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Size matters: Influence of center size on quality of diabetes control in children and adolescents with type 1 diabetes—A longitudinal analysis of the DPV cohort

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Abstract

Background: Treatment of patients with type 1 diabetes requires experience and a specific infrastructure. Therefore, center size might influence outcome in diabetes treatment.

Objective: To analyze the influence of center size on the quality of diabetes treatment in children and adolescents in Germany and Austria.

Patients and methods: In 2009 and 2018, we analyzed metabolic control, acute complications, and rates of recommended screening tests in the DPV cohort. Diabetes centers were classified according to the number of patients from "XS" to "XL" (<20 [XS], ≥20 to <50 [S], ≥50 to <100 [M], ≥100 to <200 [L], ≥200 [XL]).

Results: Over the 10-year period, metabolic control improved significantly in "M", "L" and "XL" diabetes centers. Treatment targets are best achieved in "M" centers, while "XS" centers have the highest mean hemoglobin A1c. The relation between hemoglobin A1c and center size follows a "v-shaped" curve. In 2009, conventional insulin therapy was most frequently used in "XS" centers, but in 2018, there was no difference in mode of insulin therapy according to center size. Use of CSII and sensor

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augmented CSII/hybrid closed loop increased with center size. Patients cared for in "XS" diabetes centers had the fewest follow-up visits per year. The rates of severe hypoglycemia and DKA were lowest in "XL" diabetes centers, and the rate of DKA was highest in "XS" centers.

Conclusion: Center size influences quality of care in pediatric patients with type 1 diabetes. Further investigations regarding contributing factors such as staffing and financial resources are required.

KEYWORDS

center size, diabetes mellitus type 1, pediatrics, quality improvement

1 | INTRODUCTION

Treatment of type 1 diabetes poses a challenge for families and all care-givers involved. A great variety of therapeutic options is used to achieve best possible metabolic control in the absence of acute or chronic complications. Therefore, the use of diabetes technology increased considerably with growing numbers of sensor and pump models over the last years.[1,2] Both technical components can be combined in numerous ways and thus allow a high degree of variability. Additionally, factors such as age, social environment, growth, and pubertal development require intensive medical but also psychosocial care in children and adolescents with type 1 diabetes.[3–5]

Diabetes care in general differs not only on an individual basis but also between diabetes centers on a national and even more on an international basis.[6–8] Benchmarking and comparison of diabetes care through diabetes registries improved patient outcomes significantly over the years.[9,10] Furthermore, it raised awareness for differences in diabetes care between countries.[6,11–13] The "Diabetes Patient Follow-up" (DPV), established in 1995, is a prospective longitudinal diabetes registry. It collects data on more than 90% of pediatric diabetes patients treated in Germany and more than 80% of in Austria. Both nations provide diabetes care with a similar spectrum of facilities and a comparable variance in center size, while other countries pursue a more centralized approach by pooling patients in specialized diabetes care.[6,8,12–15]

In the literature, there are few recommendations on a minimum number of patients treated per center to ensure good quality of diabetes care. In the 2018 ISPAD Guidelines, caring for at least 150 patients per center is recommended to ensure a minimum of expertise.[16] In order to provide a specialized multi-professional team service, a critical number of hospital admissions as well as outpatient cases are required. Center competence and center size may have an important impact on the successful and safe treatment of pediatric patients with type 1 diabetes.[7,8,14,17] Therefore, we investigated center size in relation to metabolic outcome of children and adolescents with type 1 diabetes, as well as frequency of acute complications and completeness of screening for chronic complications and associated diseases.

2 | METHODS

DPV is an electronic health record broadly used in Germany since 1995 and Austria since the early 2000s. Pseudonymized longitudinal data are transmitted for central validation and analysis twice yearly. Inconsistent data are reported back to the participating centers for confirmation or correction and then reentered into the joint data base, followed by complete anonymization. Based on this continuous data acquisition system for prospective surveillance, complete demographic, anthropometric and diabetes-related characteristics of patients younger than 21 years of age with type 1 diabetes treated in 2009 and 2018 were analyzed. For 2009, 217 centers (15 in Austria, 202 in Germany) with 19,400 patients and for 2018, 238 centers (24 in Austria and 214 in Germany) with 26,689 patients were included in this analysis. Data analysis in the DPV registry has been approved by the ethics committee of the University of Ulm, and data collection by local review boards.

We divided participating centers into five groups defined by the number of patients treated within a facility in a given year and labeled them accordingly ("XS": <20 patients, "S": ≥20 to <50 patients, "M": ≥50 to <100 patients, "L": ≥100 to <200 patients and "XL": ≥200 patients). Description of center size distribution and patient characteristics are shown in Table 1 a,b.

2.1 | Definitions and terms used

Hemoglobin A1c is given in percentage and mmol/mol. Hemoglobin A1c measurements were performed in local certified laboratories. Measurements were adjusted to the Diabetes Control and Complications Trial (DCCT) reference range using the multiple-of-the-mean method. Hemoglobin A1c measurements at diagnosis of type 1 diabetes and until 3 months after diabetes manifestation were excluded from the analysis. Hemoglobin A1c ≤ 7.0% (<53 mmol/mol) was defined as target hemoglobin A1c as recommended in ISPAD guideline[4] 2018. Due to the recent change in treatment target, we also included the former target for hemoglobin A1c of ≤7.5% (≤58 mmol/mol). A hemoglobin A1c ≥9% (≥ 75 mmol/mol) was defined as poor metabolic control. Patients were categorized as having migration background, if at least one parent or the child was born abroad.

TABLE 1 Center structure 2009 and 2018

(a)		2009		2018	
Center size		**Center no./pt. no. (median)**	**Total patient no.**	**Center no./pt. no. (median)**	**Total patient no.**
<20	"XS"	37/8	309	29/8	269
≥20 to <50	"S"	45/36	1565	42/36	1432
≥50 to <100	"M"	55/67	3889	57/68	4073
≥100 to <200	"L"	61/139	8368	69/130	9456
≥200	"XL"	19/228	5269	41/237	11,459
∑		217	19,400	238	26,689

(b) 2009						Year	2018					
Total	**≥200**	**≥100 to <200**	**≥50to <100**	**≥20 to <50**	**<20**	**Patients per center**	**<20**	**≥20 to <50**	**≥50 to <100**	**≥100 to <200**	**≥200**	**Total**
12.8	12.9	12.8	12.7	12.5	11.9	Median age (years)	14.3	13.4	13.4	13.4	13.5	13.4
7.4	7.4	7.2	7.6	7.2	7.8	Median age at T1DM diagnosis (years)	7.9	7.6	7.6	7.4	7.2	7.3
4.1	4.3	4.1	3.9	3.9	3.2	Median diabetes duration (years)	4.7	4.5	4.4	4.5	4.6	4.5
0.8	0.8	0.8	0.8	0.8	0.8	Median daily insulin dosage (I.E./kg)	0.9	0.8	0.8	0.8	0.8	0.8
52.4	52.3	53.3	52.0	50.4	46.6	Male (%)	56.5	54.1	53.2	52.5	53.1	53.0
18.3	16.1	18.8	19.8	18.7	19.7	Migration background (|%)	28.6	23.8	23.5	26.2	24.3	24.9

Data was analyzed for treatment modality. Conventional insulin therapy (CT), Multiple-daily-injections (MDI) and continuous subcutaneous insulin infusion (CSII) were used as categories. CT was defined as equal or less than three insulin injection time points per day. MDI was defined as more than three insulin injection time-points per day.

Acute complications were defined according to ISPAD guidelines 2018.[18,19] Severe hypoglycemia is defined as cognitive impairment requiring external assistance by another person. Hypoglycemic coma is defined as a severe hypoglycemic event resulting in coma or convulsions requiring parenteral therapy. Diabetic ketoacidosis (DKA) was defined as pH <7.3. DKA at diagnosis of type 1 diabetes was excluded for the analysis of diabetes complications during therapy.

Recommended screening intervals were defined based on ISPAD guidelines for micro- and macrovascular complications and for diabetes associated diseases and adapted to clinical practice within Austria and Germany.[20,21] Screening for microvascular complications should start at the age of 11 years or after at least 5 years of diabetes duration. Biennial screening for retinopathy obtained by a trained ophthalmologist was defined as the standard. Nephropathy screening was based on yearly measurement of urinary albumin excretion. Hypertension screening required blood pressure measurements at least yearly. Screening for dyslipidemia was defined as yearly laboratory evaluation of lipids. Thyroid disease screening was defined as measurement of thyroid stimulating hormone (TSH) or anti-thyroid peroxidase antibodies on a biennial basis. Screening for celiac disease was defined as availability of any value for immunoglobulin A or G for tissue transglutaminase (TG-A), endomysial antibodies (EMA) or immunoglobulin A or G for gliadine on a biennial basis.

2.2 | Statistical analyses

All statistical analyses were performed using SAS 9.4 (SAS Institute). Differences between groups (center sizes) were assessed by Kruskal–Wallis test for continuous variables and $\chi 2$ tests for dichotomous variables. The Bonferroni–Holm method was applied to adjust for multiple comparisons.

A linear regression model was used to analyze the effect of center size on mean hemoglobin A1c and number of outpatient contacts per year. A negative binomial regression model was used to analyze the effect of center size on acute diabetes-related complications (severe hypoglycemia, hypoglycemic coma, and diabetic ketoacidosis). A logistic regression model was used to analyze the effect of center size on therapeutic regimen (CT, MDI, CSII), completeness of screening examinations (retinopathy screening, nephropathy screening, hypertension screening, dyslipidemia screening, thyroid dysfunction screening, celiac disease screening) and center related metabolic control parameters (percentage of patients with hemoglobin A1c ≤7.0%, ≤7,5% and ≥9.0%). All regression analyses were adjusted for age, sex, diabetes-duration, and migration background. In all regression analyses, the

Tukey–Kramer test was used to adjust for comparisons between multiple groups.

Additionally, regression analyses regarding metabolic control (mean hemoglobin A1c, percentage of patients with HbA1c ≤7.0%, ≤7.5% and ≥9.0%) and complications (severe hypoglycemia, hypoglycemic coma, diabetic ketoacidosis) were adjusted for therapeutic regimen and sensor use (at least 30 days per year).

For statistical comparison of completeness of screening examinations and center related metabolic control parameters (percentage of patients with hemoglobin A1c ≤7.0%, ≤7,5% and ≥9.0%) and therapeutic regime (ICT, MDI, CSII) between 2009 and 2018, we used an unadjusted logistic regression model. The rates of acute complications in 2009 and 2018 were compared with an unadjusted negative binomial regression model.

Due to the large number of patients, a two-sided p-value <0.01 was considered statistically significant.

3 | RESULTS

3.1 | Overall longitudinal changes in metabolic control and diabetes care

From 2009 to 2018, the overall number of centers increased from 217 to 238. In detail, "XS" and "S" diabetes centers decreased ("XS": 37–29, "S" 45–42), whereas the number of "M" (55–57), "L" (61–69) and "XL" (19–41) diabetes centers increased, Table 1. At the same time there was an improvement of metabolic control, when looking at the mean hemoglobin A1c as well as the percentage of patients with hemoglobin A1c (HbA1c) <53 mmol/mol (<7.0%), <58 mmol/mol (<7.5%) and hemoglobin A1c ≥75 mmol/mol (≥9.0%), $p < 0.0001$, Table 2. Of note, in the entire cohort at both time points less than one third of patients reached the metabolic treatment goal of hemoglobin A1c <53 mmol/mol (<7.0%) according to the 2018 ISPAD guidelines.

Looking at hemoglobin A1c, Figure 1 shows an improvement in diabetes centers of all sizes over the 10-year period. Both in 2009 and 2018 a "v-shaped" relationship between center-size and metabolic control can be described. This improvement was only statistically significant for "M", "L" and "XL" centers ($p < 0.01$).

The overall rate of severe hypoglycemia (2009: 0.17/patient year vs. 2018: 0.098/patient year), hypoglycemia with coma (2009: 0.037/patient year vs. 2018: 0.015/patient year) and the rate of diabetic ketoacidosis (DKA) (2009: 0.023/patient year vs. 0.018/patient year) improved significantly, $p < 0.0001$, (results stratified by center size shown in Table 3). In "XS" centers the DKA rate increased significantly over the observed time frame ($p < 0.01$), but the total numbers of DKA events in these centers is low due to the low patient volume (2009: 5 DKA events, 2018: 17 DKA events).

There are also significant changes in the mode of insulin therapy: percentage of conventional insulin therapy (CT) decreased from 6.3% to 2.6%, $p < 0.0001$, multiple daily injections (MDI) decreased from 59.8% to 40.5%, $p < 0.0001$, whereas the use of continuous subcutaneous insulin infusion (CSII) increased from 33.8% to 56.8%, $p < 0.0001$. Sensor augmented CSII was not yet documented in 2008, but in 68.6% of insulin pump users (39.1% of all patients) in 2018.

Completeness of nephropathy, retinopathy, thyroid and dyslipidemia screening was comparable in 2008 and 2019, but screening for coeliac disease (CD) increased from 64.6% to 74.1% between 2009 and 2018, $p < 0.0001$. Completeness of blood pressure measurements, use of antihypertensive medication and lipid lowering medication was comparable at the two time points. Smoking cigarettes was less frequently addressed in 2018 (86.6% in 2009 vs. 78.4% in 2018).

3.2 | Influence of center size in 2009

In 2009, "XS" diabetes centers had the fewest follow-up visits per patient and year and the worst metabolic control, Table 2. The difference in mean hemoglobin A1c was statistically significant when "XS" centers were compared to "L" centers, $p < 0.01$. "S" diabetes centers also had a significant higher mean hemoglobin A1c when compared to "M" and "L" diabetes centers, $p < 0.01$. The best hemoglobin A1c outcome was found in "M" and larger diabetes centers.

When analyzing the fraction of patients with hemoglobin A1c <58 mmol/mol (<7.5%), "XS", "S" and "XL" diabetes centers had the smallest proportion of patients reaching this treatment target. The difference was statistically significant when "S" and "L" diabetes centers were compared, $p < 0.01$, Table 2. "XL" diabetes centers had a significant lower number of patients reaching this threshold than "M" and "L" centers, $p < 0.01$, Table 2, Figure 2.

When analyzing the fraction of patients reaching hemoglobin A1c <53 mmol/mol (<7.0%), "XL" centers had the lowest percentage of patients reaching the current ISPAD treatment target, and differed significantly from "M" and "L" centers, $p < 0.01$, Table 2, Figure 2.

"XS" and "S" diabetes centers had the highest fraction of patients with hemoglobin A1c ≥75 mmol/mol (≥9.0%) compared to all other center sizes. This difference was statistically significant when "XS" and "S" centers were compared to "M", "L", or "XL" centers, $p < 0.01$.

The rate of severe hypoglycemia was highest in "XS" and "S" diabetes centers, but the difference was statistically significant only when "S" centers were compared to "XL" centers, $p < 0.01$. Diabetic ketoacidosis (DKA) rate was lowest in "XL" diabetes centers (0.016 DKA/patient year) and highest in "L" centers (0.024 DKA/patient year), not significant.

Conventional insulin therapy (CT) was most frequently used in "XS" diabetes centers in comparison to centers of all sizes, $p < 0.001$, Table 2. Multiple daily injections (MDI) were least used in "XS" diabetes centers ("XS": 56.2% vs. "S" 63.3%, "M" 61.1%, "L" 60.4% and "XL" 59.7%). Also continuous subcutaneous insulin infusion (CSII) was least used in "XS" diabetes centers ("XS" 26.1% vs. "S" 29.0%, "M" 34.3%, "L" 33.2% and "XL" 32.5%), but the difference in MDI and CSII use according to center size was statistically not significant.

TABLE 2 Comparison of mean adjusted benchmarking parameters 2009 and 2018 according to center size

2009						2018				
≥200 ("XL")	≥100 to <200 ("L")	≥50 to <100 ("M")	≥20 to <50 ("XS")	<20 ("S")	Center size	<20 ("S")	≥20 to <50 ("XS")	≥50 to <100 ("M")	≥100 to <200 ("L")	≥200 ("XL")
62.8 °	61.8 *	61.2	63.9 ^	**64.7**	Mean adjusted HbA1c mmol/mol	**64.1**	**62.5**	59.6 *	60.3 *	61 *
7.9 °	7.8 *	7.9	8.0 ^	**8.1**	Mean adjusted HbA1c %	**8.0**	**7.9**	7.6 *	7.7 *	7.7 *
0.144 *	0.165	0.171	**0.220**	0.208	Adjusted severe hypoglycemia rate	0.140	**0.150**	0.091	**0.128**	0.067 *
0.038	0.033	0.043	0.028	0.062	Adjusted hypoglycemia with coma rate	0.039	0.014	0.012	0.016	0.013
0.016	0.024	0.021	0.021	0.020	Adjusted DKA rate	**0.060**	0.011 *	0.016 *	0.017 *	0.017 *
98.5 *	98.0	96.0	97.7	**95.0**	Percentage blood pressure screening	98.4	97.8	99.1	98.7	99.1
61.2	67.3 *	65.0 *,#	65.1 *	**52.3**	Percentage of coeliac disease screening	69.0	**57.1**	74.7 *	75.7 *	74.9 *
22.0	28.1 *	26.7 #	**24.0**	24.1	Percentage adjusted HbA1c <53 mmol/mol (<7.0%)	25.8	**24.4**	32.5 *,~	29.5 *	27.2
41.0	48.4 *	45.5 #	**41.5**	41.3	Percentage adjusted HbA1c <58 mmol/mol (<7.5%)	43.9	**44.1**	53.3 *,#	50.6 *	48.1
13.1 *	11.9 *	12.9 *	**16.6**	**20.3**	Percentage adjusted HbA1c ≥75 mmol/mol (≥ 9.0%)	**18.6**	**13.5**	9.5 *	11.0 *	10.8 *
6.2 *	5.0 *	3.7 *,#	6.2 *	**14.1**	Percentage adjusted use of conventional insulin therapy (CT)	2.1	**3.9**	2.3	2.8	2.0 *
6.1 *	6.1 *	5.9 *	6.0 *	**5.0**	Mean adjusted follow-up visits per year	**5.0**	5.7 *	5.7 *	5.5 *	5.9 *

Note: Significant difference between bold type center and * marked center (*$p < 0.01$), # = significant difference between "M" and "L" & "XL" centers (#$p < 0.01$), ^ = significant difference between "S" diabetes centers and "M" & "L" diabetes centers (^$p < 0.01$), ° = significant difference between "L" and "XL" centers (° $p < 0.01$), ~ = significant difference between "M" diabetes centers and "L" diabetes centers (~$p < 0.01$).

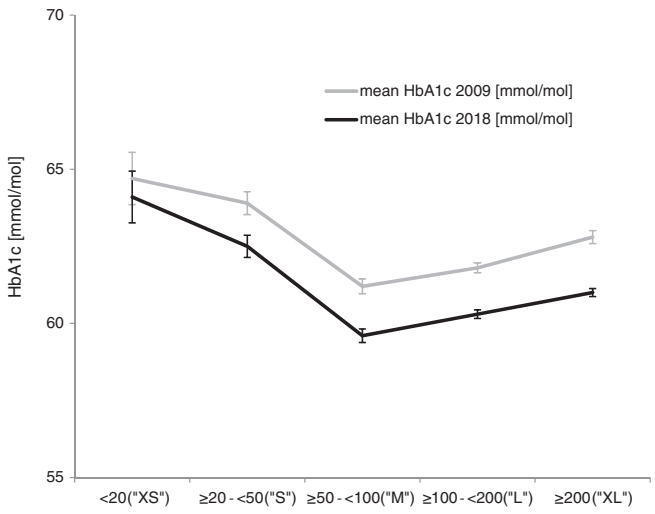

FIGURE 1 Mean adjusted HbA1c (mmol/mol) according to center size in 2009 and 2018 follows a v-shaped curve. SE of the mean as indicators. Improvement over the years was significant for "M", "L" and "XL" centers ($p < 0.01$)

3.3 | Influence of center size in 2018

Also in 2018, mean adjusted hemoglobin A1c was significantly worse in "XS" and "S" diabetes centers compared to all other center sizes, $p < 0.01$, Table 2.

TABLE 3 Rate of diabetes complications according to center size in 2009 and 2018

2009				
Center size		Rate of severe hypoglycemia (pt.year)	Rate of hypoglycemia with coma (pt.year)	Rate of diabetic ketoacidosis (DKA) (pt.year)
<20	"XS"	0.208	0.062	0.020
≥20 to <50	"S"	0.220	0.028	0.021
≥50 to <100	"M"	0.171	0.043	0.021
≥100 to <200	"L"	0.165	0.033	0.024
≥200	"XL"	0.144*	0.038	0.016
2018				
<20	"XS"	0.140	0.039	0.060***
≥20 to <50	"S"	0.150	0.014	0.011
≥50 to <100	"M"	0.091	0.012	0.016
≥100 to <200	"L"	0.128	0.016	0.017
≥200	"XL"	0.067**	0.013	0.017

Note: * Significant difference between "S" and "XL" centers, * $p < 0.01$; **significant difference between "XL" and "S" & "L" centers, ** $p < 0.01$; *** significant difference between "XS" and all other centers, *** $p < 0.01$.

"XS" and "S" diabetes centers had the lowest proportion of patients with hemoglobin A1c below 53 mmol/mol (7.0%) and 58 mmol/mol (7.5%), respectively. "S" diabetes centers had

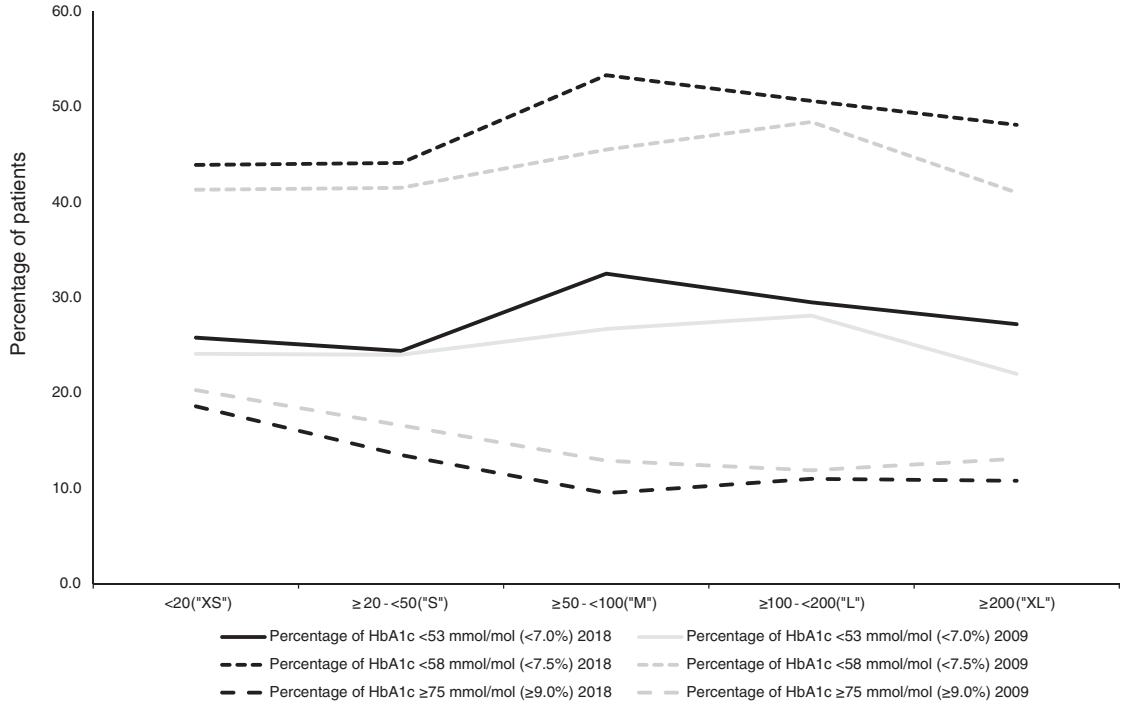

FIGURE 2 Percentage of patients with hemoglobin A1c <7.0% (53 mmol/mol), <7.5% (58 mmol/mol) and ≥9% (75 mmol/mol) according to center size in 2009 and 2018

TABLE 4 Metabolic diabetes control in 2018 according to diabetes center size

2018		hemoglobin A1c (HbA1c)				
Center size		Mean	Use of conventional therapy (CT) (%)	Use of multiple daily injections (MDI) (%)	Use of continuous subcutaneous insulin infusion (CSII) (%)	Percentage of CSII users with CGM sensor or "hybrid closed loop system" (%)
<20	"XS"	64.1 mmol/mol (8.0%)	2.1	43.8	53.6	50.9 **
≥20 to <50	"S"	62.5 mmol/mol (7.9%)	3.9	35.6	59.6	61.5
≥50 to <100	"M"	59.6 mmol/mol (7.6%)	2.3	38.7	58.4	65.5
≥100 to <200	"L"	60.3 mmol/mol (7.7%)	2.8	38.9	57.7	68.4
≥200	"XL"	61 mmol/mol (7.7%)	2.0	39.8	57.6	71.3 *

Note: * Significant difference between marked center and all other centers * = $p < 0.01$; ** Significant difference between "XS" center and "M", "L", and "XL" center.

significantly less patients reaching these two metabolic treatment targets in comparison to "M", "L" and "XL" centers, $p < 0.01$. "M" and "L" diabetes centers had the highest proportion of patients reaching the treatment target of hemoglobin A1c below 53 mmol/mol (7.0%) and 58 mmol/mol (7.5%) and this difference was statistically significant in comparison to "S" and "XL" diabetes centers, $p < 0.01$. The percentage of patients with hemoglobin A1c equal or greater than 75 mmol/mol (9.0%) was highest in "XS" diabetes centers compared to all other center sizes, $p < 0.01$ for "M" to "XL" centers, Table 2, Figure 2.

The rate of hypoglycemia with coma and diabetic ketoacidosis (DKA) was highest in "XS" diabetes centers, but this difference was only significant for DKA in comparison to all other centers, $p < 0.01$. In "XL" diabetes, centers the rate of severe hypoglycemia was significantly lower than in "S", or "L" centers, $p < 0.01$, Table 3.

In 2018, the use of conventional insulin therapy (CT) was comparably low in diabetes centers of all sizes. Multiple daily injections (MDI) were most frequently used in "XS" diabetes centers (43.8%) and use of continuous subcutaneous insulin infusion (CSII) was lowest ("XS": 53.6%) compared to 'S" to "XL" diabetes centers (57.6%–59.6%), Table 4.

Sensor augmented CSII was least used in "XS" diabetes centers ("XS": 50.9% of CSII patients/26.0% of all patients). The use of sensor augmented CSII increased with center size ("S": 61.5% of CSII patients/36.0% of all patients, "M": 65.5% of CSII patients/37.8% of all patients, "L": 68.4% of CSII patients / 38.6% of all patients, "XL": 71.3% of CSII patients/40.6% of all patients). "XL" centers had significantly more patients with sensor augmented CSII than all other centers, $p < 0.01$ and "XS" centers had a significantly lower percentage of patients with sensor augmented CSII than "M", "L", and "XL" centers, $p < 0.01$, Table 4.

3.4 | Screening examinations and follow-up visits

The smallest diabetes centers had the lowest coeliac disease screening rate. Otherwise, completeness of screening examinations was comparable between the different center sizes. In 2018 "XS", diabetes centers still had significantly fewer follow-up visits per patient and year, $p < 0.01$, Table 2.

4 | DISCUSSION

Over the 10-year time period, significant improvements of metabolic control and overall diabetes care can be documented in medium-sized and larger diabetes centers. Treatment targets are also best achieved in medium sized and larger diabetes centers. The relation between hemoglobin A1c and center size follows a "v-shaped" curve. In 2018 "M" and in 2009 "L" diabetes centers had the highest proportion of patients with hemoglobin A1c <53 mmol/mol (<7.0%) and <58 mmol/mol (<7.5%). "XS" diabetes centers have the highest proportion of patients with suboptimal diabetes control (hemoglobin A1c ≥75 mmol/mol/ ≥9.0%).

Conventional insulin therapy (CT) was most frequently used in very small "XS" diabetes centers in the past, but this difference is no longer present nowadays. In 2018 more than 50% of patients were treated with CSII irrespective of center size. The use of "technical diabetes treatment" (sensor augmented CSII and hybrid close loop systems) increases with center size.

The structure of diabetes care in Germany and Austria is organized in a different way compared to Great Britain, the United States, or northern European countries.[6] Due to historical reasons and a decentralized, federal structure of medical care in Germany and Austria, a wide variety of centers can offer diabetes care for pediatric patients. These structures range from general pediatricians with some training in pediatric diabetology to tertiary university hospitals with entire departments dedicated to pediatric endocrinology and diabetology. International comparison of registry data for the treatment–years 2013 and 2014 have shown that the mean hemoglobin A1c was 7.8% (62 mmol/mol) in Austria and 7.7% (61 mmol/mol) in Germany, but the between center-variation within the countries was substantial.[12] The aim of our analysis was to investigate center size itself as an influencing factor for metabolic outcome and care of children and adolescents with diabetes. Center size was associated with the proportion of patients meeting the metabolic target—and this finding was consistent over a 10-year time period.

Independent of center size, the longitudinal analysis confirmed previously described trends in improvement of mean hemoglobin A1c, rates of acute complications and increasing use of "diabetes technology" over the last decade. Nevertheless, "XS" diabetes centers continuously have the highest percentage of patients with hemoglobin A1c ≥9.0% (75 mmol/mol) and a significantly higher rate of DKA events among their patients, while at same time providing a similar degree of modern insulin therapy (MDI and CSII). Especially, the growing number of CSII could be a factor for improved metabolic outcomes regardless of center size over the 10-year period.[22–24] However, advanced technical diabetes therapy with sensor augmented CSII was most prevalent in "XL" diabetes centers, while at the same time "XS" and "S" centers had the lowest number of patients with this advanced treatment modality. As seen in numerous publications, the use of sensor augmented pump therapy and the use of hybrid closed loop systems results in significant improvement of hemoglobin A1c, especially in patients with insufficient metabolic control.[25–28] Therefore, the implementation of advanced technical diabetes therapy could be a contributing factor for better glycemic control in "M", "L" and "XL" centers. The increasing use of diabetes technology with center size will most likely lead to more clinical experience in educating and guiding patients under such a regime. It is important to note that, both in Austria and Germany, due to state dependent or statutory health insurance, individual financial resources do not primarily influence choice of therapy regime or facility. Therefore, family financial resources or diabetes center size per se do not impede technical diabetes treatment in both countries.

Screening for diabetes associated diseases and complications as a cornerstone of diabetes care was conducted to a similar degree independent of center size over the years. Only screening rates for celiac disease increased significantly in the observed timeframe. This can be explained by easier access to laboratory screening examinations and the growing awareness for celiac disease in general and in patients with type 1 diabetes.[21,29–31]

The number of patients treated in a facility might influence the availability of trained staff (diabetes educators, dieticians, psychologists, social workers and specialized pediatric endocrinologists and diabetologists) and financial resources. The accessibility of these resources led to the recommendation by ISPAD to treat a minimum number of patients with type 1 diabetes per center to reach a sufficient expertise.[16,32] As mentioned above, "XS" centers showed worst outcome regarding metabolic control. A factor related to worse outcome of "XS"-centers could be the frequency of patient visits per year, which was lowest in "XS"-centers. Even though "XS" centers provided more visits than recommended in international and national guidelines, there is evidence that patients with poor metabolic control benefit from a higher frequency of contacts.[33,34] Even "XL"-centers with higher patient volumes provided more yearly visits per patient than recommended in international guidelines.

In an international analysis of seven high-income countries, Birkebaek et al. showed an association of center size on hemoglobin A1c with favorable outcomes for centers with more than 50 patients.[7] Our analysis adds a longitudinal perspective and additional data on acute complications and completeness of screening examinations. Interestingly, our data from "XL"-centers suggest that practical skills and the availability of resources alone do not serve as positive predictive factors for satisfying metabolic control. Due to the lack of information on staffing within diabetes centers this key aspect of diabetes care could not be evaluated and should be further investigated in the future as a survey from the UK showed an example for huge differences in staffing within a country.[35] Besides differences in staffing and financial resources one could also speculate that larger diabetes

centers care for more "complicated" patients, for example, for patients with complex challenges or patients with psychiatric comorbidity or extremely poor adherence, who might have been referred to tertiary facilities. Additional factors such as recommendation of patient support groups, social media and online presence of centers could influence parents or patients choice for larger centers.

4.1 | Strengths and limitations

Strengths of the present study include its large population-based database of patients with type 1 diabetes, the prospective data collection over 10 treatment years and a high nationwide capture rate of pediatric patients with type 1 diabetes. The data reflect quality of routine patient care in diabetes centers of different sizes, so that centers of each size may question their potential strengths and weaknesses. Limitations of the analysis are the missing information on multiprofessional team structure and financial resources of participating institutions. Additionally, important patient associated factors such as socioeconomic and educational status of the parents or patient, or distance to clinic, just to mention a few, could not be included in the analysis and interpretation of the data. For documentation of DPV data resources are required, that smaller centers may struggle to provide. So, one could speculate that smaller centers may have failed in documenting each single patient visit. In addition, a categorization by patient number alone misses further differentiation based on position in national health care plans (e.g., university hospitals vs. general hospitals vs. outpatient diabetes care).

5 | CONCLUSION

Center size is related to diabetes care on a broad level: best metabolic control is found in medium sized centers that care for ≥50 to 100 patients. In centers that care for ≤20 patients, metabolic control is worst, occurrence of DKA is highest and visits per year are fewest. Use of "technical diabetes treatment" increases with center size. Nevertheless, up to date diabetes care can be organized without a centralized approach with overall satisfying treatment results, but the smallest and the largest centers should be aware of their potential challenges and weaknesses. From our data it remains unclear, whether patient numbers ensure a multidisciplinary diabetes team, because these data on center structure were not available for analysis. Therefore, additional information on team structure and availability of resources per center could be helpful for further research and health policy decision making.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS

Lukas Hackl, Walter Bonfig, and Reinhard W. Holl designed the research study. Reinhard W. Holl and Stefanie Lanzinger analyzed the data. Lukas Hackl and Walter Bonfig wrote the paper.Susanne Bechtold-Dalla Pozza, Nicole Treptau, Klemens Raile, Ulf Elpel, Karl-Heinz Ludwig, Gebhard Buchal, Stefanie Lanzinger and Reinhard W. Holl reviewed the manuscript multiple times and contributed essential feedback.

ETHICS STATEMENT

Data analysis in the DPV registry has been approved by the ethics committee of the University of Ulm, and data collection by local review boards.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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