 2;13:43.

(6) Maier W, Scheidt-Nave C, Holle R, Kroll LE, Lampert T, Du Y, et al. Area level
deprivation is an independent determinant of prevalent type 2 diabetes and obesity at
the national level in Germany. Results from the National Telephone Health Interview
Surveys 'German Health Update' GEDA 2009 and 2010. PLoS One 2014 Feb
27;9(2):e89661.

(7) Scott A, Chambers D, Goyder E, O'Cathain A. Socioeconomic inequalities in
 mortality, morbidity and diabetes management for adults with type 1 diabetes: A
 systematic review. PLoS One 2017 May 10;12(5):e0177210.

- (8) Carter PJ, Cutfield WS, Hofman PL, Gunn AJ, Wilson DA, Reed PW, et al.
- 509 Ethnicity and social deprivation independently influence metabolic control in children 510 with type 1 diabetes. Diabetologia 2008 Oct;51(10):1835–1842.

(9) Collier A, Ghosh S, Hair M, Waugh N. Impact of socioeconomic status and gender
on glycaemic control, cardiovascular risk factors and diabetes complications in type 1
and 2 diabetes: a population based analysis from a Scottish region. Diabetes Metab
2015 Apr;41(2):145–151.

(10) Lindner LME, Rathmann W, Rosenbauer J. Inequalities in glycaemic control,
hypoglycaemia and diabetic ketoacidosis according to socio-economic status and
area-level deprivation in Type 1 diabetes mellitus: a systematic review. Diabet Med
2018 Sep 25;35:12–32.

- (11) Zuijdwijk CS, Cuerden M, Mahmud FH. Social determinants of health on
- 520 glycemic control in pediatric type 1 diabetes. J Pediatr 2013 Apr;162(4):730–735.

(12) Hine P, Senniappan S, Sankar V, Amin R. Deprivation impedes success of
 insulin intensification in children and adolescents with type 1 diabetes; longitudinal
 linear mixed modelling of a retrospective observational cohort. Diabet Med 2011
 Mar;28(3):338–344.

(13) Noble, M., Wright, G., Smith, G., Dibben, C. Measuring multiple deprivation at
 the small-area level. Environ Planning 2006;38:169-185.

(14) Fairburn J, Maier W, Braubach M. Incorporating environmental justice into
 second generation indices of multiple deprivation: lessons from the UK and progress
 internationally. Int J Environ Res Public Health 2016 Jul

530 26;13(8):10.3390/ijerph13080750.

(15) Kuznetsov L, Maier W, Hunger M, Meyer M, Mielck A. Associations between

- regional socioeconomic deprivation and cancer risk: Analysis of population-based
- 533 Cancer Registry data from Bavaria, Germany. Prev Med 2011 Oct;53(4–5):328–330.

(16) Maier W, Fairburn J, Mielck A. Regional deprivation and mortality in Bavaria.

- 535 Development of a community-based index of multiple deprivation [German].
- 536 Gesundheitswesen 2012 Jul;74(7):416–425.

(17) Maier W. Indices of Multiple Deprivation for the analysis of regional health

disparities in Germany: Experiences from epidemiology and healthcare research.

Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz 2017
 Dec;60(12):1403–1412.

541 (18) Maier W, Holle R, Hunger M, Peters A, Meisinger C, Greiser KH, et al. The

542 impact of regional deprivation and individual socio-economic status on the

543 prevalence of Type 2 diabetes in Germany. A pooled analysis of five population-544 based studies. Diabet Med 2013 Mar;30(3):e78–86.

- (19) Schafer T, Pritzkuleit R, Jeszenszky C, Malzahn J, Maier W, Gunther KP, et al.
   Trends and geographical variation of primary hip and knee joint replacement in
- 546 Germany. Osteoarthritis Cartilage 2013 Feb;21(2):279–288.
- (20) Bohn B, Karges B, Vogel C, Otto KP, Marg W, Hofer SE, et al. 20 years of
  pediatric benchmarking in Germany and Austria: age-dependent analysis of
  longitudinal follow-up in 63,967 children and adolescents with type 1 diabetes. PLoS
  One 2016 Aug 17;11(8):e0160971.
- (21) Konrad K, Vogel C, Bollow E, Fritsch M, Lange K, Bartus B, et al. Current
  practice of diabetes education in children and adolescents with type 1 diabetes in
  Germany and Austria: analysis based on the German/Austrian DPV database.
  Pediatr Diabetes 2016 Nov;17(7):483–491.

(22) Rosario AS, Kurth BM, Stolzenberg H, Ellert U, Neuhauser H. Body mass index
percentiles for children and adolescents in Germany based on a nationally
representative sample (KiGGS 2003–2006). Eur J Clin Nutr 2010 Apr;64(4):341–349.

(23) Rosenbauer J, Dost A, Karges B, Hungele A, Stahl A, Bachle C, et al. Improved
metabolic control in children and adolescents with type 1 diabetes: a trend analysis
using prospective multicenter data from Germany and Austria. Diabetes Care 2012
Jan;35(1):80–86.

(24) Ly TT, Maahs DM, Rewers A, Dunger D, Oduwole A, Jones TW, et al. ISPAD
Clinical Practice Consensus Guidelines 2014. Assessment and management of
hypoglycemia in children and adolescents with diabetes. Pediatr Diabetes 2014
Sep;15 Suppl 20:180–192.

(25) Clarke W, Jones T, Rewers A, Dunger D, Klingensmith GJ. Assessment and
 management of hypoglycemia in children and adolescents with diabetes. Pediatr
 Diabetes 2009 Sep;10 Suppl 12:134–145.

(26) Neu A, Bürger-Büsing J, Danne T, Dost A, Holder M, Holl RW, et al. Diagnosis,
therapy and follow-up of diabetes mellitus in children and adolescents. [German].
Diabetologie Stoffwechsel 2016:35–116.

(27) Huber J, Mielck A. Morbidity and healthcare differences between insured in the
statutory ("GKV") and private health insurance ("PKV") in Germany. Review of
empirical studies. Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz
2010 Sep;53(9):925–938.

577 (28) Wild F. Supply of insulins in private health insurance compared to statutory
578 health insurance [German]. Gesundeitsökonomie Qualitätsmanagement
579 2009;14(4):200–203.

(29) Nevill AM, Duncan MJ, Lahart I, Sandercock G. Modelling the association
 between weight status and social deprivation in English school children: Can physical
 activity and fitness affect the relationship? Ann Hum Biol 2016 Nov;43(6):497–504.

(30) van Vliet JS, Gustafsson PA, Duchen K, Nelson N. Social inequality and agespecific gender differences in overweight and perception of overweight among
Swedish children and adolescents: a cross-sectional study. BMC Public Health 2015
Jul 9;15:628-015-1985-x.

(31) DuBose SN, Hermann JM, Tamborlane WV, Beck RW, Dost A, DiMeglio LA, et
al. Obesity in youth with type 1 diabetes in Germany, Austria, and the United States.
J Pediatr 2015 Sep;167(3):627–32.e1–4.

(32) Leese GP, Wang J, Broomhall J, Kelly P, Marsden A, Morrison W, et al.
Frequency of severe hypoglycemia requiring emergency treatment in type 1 and type
2 diabetes: a population-based study of health service resource use. Diabetes Care
2003 Apr;26(4):1176–1180.

(33) Haynes A, Hermann JM, Miller KM, Hofer SE, Jones TW, Beck RW, et al.
Severe hypoglycemia rates are not associated with HbA1c: a cross-sectional analysis
of 3 contemporary pediatric diabetes registry databases. Pediatr Diabetes 2016 Nov
23;18:643-650.

(34) Govan L, Maietti E, Torsney B, Wu O, Briggs A, Colhoun HM, et al. The effect of

- deprivation and HbA1c on admission to hospital for diabetic ketoacidosis in type 1
- diabetes. Diabetologia 2012 Sep;55(9):2356-2360.

(35) Bundeszentrale für politische Bildung. Dossier: Lange Wege der Deutschen

- Einheit. 2017; Available at: http://www.bpb.de/geschichte/deutsche-einheit/langewege-der-deutschen-einheit/. Accessed 02.11, 2017.
- (36) Bundesagentur für Arbeit. Statistik. Available at:
- 605 https://statistik.arbeitsagentur.de/Navigation/Statistik/Statistik-nach-

606 Regionen/Politische-Gebietsstruktur/Ost-West-Nav.html. Accessed 19.10, 2017.

- (37) Lampert T. 20 Jahre Deutsche Einheit: Gibt es noch Ost-West-Unterschiede in
- der Gesundheit von Kindern und Jugendlichen? www.rki.de/gbe-kompakt (Stand:
- 22.10.2010). GBE kompakt. Hrsg. Robert Koch-Institut Berlin. 2010;4.
- (38) Schneider EC, Squires D. From last to first Could the U.S. health care system
   become the best in the world? N Engl J Med 2017 Sep 7;377(10):901-904.
- (39) Lee AC, Maheswaran R. The health benefits of urban green spaces: a review of
- the evidence. J Public Health (Oxf) 2011 Jun;33(2):212-222.

615	
616	Tables
617	Table 1. Characteristics of the study population by GIMD 2010 quintiles
618	Table 2. Multiple adjusted mean estimates (95% CI) of indicators of diabetes care by
619	GIMD 2010 quintiles
620	
621	Figures
622	
623	Figure 1. Quintile-based distribution of the German Index of Multiple
624	Deprivation 2010 (GIMD 2010) (A) and of selected indicators of diabetes care at
625	district level (B–F)
626	Legend (B–F):
627	Adjusted mean estimates (least square means) from regression models (linear,
628	logistic, and Poisson), adjusting for sex, age group, migration, and diabetes duration,
629	with district as the categorical independent variable, categorized into outcome
630	quintiles.
631	
632	Figure 2. Multiple adjusted mean estimates of indicators of diabetes care by
633	GIMD 2010 quintiles
634	Legend:
635	Black triangles: Adjusted mean estimates (least square means) from regression
636	models (linear, logistic, and Poisson), with GIMD 2010 quintiles as the categorical
637	independent variable, adjusting for sex, age group, migration, and diabetes duration
638	(Model 1)

639	White 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
- 642 federal state (Model 2)

643

644

- 645 Online-Only Supplemental Material: 1 figure, 1 table, 1 appendix
- 646 **Supplemental Figure S1.** Selection of the study population
- 647 Supplemental Table S2. Multiple adjusted mean estimates (95% CI) of indicators of
- diabetes care by GIMD 2010 quintiles, stratified by sex
- 649 Supplemental Appendix S3: List of all centers contributing data to this analysis

650

651

# **Table 1. Characteristics of the study population by GIMD 2010 quintiles**

654

	All patients	Q1	Q2	Q3	Q4	Q5
	(n= 29,284)	(n= 7,109)	(n= 7,541)	(n= 5,353)	(n= 5,804)	(n= 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	15.9	0.0	0.4	3.1	30.5	77.3
(new federal states), %						

655

656

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

658

659

Outcome	n	Q1	Q2	Q3	Q4	Q5	p-value**
Treatment							
CGMS, %	29,284	7.3 (6.7 to 7.9)	5.6 (5.2 to 6.2)	5.6 (5.1 to 6.3)	4.8 (4.3 to 5.4)	4.5 (3.9 to 5.2)	<0.001
		6.3 (5.7 to 7.0) <sup>‡</sup>	5.6 (5.1 to 6.2) <sup>‡</sup>	5.7 (5.1 to 6.4) <sup>‡</sup>	5.3 (4.7 to 6.0) <sup>‡</sup>	3.4 (2.7 to 4.3) <sup>‡</sup>	<0.001 <sup>‡</sup>
Rapid-acting insulin	15,719 <sup>†</sup>	66.8 (65.3 to 68.3)	70.4 (68.8 to 71.9)	66.7 (64.8 to 68.5)	78.0 (76.5 to 79.5)	87.8 (86.2 to 89.2)	<0.001
analogs, %		74.7 (73.1 to 76.2) <sup>‡</sup>	75.9 (74.3 to 77.4) <sup>‡</sup>	70.9 (68.9 to 72.7) <sup>‡</sup>	76.7 (74.9 to 78.3) <sup>‡</sup>	79.0 (75.8 to 81.8) <sup>‡</sup>	<0.001 <sup>‡</sup>
Long-acting insulin	15,719 <sup>†</sup>	77.8 (76.5 to 79.2)	71.5 (69.9 to 73.0)	75.2 (73.4 to 76.8)	72.5 (70.8 to 74.1)	81.2 (79.4 to 82.9)	<0.001
analogs, %		80.8 (79.4 to 82.2) <sup>‡</sup>	77.3 (75.8 to 78.8) <sup>‡</sup>	80.8 (79.3 to 82.3) <sup>‡</sup>	72.4 (70.5 to 74.3) <sup>‡</sup>	64.3 (60.4 to 68.0) <sup>‡</sup>	<0.001 <sup>‡</sup>
SMBG	27,335	5.8 (5.7 to 5.8)	5.7 (5.7 to 5.8)	5.8 (5.7 to 5.8)	5.7 (5.7 to 5.8)	5.6 (5.6 to 5.7)	0.02
		5.7 (5.7 to 5.8) <sup>‡</sup>	5.7 (5.7 to 5.8) <sup>‡</sup>	5.7 (5.7 to 5.8) <sup>‡</sup>	5.8 (5.8 to 5.9) <sup>‡</sup>	5.7 (5.6 to 5.8) <sup>‡</sup>	0.02 <sup>‡</sup>
Diabetes education	29,284	44.2 (43.0 to 45.4)	46.8 (45.7 to 48.0)	46.1 (44.8 to 47.5)	47.7 (46.4 to 49.0)	51.7 (50.0 to 53.5)	<0.001
program, %		46.0 (44.6 to 47.4) <sup>‡</sup>	48.2 (47.0 to 49.5) <sup>‡</sup>	46.6 (45.1 to 48.1) <sup>‡</sup>	46.6 (45.1 to 48.1) <sup>‡</sup>	46.0 (43.4 to 48.7) <sup>‡</sup>	0.13 <sup>‡</sup>
Outcome quality							
Severe hypoglycemia with	29,284	1.8 (1.5 to 2.2)	2.1 (1.8 to 2.5)	2.5 (2.1 to 3.0)	2.0 (1.7 to 2.4)	1.6 (1.3 to 2.2)	0.06
coma, events/100 PY		1.9 (1.6 to 2.3) <sup>‡</sup>	1.9 (1.6 to 2.3) <sup>‡</sup>	2.2 (1.8 to 2.7) <sup>‡</sup>	1.9 (1.5 to 2.3) <sup>‡</sup>	1.8 (1.2 to 2.6) <sup>‡</sup>	0.71 <sup>‡</sup>
Severe DKA (pH <7.1),	28,965	0.2 (0.1 to 0.3)	0.2 (0.1 to 0.3)	0.3 (0.2 to 0.4)	0.2 (0.2 to 0.4)	0.4 (0.3 to 0.7)	0.03
events/100 PY		0.2 (0.1 to 0.3) <sup>‡</sup>	0.1 (0.1 to 0.3) <sup>‡</sup>	0.2 (0.1 to 0.5) <sup>‡</sup>	0.2 (0.1 to 0.5) <sup>‡</sup>	0.3 (0.1 to 0.8) <sup>‡</sup>	0.42 <sup>‡</sup>
BMI SDS	28,327	0.28 (0.26 to 0.30)	0.33 (0.31 to 0.35)	0.35 (0.33 to 0.37)	0.33 (0.31 to 0.35)	0.36 (0.33 to 0.39)	<0.001
		0.26 (0.24 to 0.29) <sup>‡</sup>	0.29 (0.27 to 0.32) <sup>‡</sup>	0.33 (0.31 to 0.36) <sup>‡</sup>	0.35 (0.33 to 0.38) <sup>‡</sup>	0.46 (0.41 to 0.50) <sup>‡</sup>	<0.001 <sup>‡</sup>
Obesity, %	28,327	3.2 (2.8 to 3.6)	3.0 (2.6 to 3.4)	3.7 (3.2 to 4.2)	3.6 (3.2 to 4.2)	3.8 (3.2 to 4.5)	0.07
		3.2 (2.8 to 3.7) <sup>‡</sup>	2.8 (2.5 to 3.3) <sup>‡</sup>	3.6 (3.1 to 4.2) <sup>‡</sup>	3.7 (3.2 to 4.3) <sup>‡</sup>	3.9 (3.0 to 5.0) <sup>‡</sup>	0.07 <sup>‡</sup>
Number of hospital	29,284	3.9 (3.3 to 4.6)	4.5 (3.9 to 5.3)	4.5 (3.8 to 5.4)	4.7 (4.0 to 5.6)	6.8 (5.7 to 8.2)	<0.001
days/PY		4.2 (3.5 to 5.0) <sup>‡</sup>	4.7 (4.0 to 5.5) <sup>‡</sup>	4.5 (3.8 to 5.5) <sup>‡</sup>	4.7 (3.9 to 5.6) <sup>‡</sup>	5.1 (3.8 to 7.0) <sup>‡</sup>	0.85 <sup>‡</sup>

# Table 2. Multiple adjusted mean estimates (95% CI) of indicators of diabetes care by GIMD 2010 quintiles\*

\* Adjusted mean estimates (least square means) with respective 95% confidence intervals are 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.

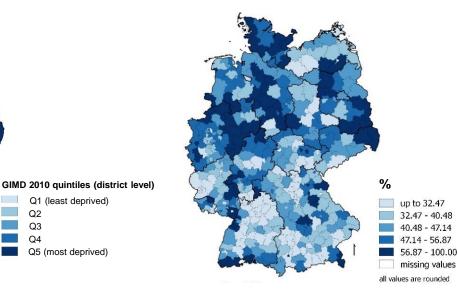
<sup>†</sup>Only patients without CSII.

<sup>‡</sup>Estimates from regression models additionally adjusted for German federal states.

\*\*p-value of test of no difference in outcome distribution across GIMD quintiles.

Page 30 of 38 Figure 1. Quintile-based distribution of the German Index of Multiple Deprivation 2010 (GIMD 2010) (A) and of selected indicators of diabetes care at district level (B-F)

- Α. German Index of multiple deprivation 2010
- Use of insulin pump therapy (CSII) В.

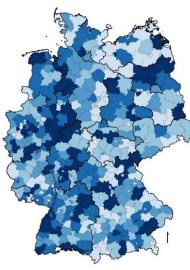


D. Severe hypoglycemia

% up to 7.57 7.57 - 7.83 7.83 - 8.03 8.03 - 8.27 8.27 - 9.41 missing values all values are rounded

C.

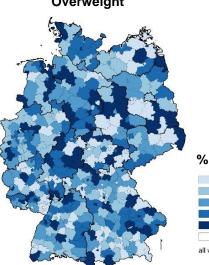
HbA1c



## Events /100 PY

	up to 2.2
	2.2 - 5.8
	5.8 - 8.7
	8.7 - 13.7
	13.7 - 132.2
	missing values
all va	lues are rounded

Overweight



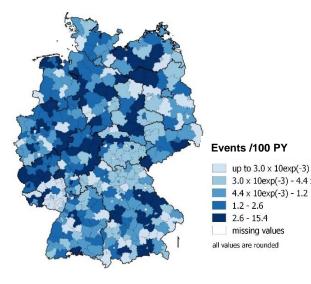
up to 8.91 8.91 - 11.98 11.98 - 14.36 14.36 - 17.33 17.33 - 45.97 missing values all values are rounded

Scale 1:4,000,000 for A4 prints

F.

C টেম্পিট্টিটিমি শিশ্বিপ্রিন্দেরে প্রিন্থিনের প্রিয়ান্টের্বার্যটোল প্রিটানেরে (IGM), 2017 Data source: VG250 (utm32w; 31/12/2010), German Federal Agency for Cartography and Geodesy

Ε. **Diabetic ketoacidosis (DKA)** 





3.0 × 10exp(-3) - 4.4 × 10exp(-3)

4.4 x 10exp(-3) - 1.2

1.2 - 2.6

2.6 - 15.4

missing values

Q1 (least deprived)

Q5 (most deprived)

Q2

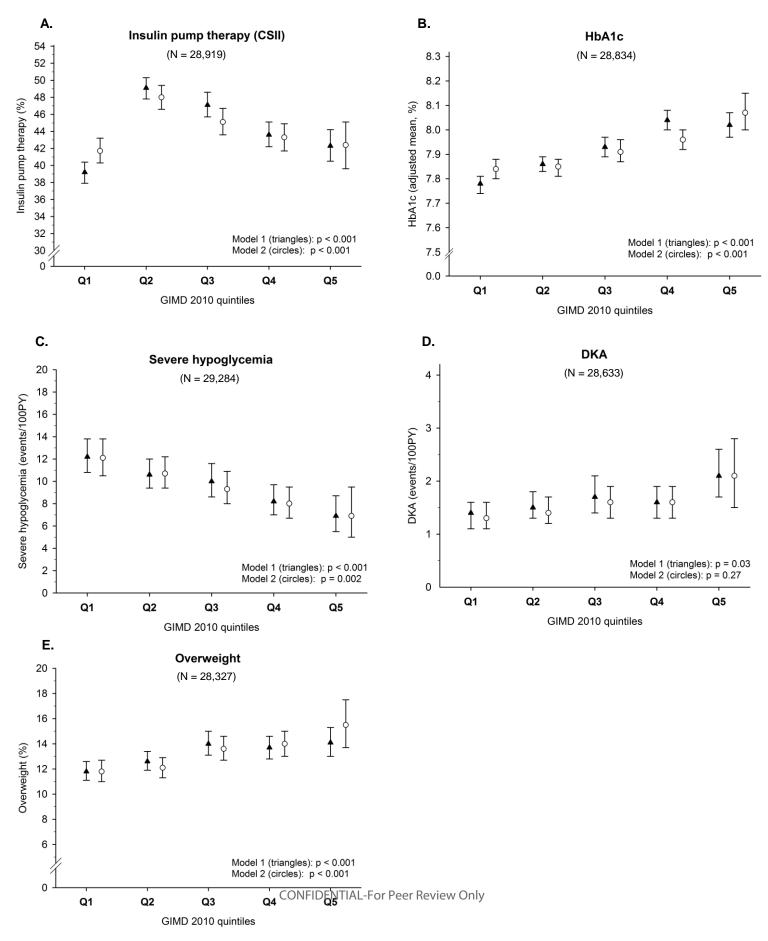
Q3

Q4

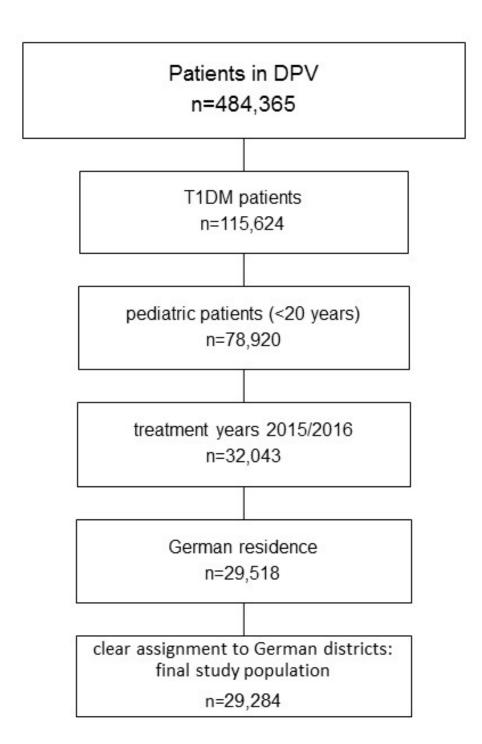
# Figure 2. Multiple adjusted mean estimates of indicators of diabetes care by GIMD 2010 quintiles

<u>Black triangles:</u> 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 1)

<u>White circles:</u> 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 (Model 2)



Supplemental figure S1. Selection of the study population



Page 33 of 38

**Supplemental table S2.** Multiple adjusted mean estimates (95% CI) of indicators of diabetes care by GIMD 2010 quintiles, stratified by sex\*

Outcome	n	sex	Q1	Q2	Q3	Q4	Q5	p- value**
Treatment								
Insulin pump therapy	13,654	Girls	45.6 (43.5 to 47.7)	51.1 (49.1 to 53.0)	50.0 (47.8 to 52.3)	47.9 (45.6 to 50.2)	45.9 (41.9 to 49.9)	0.001
(CSII), %	15,265	Boys	38.2 (36.3 to 40.2)	45.2 (43.3 to 47.1)	40.8 (38.7 to 42.9)	39.2 (37.1 to 41.4)	39.1 (35.4 to 42.9)	<0.001
CGMS, %	13,828	Girls	6.3 (5.4 to 7.3)	5.4 (4.7 to 6.3)	5.7 (4.9 to 6.7)	5.2 (4.4 to 6.2)	3.1 (2.1 to 4.4)	0.02
	15,456	Boys	6.5 (5.7 to 7.5)	6.0 (5.2 to 6.8)	5.6 (4.8 to 6.6)	5.2 (4.4 to 6.1)	3.3 (2.4 to 4.5)	0.009
Rapid-acting insulin	6,975 <sup>†</sup>	Girls	73.3 (70.7 to 75.6)	75.7 (73.3 to 77.9)	70.9 (68.0 to 73.6)	77.3 (74.6 to 79.8)	82.0 (77.4 to 85.9)	<0.001
analogs, %	8,744	Boys	75.2 (73.1 to 77.3)	76.1 (73.9 to 78.1)	70.6 (68.0 to 73.0)	76.2 (73.9 to 78.5)	78.4 (74.1 to 82.2)	<0.001
Long-acting insulin	6,975 <sup>†</sup>	Girls	81.8 (79.7 to 83.8)	78.0 (75.7 to 80.1)	80.8 (78.4 to 83.0)	73.5 (70.6 to 76.2)	70.2 (64.6 to 75.2)	<0.001
analogs, %	8,744	Boys	80.0 (78.0 to 81.8)	77.1 (74.9 to 79.0)	81.1 (78.9 to 83.0)	71.8 (69.2 to 74.2)	60.5 (55.1 to 65.6)	<0.001
SMBG	12,925	Girls	5.8 (5.7 to 5.9)	5.8 (5.7 to 5.9)	5.8 (5.7 to 5.8)	5.9 (5.8 to 6.0)	5.9 (5.7 to 6.0)	0.39
	14,410	Boys	5.7 (5.6 to 5.7)	5.7 (5.6 to 5.8)	5.7 (5.6 to 5.8)	5.8 (5.7 to 5.9)	5.5 (5.3 to 5.6)	0.003
Diabetes education	13,828	Girls	47.4 (45.4 to 49.5)	50.6 (48.8 to 52.4)	47.9 (45.8 to 50.0)	48.3 (46.2 to 50.5)	45.4 (41.6 to 49.2)	0.06
program, %	15,456	Boys	44.6 (42.8 to 46.5)	46.0 (44.2 to 47.8)	45.3 (43.3 to 47.4)	45.1 (43.1 to 47.1)	46.9 (43.3 to 50.6)	0.76
Outcome quality								
HbA1c, %	13,622	Girls	7.89 (7.83 to 7.95)	7.89 (7.83 to 7.94)	7.96 (7.90 to 8.02)	8.02 (7.95 to 8.08)	8.11 (7.99 to 8.22)	0.003
	15,212	Boys	7.80 (7.74 to 7.85)	7.81 (7.76 to 7.86)	7.88 (7.82 to 7.94)	7.91 (7.85 to 7.97)	8.04 (7.94 to 8.14)	<0.001
Severe hypoglycemia (all),	13,828	Girls	11.9 (9.7 to 14.6)	9.7 (8.0 to 11.8)	9.1 (7.3 to 11.4)	7.4 (5.7 to 9.6)	7.1 (4.5 to 11.3)	0.08
events/100 PY	15,456	Boys	12.1 (10.2 to 14.5)	11.5 (9.7 to 13.6)	9.3 (7.5 to 11.4)	8.4 (6.8 to 10.4)	6.6 (4.4 to 10.0)	0.02
Severe hypoglycemia with	13,828	Girls	2.1 (1.6 to 2.8)	1.8 (1.4 to 2.4)	2.1 (1.6 to 2.8)	1.8 (1.3 to 2.4)	1.9 (1.1 to 3.3)	0.86
coma, events/100 PY	15,456	Boys	1.7 (1.3 to 2.2)	1.9 (1.5 to 2.4)	2.2 (1.7 to 2.8)	1.9 (1.5 to 2.5)	1.5 (0.9 to 2.6)	0.61
DKA, events/100 PY	13,548	Girls	1.6 (1.2 to 2.1)	1.6 (1.3 to 2.1)	2.0 (1.5 to 2.5)	1.9 (1.4 to 2.4)	2.4 (1.5 to 3.7)	0.47

	15,085	Boys	1.0 (0.8 to 1.4)	1.2 (0.9 to 1.6)	1.2 (0.9 to 1.6)	1.4 (1.0 to 1.8)	2.0 (1.3 to 3.2)	0.24
Severe DKA (pH <7.1),	13,697	Girls	0.2 (0.1 to 0.3)	0.2 (0.1 to 0.4)	0.3 (0.2 to 0.6)	0.4 (0.2 to 0.6)	0.6 (0.3 to 1.1)	0.06
events/100 PY	15,268	Boys	0.1 (0.0 to 3.4)	0.1 (0.1 to 2.3)	0.1 (0.1 to 4.4)	0.1 (0.1 to 3.0)	0.1 (0.1 to 6.5)	0.90
BMI SDS	13,372	Girls	0.35 (0.32 to 0.38)	0.39 (0.36 to 0.42)	0.41 (0.37 to 0.44)	0.45 (0.42 to 0.49)	0.55 (0.49 to 0.62)	<0.001
	14,955	Boys	0.19 (0.15 to 0.22)	0.21 (0.18 to 0.24)	0.27 (0.23 to 0.30)	0.26 (0.23 to 0.30)	0.37 (0.31 to 0.43)	<0.001
Overweight, %	13,372	Girls	13.5 (12.2 to 14.9)	13.8 (12.6 to 15.1)	15.1 (13.7 to 16.5)	15.8 (14.3 to 17.4)	16.9 (14.3 to 20.0)	0.09
	14,955	Boys	10.3 (9.3 to 11.4)	10.5 (9.5 to 11.6)	12.3 (11.1 to 13.7)	12.4 (11.2 to 13.8)	14.2 (11.9 to 17.0)	0.007
Obesity, %	13,372	Girls	3.3 (2.7 to 4.0)	3.1 (2.6 to 3.8)	3.9 (3.2 to 4.8)	4.1 (3.4 to 5.0)	5.2 (3.7 to 7.2)	0.09
	14,955	Boys	2.9 (2.4 to 3.6)	2.5 (2.0 to 3.1)	3.2 (2.6 to 4.0)	3.3 (2.7 to 4.1)	3.1 (2.1 to 4.5)	0.35
Number of hospital	13,828	Girls	4.4 (3.3 to 5.8)	5.0 (3.9 to 6.3)	4.9 (3.7 to 6.4)	5.0 (3.7 to 6.6)	5.5 (3.5 to 8.7)	0.93
days/PY	15,456	Boys	4.1 (3.2 to 5.2)	4.4 (3.5 to 5.5)	4.2 (3.3 to 5.5)	4.3 (3.4 to 5.6)	4.7 (3.1 to 7.3)	0.98

\* Adjusted mean estimates (least square means) with respective 95% confidence intervals are derived from logistic regression analysis (for outcomes use of insulin pump therapy (CSII), use of CGMS, use of rapid-acting insulin analogs, use of long-acting insulin analogs, participation in diabetes education program, prevalence of overweight, prevalence of obesity), linear regression analysis (for outcomes HbA1c, SMBG, BMI SDS), or Poisson regression analysis considering overdispersion (for outcomes rate of severe hypoglycemia, rate of severe hypoglycemia with coma, rate of DKA, 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 age group, migration background, and diabetes duration.

<sup>†</sup>Only patients without CSII.

\*\* p-value of test of no difference in outcome distribution across GIMD quintiles.

Supplemental Appendix S3: List of all centers contributing data to this analysis.

Aachen - Uni-Kinderklinik RWTH, Aalen Kinderklinik, Ahlen St. Franziskus Kinderklinik, Amberg Kinderklinik St. Marien, Aue Helios Kinderklink, Augsburg IV. Med. Klinik, Augsburg Josefinum Kinderklinik, Augsburg Kinderklinik Zentralklinikum, Aurich Kinderklinik, Bad Aibling Internist. Praxis, Bad Driburg / Bad Hermannsborn Innere, Bad Hersfeld Innere, Bad Hersfeld Kinderklinik, Bad Kreuznach-Viktoriastift, Bad Kösen Median Kinderklinik, Bad Lauterberg Diabeteszentrum Innere, Bad Mergentheim -Diabetesfachklinik, Bad Mergentheim - Gemeinschaftspraxis DM-dorf Althausen, Bad Oeynhausen Herz-und Diabeteszentrum NRW, Bad Orb Spessart Klinik, Bad Reichenhall Kreisklinik Innere Med., Bad Salzungen Kinderklinik, Bautzen Oberlausitz KK, Bayreuth Innere Medizin, Berchtesgaden CJD, Berlin DRK-Kliniken Mitte Innere, Berlin DRK-Kliniken Pädiatrie, Berlin Evang. Krankenhaus Königin Elisabeth, Berlin Klinik St. Hedwig Innere, Berlin Lichtenberg - Kinderklinik, Berlin Oskar Zieten Krankenhaus Innere, Berlin Parkklinik Weissensee, Berlin Schlosspark-Klinik Innere, Berlin Virchow-Kinderklinik, Berlin Vivantes Hellersdorf Innere, Bielefeld Kinderarztpraxis, Bielefeld Kinderklinik Gilead, Bocholt Kinderklinik, Bochum Universitäts St. Josef, Bochum Universitätskinderklinik St. Josef, Bonn Uni-Kinderklinik, Bottrop Knappschaftskrankenhaus Innere, Braunschweig Kinderarztpraxis, Bremen - Kinderklinik Nord, Bremen - Mitte Innere, Bremen Zentralkrankenhaus Kinderklinik, Bremerhaven Kinderklinik, Bruchweiler Edelsteinklinik Kinder-Reha, Böblingen Kinderklinik, Castrop-Rauxel Evangelisches Krankenhaus, Castrop-Rauxel Rochus-Hospital, Celle Klinik für Kinder- und Jugendmedizin, Chemnitz Kinderklinik, Chemnitz-Hartmannsdorf Innere Medizin - DIAKOMED-1, Coburg Innere Medizin, Coburg Kinderklinik, Coesfeld Kinderklinik, Coesfeld/Dülmen Innere Med., Darmstadt Innere Medizin, Darmstadt Kinderklinik Prinz. Margaret, Datteln Vestische Kinderklinik, Deggendorf Gemeinschaftspraxis, Deggendorf Medizinische Klinik II, Deggendorf Pädiatrie-Praxis, Delmenhorst Kinderklinik, Dessau Kinderklinik, Detmold Kinderklinik, Dinslaken Kinderklinik, Dortmund Kinderklinik, Dortmund Medizinische Kliniken Nord, Dortmund-Hombruch Marienhospital, Dortmund-St. Josefshospital Innere, Dortmund-West Innere, Dresden Neustadt Kinderklinik, Dresden Uni-Kinderklinik, Duisburg Malteser Rhein-Ruhr St. Anna Innere, Duisburg Sana Kinderklinik, Duisburg-Huckingen Malteser Rhein-Ruhr ST. Johannes, Duisburg-St. Johannes Helios, Düren-Birkesdorf Kinderklinik, Düsseldorf Uni-Kinderklinik, Eisleben Lutherstadt Helios-Klinik, Erfurt Kinderklinik, Erlangen Uni Innere Medizin, Erlangen Uni-Kinderklinik, Essen Diabetes-Schwerpunktpraxis, Essen Elisabeth Kinderklinik, Essen Kinderarztpraxis, Essen Uni-Kinderklinik, Esslingen Klinik für Kinder und Jugendliche, Eutin Kinderklinik, Filderstadt Kinderklinik, Flensburg Diakonissen Kinderklinik, Forchheim Diabeteszentrum SPP, Frankenthal Kinderarztpraxis, Frankfurt Diabeteszentrum Rhein-Main-Erwachsenendiabetologie (Bürgerhospital), Frankfurt

Page 37 of 38

### **Diabetes** Care

Diabeteszentrum Rhein-Main-pädiat. Diabetologie (Clementine-Hospital), Frankfurt Uni-Kinderklinik, Frankfurt Uni-Klinik Innere, Frankfurt-Sachsenhausen Innere, Frankfurt-Sachsenhausen Innere MVZ, Freiburg St. Josef Kinderklinik, Freiburg Uni Innere, Freiburg Uni-Kinderklinik, Freudenstadt Kinderklinik, Fürth Kinderklinik, Gaissach Fachklinik der Deutschen Rentenversicherung Bayern Süd, Garmisch-Partenkirchen Kinderklinik, Geislingen Klinik Helfenstein Innere, Gelnhausen Innere, Gelnhausen Kinderklinik, Gelsenkirchen Kinderklinik Marienhospital, Gera Kinderklinik, Gießen Ev. Krankenhaus Mittelhessen, Gießen Uni-Kinderklinik, Greifswald Uni-Kinderklinik, Göppingen Innere Medizin, Göppingen Kinderklinik am Eichert, Görlitz Städtische Kinderklinik, Göttingen Uni Gastroenterologie, Göttingen Uni-Kinderklinik, Hachenburg Kinderpraxis, Hagen Kinderklinik, Halberstadt Innere Med. AMEOS Klinik, Halberstadt Kinderklinik AMEOS, Halle Uni-Kinderklinik, Hamburg Altonaer Kinderklinik, Hamburg Kinderklinik Wilhelmstift, Hamburg-Nord Kinder-MVZ, Hameln Kinderklinik, Hamm Kinderklinik, Hanau Kinderklinik, Hannover DM-SPP, Hannover Kinderklinik MHH, Hannover Kinderklinik auf der Bult, Haren Kinderarztpraxis, Heide Kinderklinik, Heidelberg St. Josefskrankenhaus, Heidelberg Uni-Kinderklinik, Heidenheim Kinderklinik, Heilbronn Innere Klinik, Heilbronn Kinderklinik, Herdecke Kinderklinik, Herford Kinderarztpraxis, Herford Klinikum Kinder & Jugendliche, Heringsdorf Inselklinik, Herne Evan. Krankenhaus Innere, Hildesheim GmbH - Innere, Hildesheim Kinderarztpraxis, Hildesheim Kinderklinik, Hof Kinderklinik, Homburg Uni-Kinderklinik Saarland, Itzehoe Kinderklinik, Jena Uni-Kinderklinik, Kaiserslautern Kinderarztpraxis, Kaiserslautern-Westpfalzklinikum Kinderklinik, Kamen Klinikum Westfalen Hellmig Krankenhaus, Karlsburg Klinik für Diabetes & Stoffwechsel, Karlsruhe Städtische Kinderklinik, Kassel Klinikum Kinder- und Jugendmedizin, Kempten Oberallgäu Kinderklinik, Kiel Städtische Kinderklinik, Kiel Universitäts-Kinderklinik, Kirchen DRK Krankenhaus Kinderklinik, Kirchheim-Nürtingen Innere, Kleve Innere Medizin, Koblenz Kemperhof 1. Med. Klinik, Koblenz Kinderklinik Kemperhof, Konstanz Innere Klinik, Konstanz Kinderklinik, Krefeld Innere Klinik, Krefeld Kinderklinik, Kreischa-Zscheckwitz Klinik Bavaria, Köln Kinderklinik Amsterdamerstrasse, Köln Uni-Kinderklinik, Landau Innere, Landshut Kinderklink, Lappersdorf Kinderarztpraxis, Leer Klinikum - Klinik Kinder & Jugendmedizin, Leipzig Uni-Kinderklinik, Leverkusen Kinderklinik, Lilienthal Diabeteszentrum, Lindenfels Luisenkrankenhaus Innere 2, Lingen Kinderklinik St. Bonifatius, Lippstadt Evangelische Kinderklinik, Ludwigsburg Kinderklinik, Ludwigshafen Kinderklinik St. Anna-Stift, Ludwigshafen diabetol. SPP, Lübeck Uni-Kinderklinik, Lüdenscheid Märkische Kliniken - Kinder & Jugendmedizin, Magdeburg Städtisches Klinikum Innere, Magdeburg Uni-Kinderklinik, Mainz Uni-Kinderklinik, Mannheim Uni-Kinderklinik, Marburg Uni-Kinderklinik, Marktredwitz Innere Medizin, Mechernich Kinderklinik, Meissen Kinderklinik Elblandklinikum, Memmingen Internistische Praxis, Memmingen Kinderklinik, Minden Kinderklinik, Moers Kinderklinik, Murnau am Staffelsee - diabetol. SPP, Mutterstadt Kinderarztpraxis, Mönchengladbach Kinderklinik Rheydt Elisabethkrankenhaus, Mühldorf am Inn Kinderarztpraxis, München 3. Orden Kinderklinik, München Kinderarztpraxis diabet. SPP, München von Haunersche Kinderklinik, München-Gauting Kinderarztzentrum, München-Harlaching Kinderklinik, München-Schwabing Kinderklinik, Münster Herz

Jesu Innere, Münster Ludgerus-Kliniken GmbH, Münster St. Franziskus Kinderklinik, Münster Uni-Kinderklinik, Münster pädiat. Schwerpunktpraxis, Neuburg Kinderklinik, Neumarkt Innere, Neunkirchen Marienhausklinik Kohlhof Kinderklinik, Neuruppin Kinderklinik, Neuss Lukas-Krankenhaus Kinderklinik, Neuss Lukaskrankenhaus Kinderklinik, Neuwied Kinderklinik Elisabeth, Neuwied Marienhaus Klinikum St. Elisabeth Innere, Nürnberg Cnopfsche Kinderklinik, Nürnberg Med. Klinik 4, Nürnberg Zentrum f Neugeb./Kinder & Jugendl., Oberhausen Kinderklinik, Oberhausen Kinderpraxis, Oberhausen St.Clemens Hospitale Sterkrade, Oberndorf Gastroenterologische Praxis Schwerpunkt Diabetologie, Offenbach/Main Innere Medizin, Offenburg Kinderklinik, Oldenburg Kinderklinik, Oldenburg Schwerpunktpraxis, Olpe pädiatrische Gemeinschaftspraxis, Osnabrück Christliches Kinderhospital, Paderborn St. Vincenz Kinderklinik, Passau Kinderklinik, Pforzheim Kinderklinik, Pfullendorf Innere Medizin, Pirmasens Städtisches Krankenhaus Innere, Plauen Vogtlandklinikum, Rastatt Kreiskrankenhaus Innere, Ravensburg Kinderklink St. Nikolaus, Regensburg Kinderklinik St. Hedwig, Rendsburg Kinderklinik, Reutlingen Kinderarztpraxis, Reutlingen Kinderklinik, Reutlingen Klinikum Steinenberg Innere, Rheine Mathiasspital Kinderklinik, Rodalben St. Elisabeth, Rosenheim Innere Medizin, Rosenheim Kinderklinik, Rosenheim Schwerpunktpraxis, Rostock Uni-Kinderklinik, Rotenburg/Wümme Agaplesion Diakonieklinikum Kinderabteilung, Rüsselsheim Kinderklinik, Saaldorf-Surheim Diabetespraxis, Saarbrücken Kinderklinik Winterberg, Saarlouis Kinderklinik, Scheidegg Prinzregent Luitpold, Schw. Gmünd Stauferklinik Kinderklinik, Schweinfurt Kinderklinik, Schwerin Innere Medizin, Schwerin Kinderklinik, Schwäbisch Hall Diakonie Kinderklinik, Siegen Kinderklinik, Singen - Hegauklinik Kinderklinik, Singen Kinderarztpraxis, Spaichingen Innere, Speyer Diakonissen Stiftungskrankenhaus Pädiatrie, St. Augustin Kinderklinik, Stade Kinderklinik, Stolberg Kinderklinik, Stuttgart Olgahospital Kinderklinik, Suhl Kinderklinik, Sylt Rehaklinik, Tettnang Innere Medizin, Traunstein Kinderklinik, Traunstein diabetol. Schwerpunktpraxis, Trier Kinderklinik der Borromäerinnen, Tübingen Uni-Kinderklinik, Ulm Endokrinologikum, Ulm Uni-Kinderklinik, Vechta Kinderklinik, Viersen Kinderkrankenhaus St. Nikolaus, Villingen-Schwenningen Schwarzwald Baar Klinikum Kinderklinik, Villingen-Schwenningen Schwarzwald-Baar-Klinikum Innere, Waldshut Kinderpraxis, Waldshut-Tiengen Kinderpraxis Biberbau, Wangen Oberschwabenklinik Innere Medizin, Waren-Müritz Kinderklinik, Weiden Kinderklinik, Weingarten Kinderarztpraxis, Weisswasser Kreiskrankenhaus, Wesel Marienhospital Kinderklinik, Wiesbaden Helios Horst-Schmidt-Kinderkliniken, Wiesbaden Kinderklinik DKD, Wilhelmshaven Klinikum Kinderklinik, Winnenden Rems-Murr Kinderklinik, Wismar Kinderklinik, Wittenberg Kinderklinik, Worms - Weierhof, Worms Kinderklinik, Wuppertal Kinderklinik, Würzburg Kinderarztpraxis, Zweibrücken Kinderarztpraxis.