Hospitalization in pediatric diabetes: a nationwide analysis of all admission causes for Germany in 2015

b) Short-running-title:

Hospitalization in pediatric diabetes

c)

Marie Auzanneau*[1,2], Joachim Rosenbauer*[2,3], Andrea Icks[2,4,5], Beate Karges[6], Andreas Neu[7], Ralph Ziegler[8], Wolfgang Marg[9], Thomas Kapellen[10], Paul-Martin Holterhus[11], R. W. Holl[1, 2]

[1] Institute of Epidemiology and Medical Biometry, ZIBMT, University of Ulm, Ulm, Germany

[2] German Center for Diabetes Research (DZD), Munich-Neuherberg, Germany

[3] Institute for Biometrics and Epidemiology, German Diabetes Center, Leibniz Center for Diabetes Research at Heinrich Heine University, Düsseldorf, Germany

[4] Institute for Health Services Research and Health Economics, German Diabetes Center, Düsseldorf, Germany.

[5] Institute for Health Services Research and Health Economics, Centre for Health and Society, Faculty of Medicine, Heinrich Heine University Düsseldorf, Germany.

[6] Division of Endocrinology and Diabetes, Medical Faculty, RWTH Aachen University, Aachen, Germany

[7] University Children's Hospital Tübingen, Tübingen, Germany

[8] Diabetes Clinic for Children and Adolescents, Muenster, Germany

[9] Center for Pediatrics and Adolescent Medicine, Bremen-Mitte Hospital, Bremen, Germany

[10] Department of Women and Child Health, Hospital for Children and Adolescents, University of Leipzig, Leipzig, Germany

[11] Division of Pediatric Endocrinology and Diabetes, Department of Pediatrics, University Hospital of Schleswig-Holstein, Campus Kiel/Christian-Albrechts University of Kiel, Kiel, Germany

* These authors contributed equally to this paper.

d) Corresponding author:

Marie Auzanneau, MPH

Institute of Epidemiology and Medical Biometry

ZIBMT

University of Ulm

Albert-Einstein-Allee 41

D-89081 Ulm

Germany

Tel.: +49/731/5025483

Fax: +49/ 731/5025309

marie.auzanneau@uni-ulm.de

a) Abstract   (263 words)

Introduction

Regarding pediatric diabetes, hospital admission for acute complications of type 1 diabetes (T1D) has often been investigated, but little is known about other causes of hospitalization. This study aimed to explore the total burden of hospitalization in individuals with diabetes <20 years of age in Germany.

Methods

Using the German Diagnosis-Related Groups data for 2015, we examined the frequencies of hospitalization with diabetes (20,251 inpatient cases), stratified by diabetes type [T1D, type 2 diabetes (T2D), other specified diabetes types (T3D), and unclear diabetes], and without diabetes (1,269,631 inpatient cases). Using estimates of the population at risk with T1D, T2D, and without diabetes, we evaluated hospitalization rates (per patient-year) by Poisson regression. For T1D, T2D, and T3D, we investigated the most frequent diagnoses and the median length of stay. Most analyses were stratified by sex, age-group and east/west residence.

Results

Children and adolescents with diabetes had a 6 to 9 times higher hospitalization risk than peers without diabetes (hospitalization rate 0.09). The hospitalization rate was higher for T2D compared with T1D (0.84 vs. 0.53, P<0.001). In T2D, two-third of inpatient cases were not directly related to diabetes, and stay was shorter compared with T1D and T3D (3 vs. 4 and 5 days, respectively). In T1D, hospitalization was more frequent among girls than boys (0.58 vs. 0.49, P<0.001), and mostly due to

"diabetes without complications" (65.7%). Hospitalization tended to be more frequent and longer in the youngest patients, and in those with east residence.

Conclusion

Hospitalization rate in pediatric diabetes in Germany remained high, especially for T2D patients, girls with T1D, and young children.

Word count: 3,986 words, 3 tables and 1 figure, 3 supplementary tables.

Introduction

Diabetes in children and adolescents is associated with a high hospitalization rate compared to the general pediatric population [1-3]. However, inpatient care in pediatric diabetes varies a lot between countries. For example, outpatient/home care of newly diagnosed diabetes is common in the US or in Australia, whereas in other countries as in Japan, Sweden, Finland or Germany, children are mostly hospitalized at onset of type 1 diabetes (T1D) [4,5].

Hospitalization in pediatric diabetes has mostly been studied with a focus on acute complications of T1D as severe hypoglycemia or ketoacidosis [6]. However, in many countries with a high hospitalization rate for pediatric diabetes, most of inpatient cases are not due to T1D complications [1,7,8]. In Germany for instance, elective hospital admissions for T1D without complications, like management of newly diagnosed diabetes, diabetes education or insulin dose adjustment, represent most of the inpatient cases in pediatric diabetes [1,7,9]. Among other things, hospitalization can be necessary for the implementation of multimodal therapy concepts, for pre/postprandial and nocturnal glucose monitoring, or for the reimbursement of multidisciplinary education programs for the patients and their families.

Nevertheless, studies investigating overall inpatient pediatric diabetes care in Germany are scarce [1,7]. Furthermore, inpatient care may have been underestimated in previous studies. In a work based on a voluntary registry, the authors assumed that hospital admissions could have been underreported [7]. In a recent study using data from statutory health insurance covering 86% of the German

population, an unknown number of cases had to be excluded because of inconsistent information [1].

Since 2004, the Diagnosis-Related Groups (DRG) system is mandatory in Germany and all German hospitals are obligated to submit their hospitalization data annually to the Hospital Remuneration System (Institut für das Entgeltsystem im Krankenhaus, InEK) for reimbursement. Anonymized DRG data are then transmitted by the InEK to the Federal Statistical Office. Thus, DRG data constitute a comprehensive dataset on all hospital stays in Germany.

The aim of this study was to gain a comprehensive overview of hospitalization (frequency, causes, length of stay) in children and adolescents with diabetes in Germany using the nationwide DRG data. Taking into account a recent report indicating significant regional disparities in pediatric diabetes care in Germany, in particular between the western and the eastern part of the country [10], we additionally compared hospitalizations between east and west residence.

Material and Methods

Data source

Since the introduction of the DRG system in Germany in 2004, all general hospitals have to report annually information on all inpatient cases to the Hospital Remuneration System (InEK) for reimbursement. Beside sociodemographic characteristics, hospitals code primary and secondary diagnoses as well as complications according to the International Classification of Diseases, 10th revision,

German modification (ICD-10-GM). Validated and anonymized DRG data are then transmitted by the InEK to the Federal Statistical Office.

We applied for the use of DRG data provided by the Research Data Center (RDC) of the Federal Statistical Office in Wiesbaden, Germany (www.forschungsdatenzentrum.de/en/database/drg). We obtained a three years access to the DRG data of 2015, which was the most recent available year. Analysis codes were sent to the RDC, which controlled data confidentiality and reported results back. To maintain strict data anonymity, the RDC blinded all frequencies under 3 counts per cell in frequency tables as well as one additional count to prevent deductive calculations (n=17 inpatient cases in all). The ethical committee of the University of Ulm confirmed that the present analysis, which is based on strictly anonymized administrative data (secondary data), does not require informed consent or ethical approval, according to the German law.

Study population

We included all inpatient cases of individuals under 20 years of age with a primary or secondary diagnosis of diabetes for the year 2015. In the DRG statistics as well as in the present work, each case refers to one hospital admission. Thus, one patient hospitalized several times corresponds to several different inpatient cases. Since for reasons of data protection no unique identifier of individual patients is available in the DRG data, there is no possibility to identify one individual patient behind several cases.

We identified as type 1 diabetes (T1D) and type 2 diabetes (T2D) all cases with ICD-10 codes E10 and E11, respectively. Cases with ICD-10 code E13 (other specified diabetes mellitus), which includes diabetes following disorders of the exocrine pancreas (pancreatic diabetes) were classified under the category type 3 diabetes (T3D). Finally, we merged cases with ICD-10 codes E12, E14, as well as cases with double codes E10 and E12 under the category "unclear diabetes".

Data analysis

For each diabetes category, we assessed the absolute frequencies of hospitalization in 2015, stratified by sex, age-group (0-4, 5-9, 10-14, 15-19 years), and residence in the East (Berlin, Brandenburg, Mecklenburg-Vorpommern, Saxony, Saxony-Anhalt, and Thuringia) or West (all other federal states).

We estimated hospitalization rates including 95% CI in persons with T1D, T2D and without diabetes according to the person-years method assuming a Poisson distribution of the cases [11]. Rates were estimated for the total groups, as well as by sex, age group, and east-west residence, and compared between groups using Poisson regression. For these estimations, we assessed for each sub-group the population at risk with T1D or T2D in Germany based on sex-and age-specific prevalence estimates of T1D and T2D diabetes for North Rhine-Westphalia (the most populous German federal state covering 27% of the West and 22% of the total German childhood and youth population) for 2016, corrected for underreporting in the North Rhine-Westphalian diabetes registry by the capture-recapture method (J. Rosenbauer [12]). T1D / T2D prevalence estimates from North Rhine-Westphalia were assumed to hold for the whole of West Germany, while T1D / T2D prevalence

for East Germany was assumed to be 20% lower / 30% higher than respective prevalence estimates from North Rhine-Westphalia, according to a previous report [13] (Supplementary Table S1). First, sex- and age-specific populations at risk with T1D or T2D for West- and East-Germany were estimated by multiplying the assumed prevalence with the size of the respective general population (Supplementary Table S1). These numbers were then conveniently aggregated to estimate the population at risk for the total group, the male and female subgroups, the age groups, and the West/East subgroups. Population data were obtained from the German Federal Statistical Office [14]. Frequencies for the population without diabetes were calculated as the difference of the frequencies for the whole population (inpatient cases [15] and population at risk [14]) and the frequencies in individuals with diabetes calculated as described above. Assuming that diabetes prevalence in children <1 year of age being almost zero, we excluded individuals and inpatient cases <1 year of age in the population without diabetes. As a result, hospitalization at birth and inpatient newborn care were not considered in the comparison.

For T1D, T2D, and T3D, we analyzed the ten most frequent principal diagnoses (reason for hospitalization), as well as the median length of stay, stratified by sex, age-group, and east/west residence. The greater number of inpatient cases with T1D allowed further explorations for this type of diabetes. Therefore, we investigated the frequency of complications (fourth place of the ICD code) for all inpatient cases with T1D as principal diagnosis, as well as the frequency of the most documented secondary diagnoses for all cases with T1D as principal or secondary diagnosis. For that purpose, we extracted the first three secondary diagnoses for each case.

Subsequently, we identified the ten most frequent documented secondary diagnoses, and assessed their overall frequency among all secondary diagnoses in T1D cases. Finally, we compared the distribution by month of inpatient cases in children with T1D younger than 5 years of age with hospitalizations of peers of the same age from the general population, also using DRG statistics from the same year. We chose young children to assess whether the higher prevalence of infections in the cold season affects hospitalization.

Results are presented as median (lower - upper quartile) for continuous variables and as percentage for categorical variables. Hospitalizations rates are presented per patient-year. To assess group differences in the hospitalization rate, we used Likelihood ratio test derived from Poisson regression. Group differences in the length of stay were assessed using Wilcoxon-test. The level of significance of two-sided tests was set at $P < 0.05$. All statistical analyses were conducted via remote computing using the software SAS 9.4 (Statistical Analysis Software, SAS Institute, Cary, NC, USA).

Results

Overall 2,961,131 inpatient cases with a primary or secondary diagnosis of diabetes were documented by the German hospitals for the year 2015. Of these hospitalizations, 20,251 were for individuals under 20 years of age. Considering the absolute frequencies of hospital admissions, T1D was by far the most frequent diagnosis (90.5%, versus 5.0% and 4.0% for T2D and T3D respectively) (Table 1). However, related to the respective population at risk (estimations of the pediatric population with T1D and T2D are given in table 1), the hospitalization rate per

patient-year was higher for T2D than for T1D (0.84 vs. 0.53, P<0.001) (Table 1). Comparing hospitalization rates with those of peers without diabetes, we found that children and adolescents with diabetes had a 6 to 9 times higher hospitalization risk (Table 1).

Hospitalization by sex, age and residence

Results stratified by sex, age, and east/west residence are given for cases with T1D, T2D, T3D, and unclear diabetes in table 1. Results were also presented for the children without diabetes by sex and age, but not by east/west residence (data not available). Hospitalizations among girls were preponderant in all types of diabetes, particularly in T2D (63.3%) or T3D (57.1%) (Table 1). However, considering the hospitalization rates (which take into account the respective population at risk), a significant sex difference was only found in T1D patients (0.58 hospitalizations per patient-year among girls vs. 0.49 among boys, P<0.001, Table 1). Similarly, the difference in the hospitalization rates between individuals with and without diabetes was larger for girls than for boys with T1D (6.4 vs. 5.6 times higher hospitalization risk), whereas no gender difference was observed in the hospitalization risk of children with T2D.

Among T1D patients, the hospitalization rate was highest for the patients under 5 years of age, followed by patients aged 10-14, 5-9 and 15-19 years (1.13, 0.62, 0.57 and 0.42, respectively). Compared with peers without diabetes, the difference in the hospitalization rates decreased with age (from a 9.6 to a 4.0 times higher hospitalization risk). In T2D patients, the hospitalization rate decreased significantly with age (5-9, 10-14 and 15-19 years: 1.65, 1.13 and 0.74, respectively, P<0.001,

Table 1), as well as the hospitalization risk compared with peers without diabetes (from a 22.7 to a 7.1 times higher hospitalization risk).

In T1D and T2D, the hospitalization rate was significantly higher in residents of the east compared to west part of the country (0.65 vs. 0.51 and 0.95 vs. 0.79 respectively, P<0.001, Table 1).

Principal diagnosis

Diabetes was by far the most frequent reason for hospitalization in pediatric T1D (78.3% of the inpatient cases, table 2). For pediatric patients with T2D, less than one third of the hospitalizations were attributed to diabetes (Table 2). Otherwise, obesity or abdominal and pelvic pain (both 2.6%) as well as gastroenteritis or pilonidal cyst (both 1.8%) were frequent principal diagnoses (Table 2). Regarding patients with T3D, about 43% of all inpatient cases were due to pancreatic diabetes and cystic fibrosis (Table 2). Other T3D inpatient cases were related with lymphoid leukemia, pregnancy, failure and rejection of transplanted organs and tissues, or interstitial pulmonary diseases (each in 3 to 5% of cases).

Length of hospital stay

The overall median length of hospital stay was the highest for T3D (5 days) and the lowest for T2D (3 days) (Table 3). For T1D and T3D, the length of hospital stay was highest for patients under 5 years of age and decreased with age (P<0.001 and P=0.011 respectively, table 3). In T3D, hospital stay was significantly longer for residents of the eastern part of Germany (P<0.001, table 3). Additionally, the number of hospital days varied according to the principal diagnosis from 1 day ("mental or

behavioral disorders due to use of alcohol" in patients with T1D) to 8 days (lymphoid leukemia in patients with T3D) (Table 3). No differences in the length of stay were observed between girls and boys, whatever the type of diabetes (Table 3).

T1D: complications, secondary diagnoses and seasonality

Further analyses performed among inpatient cases with T1D as principal diagnosis (n=14,366) provided information on complications (Supplementary Table S2). In 65.7% of cases "T1D without complications" (14.3 % "without" and 51.4% "with metabolic derangement") was documented, followed by "T1D with ketoacidosis" in 23.4%, and "T1D with other specified complications" (including hypoglycemia) in 8.7%. All other complications were documented in less than 1% of all inpatients cases due to T1D.

Among the 18,340 hospitalizations of children and adolescents with T1D, the most frequent documented secondary diagnoses were "T1D without complications" (22.3% of cases), as well as codes related to the presence, adjustment or management of an insulin pump (19.9% of cases) (Supplementary Table S3). Hypoglycemia without coma was documented in about 3% of the cases (Supplementary Table S3).

Children with T1D younger than 5 years of age were more frequently hospitalized in the cold season, from October to March, in exactly the same way as children from the general population (Figure 1). However, a trough in the frequency of hospitalizations can be observed in August and December in children of the general population, but not in children with diabetes (Figure 1).

Discussion and conclusions

The current analysis of the German DRG Data for 2015 shows that the large majority of the inpatient cases in pediatric diabetes was related to T1D. Considering the hospitalization rates per patient-year, children and adolescents with T2D were more frequently admitted to inpatient care compared with peers with T1D. However, in T2D patients, only one third of hospital admissions were directly due to diabetes (compared with nearly 80% in T1D patients), and the median stay was shorter compared with other types of diabetes. Hospitalizations in pediatric T1D were more frequent among girls, and mostly due to "diabetes without complications". In most of cases, hospitalizations were most frequent and longer in the youngest patients, as well as in patients living in the eastern part of the country.

This analysis confirms that hospitalization rates in pediatric diabetes in Germany are very high compared to the population without diabetes [1,7]. Our results additionally suggest that the difference in hospitalization rates between children with T1D and children without diabetes is largest for the age group <5 years. A previous analysis in Germany based on statutory health insurance data [1] reported a smaller difference between the population with or without diabetes for this age-group. However, in the present work, we excluded all inpatient cases <1 year of age in the population without diabetes, including a large number of hospitalizations at birth and newborn inpatient care.

Compared with T1D, children and adolescents with T2D constitute a small group, and previous research on hospitalization in pediatric T2D is sparse. Though, one study found that young patients with T2D have had more hospitalizations in the past 6

months than their peers with T1D [16] and this result is similar to our findings. The high prevalence of psychological and somatic comorbidities associated with childhood obesity and T2D [17,18] may be one explanation for the higher prevalence of hospital admissions [19]. Additionally, we found that the major part of inpatient cases with T2D were not directly attributed to diabetes, and this may also be a consequence of the high number of comorbidities in this population. This could also explain the very higher risk of hospitalization compared to peers without diabetes, especially in the youngest individuals.

Concerning children and adolescents with T1D, there is some evidence that hospital admissions are more frequent among girls than among boys [1,7,19-21], and our results confirm this pattern. Previous studies have shown that girls with T1D tend to have worse metabolic control [22], a higher BMI-SDS [23], and more frequent DKA than boys [6]. These facts may contribute to an increased hospitalization among girls.

We found that "diabetes without complications" was the predominant reason for hospitalization in pediatric T1D. This finding also conforms to previous analyses [1,7]. Whereas outpatient/home care of newly diagnosed T1D is the rule in the US or in Australia, hospitalization at T1D onset is common in Germany [4]. Moreover, pediatric diabetes education programs or therapy adjustment are frequently offered as inpatient care in Germany [9,24].

According to our results, hospitalizations were more frequent and longer in the younger individuals, especially for T1D in the age-groups under 5 years and 10-14 years, and this is consistent with previous findings [7,25]. The present data indicates

on average approximately one hospitalization per child with T1D aged under 5 years during the year 2015. Comorbidities or parent's uncertainty can lead to repeated admissions in this age-group. Besides this, we presume against the background of German registry data [26] that nearly half of the inpatient cases under 5 years correspond to new onset of T1D, while the respective portion in the older age groups 5-9, 10-14 and 14-19 years are estimated at 29%, 16% and 6%, respectively. As already mentioned, inpatient management of newly diagnosed T1D is widely used in Germany, especially regarding very young children [24]. Regular screening in high risk groups (identified through islet-specific multiple antibody positivity and/or genetic risk markers) has been suggested to reduce ketoacidosis at T1D onset [27] and might therefore help to reduce hospitalization at diabetes onset. Furthermore, we found that children with T1D under 5 years of age were more frequently hospitalized in the cold months, similarly to their peers from the same age group in the general population. The preponderance of inpatient cases in young children in the cold season might be related to the increase of infectious diseases, which can lead to blood glucose variations in children with diabetes [28]. Interestingly, hospitalization in children with T1D under 5 years seemed to be less influenced by school holidays (e.g. August and December), compared with hospitalization in children in the general population. Hospitalizations were also particularly frequent in the age group 10-14 years. Currently in Germany, onset of T1D mostly occurs in this age group [26]. Moreover, the greater prevalence of acute complications in this age group, and worse metabolic control partly explained by puberty and hormonal changes, and needing adjustment of diabetes treatment [29], may lead to a higher number of hospitalizations.

In addition, the present analysis shows that hospitalizations in T1D and T2D were more frequent in residents of the eastern part of the country. Outpatient management of pediatric diabetes, e.g. for education or therapy adjustment, may be more prevalent in the western than in the eastern part of Germany. Another explanation could be the higher proportion of families with low socioeconomic status in the eastern part of the country [30]; a recent study showed that children and adolescents from families with low socioeconomic status in Germany are hospitalized more frequently and longer than other children [31]. Moreover, there is some evidence that a higher regional deprivation in the eastern part of Germany leads to worse diabetes outcomes, and also to increased hospital admissions [10,32].

Finally, hospitalizations were longer for individuals with T3D. As defined in the methods section, T3D represents a very heterogeneous group, mainly including diabetes due to disorders of the exocrine pancreas (pancreatic diabetes). Recently, clinical characteristics of children and adolescents under 20 year of age with pancreatic diabetes were examined in a German cohort [33]. In line with our results, the most frequent diagnosis was cystic fibrosis (84%) and female individuals were preponderant (59%) [33]. The authors also found, similarly to our findings, that children and adolescents with pancreatic diabetes had a twofold higher number of hospitalization days per person-year compared to peers with T1D [33].

Strengths and limitations

The major strength of this study is the use of the nationwide DRG dataset, which includes information on all inpatient cases of all German hospitals. Thus, not only patients insured through statutory health insurance but also privately insured patients

are included. Only rehabilitation and psychiatry /psychosomatic care are excluded from the DRG statistics, because they are financed through other systems in Germany. Consequently, the present analysis may reflect exactly the current pediatric inpatient diabetes care in Germany, in contrast to previous studies.

However, this analysis has important limitations. The most relevant shortcoming is the administrative nature of the DRG data, the purpose is not patient care or research but hospital reimbursement. Clinical details, e.g. parameters of metabolic control, are not documented in the DRG data, and thus the quality of the coded diagnoses and complications cannot be verified. For example, the documentation of 19 inpatient cases with T2D under 5 years old, as well as most of the cases of T2D under 10 years old, is probably attributable to diagnostic errors, because most of these cases are likely to have different diabetes type. In addition, comorbidities (documented as secondary diagnoses) could have been underreported. However, since appropriate coding assures correct reimbursement in the DRG system, the probability of omission of comorbidities is limited. On the other hand, overcoding of cases and diagnoses cannot be excluded. According to the DRG system, the transfer of one patient to another department within the same hospital is not resulting in two different cases. However, if the patient is transferred to another hospital, two different inpatient cases are coded for the same patient. Moreover, if a patient was discharged, for example over the week-end, and readmitted afterwards, two different cases could have been coded. So, we cannot exclude that the number of inpatient cases is overestimated in the DRG statistics. Nevertheless, problems with coding quality may influence all subgroups (type of diabetes, sex, age-group, or residence) in a similar manner (non-

differential bias). Thus, comparisons between subgroups may not have been seriously affected.

A further limitation is the imprecision of certain administrative terms. For instance, there is no possibility to explore what really underlies the code "T1D without complications" (ICD-10 code E10.9). This could refer to diabetes education (for example for the management of an insulin pump), in the same way as "Adjustment and management of infusion pump" (Z45.1), or even "Presence of endocrine implants" (Z96.4). As well, the precision "without" or "with metabolic derangement" (code E10.90 or E10.91) is not based on HbA1c or on any other objective measurement. Moreover, some of the frequently documented secondary diagnoses, as "Healthy person accompanying sick person" (Z76.3) and "Persons encountering health services for other counselling and medical advice, not elsewhere classified" (Z71), remained unclear or are not clinically relevant, and were thus not taken into account.

Another weakness is that the DRG statistic refers to inpatient cases and not to individuals, and data do not allow to know how many patients were hospitalized in 2015 or which of them have experienced more than one hospitalization. However, this aspect has no consequences for our conclusions based on hospitalization rates.

In this study, the total populations with T1D or T2D in Germany (populations at risk) have to be estimated based on prevalence data from the West German federal state of NRW and additional assumptions on the prevalence of T1D and T2D in the remaining West German federal states and East Germany. This may have introduced

some bias into the population estimates, although NRW covers 27%/22% of the West/total German childhood and youth population, and assumptions on prevalence ratios between East and West Germany were based on recent nationwide data.

In conclusion, the current analysis of the DRG data provides new insight into all inpatient cases of children and adolescents with diabetes in Germany in 2015, not only focusing on T1D complications. Results confirm that hospitalization rate in pediatric diabetes in Germany is very high compared to the population without diabetes, and indicate that hospital admission varied by diabetes type, age, sex and residence. Overall, hospitalization rates were higher in patients with T2D, girls with T1D, young patients, and eastern-residents.

Author contribution statement

 M.A. conducted the statistical analysis, wrote and edited the manuscript, and created
figures. She is the guarantor of this work and, as such, takes responsibility for the
accuracy of the data analysis. J.R. contributed to statistical analysis, estimated the
pediatric population with diabetes in Germany by sex, age group and residence,
contributed to the discussion and reviewed/edited the manuscript. A.I., B.K., A.N.,
R.Z., W.M., T.K., and P-M. H. contributed to the discussion and reviewed/edited the
manuscript. R.W.H. conceptualized the study, contributed to the discussion, and
reviewed/edited the manuscript.

References

1. Bohn B, Schwandt A, Ihle P, et al. Hospital admission in children and adolescents with or without type 1 diabetes from Germany: An analysis of statutory health insurance data on 12 million subjects. Pediatr Diabetes 2018;19:721-726.

2. Bachle CC, Holl RW, Strassburger K, et al. Costs of paediatric diabetes care in Germany: current situation and comparison with the year 2000. Diabet Med 2012;29:1327-1334.

3. Sayers A, Thayer D, Harvey JN, et al. Evidence for a persistent, major excess in all cause admissions to hospital in children with type-1 diabetes: results from a large Welsh national matched community cohort study. BMJ Open 2015;5:e005644-2014-005644.

4. Clapin H, Hop L, Ritchie E, et al. Home-based vs inpatient education for children newly diagnosed with type 1 diabetes. Pediatr Diabetes 2017;18:579-587.

5. Morgan-Trimmer S, Channon S, Gregory JW, et al. Family preferences for home or hospital care at diagnosis for children with diabetes in the DECIDE study. Diabet Med 2016;33:119-124.

6. Karges B, Rosenbauer J, Holterhus PM, et al. Hospital admission for diabetic ketoacidosis or severe hypoglycemia in 31,330 young patients with type 1 diabetes. Eur J Endocrinol 2015;173:341-350.

7. Icks A, Rosenbauer J, Holl RW, et al. Hospitalization among diabetic children and adolescents and the general population in Germany. German Working Group for Pediatric Diabetology. Diabetes Care 2001;24:435-440.

8. Curtis JR, To T, Muirhead S, et al. Recent trends in hospitalization for diabetic ketoacidosis in ontario children. Diabetes Care 2002;25:1591-1596.

9. Konrad K, Vogel C, Bollow E, 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;17:483-491.

10. Auzanneau M, Lanzinger S, Bohn B, et al. 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. Diabetes Care 2018;41:2517-2525.

11. Woodward M. Epidemiology – Study Design and Data Analysis. London, New York. pp223: Chapman & Hall/CRC; 1999.

12. Patterson CC, Harjutsalo V, Rosenbauer J, et al. Trends and cyclical variation in the incidence of childhood type 1 diabetes in 26 European centres in the 25 year period 1989-2013: a multicentre prospective registration study. Diabetologia 2018.

13. Goffrier B, Schulz M, Bätzing-Feigenbaum J. Administrative Prävalenzen und Inzidenzen des Diabetes mellitus von 2009 bis 2015 - Versorgungsatlas-Bericht Nr. 17/03. Berlin; 2017.

14. German Federal Statistical Office (Destatis). Ergebnisse auf Grundlage des Zensus 2011. 31 December 2016. https://www-genesis.destatis.de/genesis/online. Accessed 5 November 2018.

15. Gesundheit. Fallpauschalenbezogene Krankenhausstatistik (DRG-Statistik). 2015. Fachserie 12 Reihe 6.4 ed. Wiesbaden: Statistisches Bundesamt; 2016.

16. Naughton MJ, Ruggiero AM, Lawrence JM, et al. Health-related quality of life of children and adolescents with type 1 or type 2 diabetes mellitus: SEARCH for Diabetes in Youth Study. Arch Pediatr Adolesc Med 2008;162:649-657.

17. Pulgaron ER. Childhood obesity: a review of increased risk for physical and psychological comorbidities. Clin Ther 2013;35:A18-32.

18. Pinhas-Hamiel O, Zeitler P. Acute and chronic complications of type 2 diabetes mellitus in children and adolescents. Lancet 2007;369:1823-1831.

19. Estrada CL, Danielson KK, Drum ML, Lipton RB. Hospitalization subsequent to diagnosis in young patients with diabetes in Chicago, Illinois. Pediatrics 2009;124:926-934.

20. Cohn BA, Cirillo PM, Wingard DL, et al. Gender differences in hospitalizations for IDDM among adolescents in California, 1991. Implications for prevention. Diabetes Care 1997;20:1677-1682.

21. Lipton RB, Zierold KM, Drum ML, et al. Re-hospitalization after diagnosis of diabetes varies by gender and socioeconomic status in urban African-American and Latino young people. Pediatr Diabetes 2002;3:16-22.

22. Samuelsson U, Anderzen J, Gudbjornsdottir S, et al. Teenage girls with type 1 diabetes have poorer metabolic control than boys and face more complications in early adulthood. J Diabetes Complications 2016;30:917-922.

23. Frohlich-Reiterer EE, Rosenbauer J, Bechtold-Dalla Pozza S, et al. Predictors of increasing BMI during the course of diabetes in children and adolescents with type 1 diabetes: data from the German/Austrian DPV multicentre survey. Arch Dis Child 2014;99:738-743.

24. Hilgard D, Johannsen C, Herbst A, et al. Development in hospitalisation and average length of hospital stay in children and youth with diabetes mellitus type 1 in 1995 to 2005 [in German]. Diabetol Stoffwechs. 2007;2:153-160.

25. Bachle C, Haastert B, Holl RW, et al. Inpatient and outpatient health care utilization of children and adolescents with type 1 diabetes before and after introduction of DRGs. Exp Clin Endocrinol Diabetes 2010;118:644-648.

26. Holl R, Prinz N. Medizinische Versorgung von Kindern und Jugendlichen mit Diabetes – Entwicklungen der letzten 21 Jahre. In: Deutsche Diabetes Gesellschaft (DDG) und diabetes DE (ed), *Deutscher Gesundheitsbericht Diabetes 2017*: 133.

27. Ziegler AG, Hoffmann GF, Hasford J, et al. Screening for asymptomatic beta-cell autoimmunity in young children. Lancet Child Adolesc Health 2019;3:288-290.

28. Korbel L, Easterling RS, Punja N, Spencer JD. The burden of common infections in children and adolescents with diabetes mellitus: A Pediatric Health Information System study. Pediatr Diabetes 2018;19:512-519.

29. Cameron FJ, Amin R, de Beaufort C, et al. ISPAD Clinical Practice Consensus Guidelines 2014. Diabetes in adolescence. Pediatr Diabetes 2014;15 Suppl 20:245-256.

30. Albrech J, Fink P, Tiemann H. Unequal Germany: socio-economic disparity report 2015 [German]. www.fes-2017plus.de: Friedrich-Ebert-Stiftung; 2016.

31. Lampert T, Prütz F, Rommel A, Kuntz B. Social differences in the utilization of medical services by children and adolescents in Germany. Results of the cross-sectional KiGGS Wave 2 study. Journal of Health Monitoring 2018;3:35-51.

32. Apperley LJ, Ng SM. Socioeconomic Deprivation, Household Education, and Employment are Associated With Increased Hospital Admissions and Poor Glycemic Control in Children With Type 1 Diabetes Mellitus. Rev Diabet Stud 2017;14:295-300.

33. Lanzinger S, Welters A, Thon A, et al. Clinical characteristics of pancreatic diabetes in children and adolescents documented in the German/Austrian/Swiss/Luxemburg DPV registry. Pediatric diabetes. Supplement: Abstracts for the 44th Annual Meeting of the International Society for Pediatric and Adolescent Diabetes (ISPAD), 11–14 October 2018, Hyderabad, India 2018;19:14-40.

Figures and legends

Tables

Table 1. Hospitalization in children and adolescents with or without diabetes in Germany in 2015, stratified by diabetes type, sex, age, and residence

Table 2. Most frequent principal diagnoses for the hospitalization of children and adolescents with diabetes in Germany in 2015, stratified by diabetes type

Table 3. Median length of hospital stay, stratified by diabetes type, sex, age, residence, and principal diagnosis
Legend: For each type of diabetes, median number of hospital days (lower – upper quartile). Group differences in the length of stay were assessed using the Wilcoxon-test.

Figures

Figure 1. Number of hospitalizations in children with T1D and in the general population in the age group under 5 years in Germany in 2015, stratified by month

Online-only supplementary material

Supplementary Table S1. Estimated prevalence and number of cases of type 1 diabetes (T1D, 0-19 years) and type 2 diabetes (T2D, 5-19 years) in Germany in 2016 by sex, age, and region

Supplementary Table S2. Complications among inpatient cases with T1D as principal diagnosis (n=14,366)

Supplementary Table S3. Most frequent secondary diagnoses among inpatient cases with T1D (n=18,340)

Figure 1. Number of hospitalizations in children with T1D and in the general population in the age group under 5 years in Germany in 2015, stratified by month
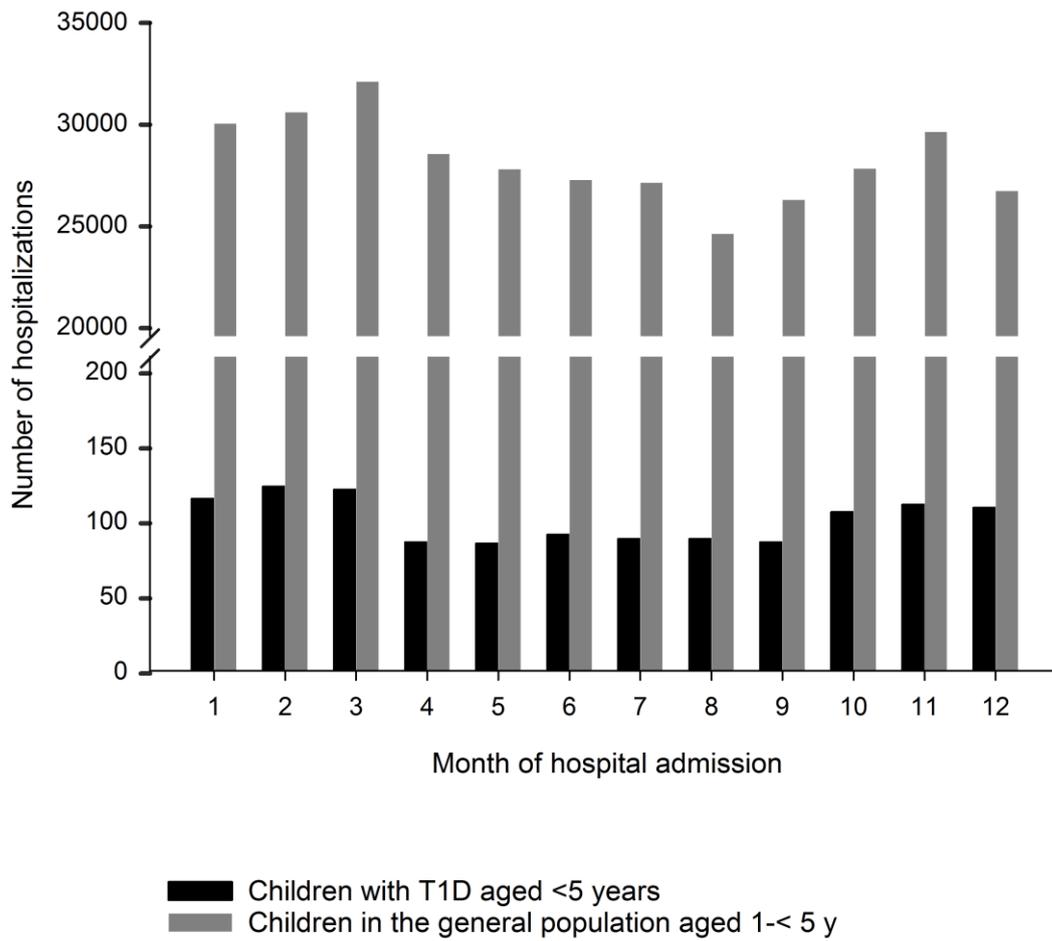
Table 1. Hospitalization in children and adolescents with or without diabetes in Germany in 2015, stratified by diabetes type, sex, age, and residence

Diabetes type[1]		Sex		P-Value*	Age group				P-Value*	Residence[2]		P-Value*	All
		Girls	Boys		0 - 4	5 - 9	10 - 14	15 - 19		West	East		
T1D	Inpatient cases, n (%)	9,341 (50.9)	8,999 (49.1)		1,209 (6.6)	3,279 (17.9)	7,091 (38.6)	6,761 (36.9)		15,108 (82.4)	3,133 (17.1)		18,340
	Population at risk[3], n	16,173	18,240		1,074	5,780	11,479	16,080		29,569	4,844		34,413
	Hospitalization rate per patient-year (95% CI)[4]	0.58 (0.57; 0.59)	0.49 (0.48; 0.50)	<0.001	1.13 (1.06; 1.19)	0.57 (0.55; 0.59)	0.62 (0.60; 0.63)	0.42 (0.41; 0.43)	<0.001	0.51 (0.50; 0.52)	0.65 (0.62; 0.67)	<0.001	0.53 (0.53; 0.54)
T2D	Inpatient cases, n (%)	636 (63.3)	369 (36.7)		19 (1.9)	33 (3.3)	207 (20.6)	746 (74.2)		764 (76.0)	226 (22.5)		1,005
	Population at risk[3], n	753	447		-	23	179	998		963	237		1,200
	Hospitalization rate per patient-year (95% CI)[4]	0.84 (0.78; 0.91)	0.83 (0.75; 0.91)	0.73	-	1.43 (1.02; 2.02)	1.16 (1.01; 1.33)	0.75 (0.70; 0.80)	<0.001	0.79 (0.74; 0.85)	0.95 (0.84; 1.09)	0.017	0.84 (0.79; 0.89)
T3D	Inpatient cases, n (%)	462 (57.1)	347 (42.9)		37 (4.6)	59 (7.3)	163 (20.1)	550 (68.0)		639 (79.0)	160 (19.8)		809
Unclear Diabetes	Inpatient cases, n (%)	55 (56.7)	42 (43.3)		x	x	32 (33.0)	48 (49.5)		-	-		97

All diabetes types	Inpatient cases, n (%)	10,494 (51.8)	9,757 (48.2)		1,269 (6.3)	3,384 (16.7)	7,493 (37.0)	8,105 (40.0)		-	-	20,251
No diabetes	Inpatient cases[5], n (%)	622,235 (49.0)	647,351 (51.0)		338,527 (26.6)	225,849 (17.8)	261,392 (20.6)	443,863 (35.0)		-	-	1,269,631
	Population at risk[6], n	6,908,473	7,382,283		2,867,751	3,566,111	3,684,008	4,172,886		-	-	14,290,756
	Hospitalization rate per patient-year (95% CI)[4]	0.090 (0.090; 0.090)	0.088 (0.087; 0.088)	<0.001	0.118 (0.118; 0.118)	0.063 (0.063; 0.064)	0.071 (0.071; 0.071)	0.106 (0.106; 0.107)	<0.001	-	-	0.089 (0.089; 0.089)

[1] Diabetes as principal or secondary diagnosis.

[2] Sum of East and West below 100% due to missing values (residence not documented or residence abroad).

[3] Population at risk in Germany, based on prevalence estimates of the T1D and T2D diabetes for North Rhine-Westphalia for 2016, and assuming for East-Germany T1D prevalence 20% lower and T2D prevalence 30% higher than in West-Germany. Details are given in the methods section.

[4] Hospitalization rates including 95% CI were estimated according to the person-years method assuming a Poisson distribution of the cases [11]. Comparison of rates between groups were performed by Poisson regression.

[5] Children >1 year of age. 45 Missing values for the variable "sex". Results for residence (East/West) were not available. Source: DRG-data

[6] Population without diabetes in Germany >1 year of age, calculated as the difference of the total population >1 year of age in 2015 [14] and the population with T1D or T2D, estimated as defined above.

*Likelihood ratio test derived from Poisson regression.

x: frequencies under 3 counts per table cell as well as one additional result were blinded by the RDC in order to maintain a strict data anonymity. Overall, 17 inpatient cases with unclear diabetes and age <10 years were blinded.

Table 2. Most frequent principal diagnoses for the hospitalization of children and adolescents with diabetes in Germany in 2015, stratified by diabetes type

Diabetes type	Principal diagnosis	Frequency (%)
T1D	Diabetes mellitus type 1 (E10)	14,366 (78.3)
	Gastroenteritis (A08/A09)	365 (2.0)
	Mental and behavioural disorders due to alcohol use (F10)	144 (0.8)
	Abdominal and pelvic pain (R10)	143 (0.8)
	Intracranial injury (S06)	112 (0.6)
	Epilepsy (G40)	83 (0.5)
	Cutaneous abscess, furuncle and carbuncle (L02)	82 (0.4)
	Intestinal malabsorption, incl. coeliac disease (K90)	79 (0.4)
	Acute appendicitis (K35)	78 (0.4)
T2D	Diabetes mellitus type 2 (E11)	294 (29.3)
	Obesity (E66)	26 (2.6)
	Abdominal and pelvic pain (R10)	26 (2.6)
	Gastroenteritis (A09)	18 (1.8)
	Pilonidal cyst (L05)	18 (1.8)
	Hypofunction and other disorders of pituitary gland (E23)	16 (1.6)
	Essential (primary) hypertension (I10)	16 (1.6)
	Other metabolic disorders (E88)	15 (1.5)

	Mental and behavioural disorders due to alcohol use (F10)	14 (1.4)
	Diabetes mellitus in pregnancy (024)	14 (1.4)
T3D	Cystic fibrosis (E84)	248 (30.7)
	Other specified diabetes mellitus, incl. pancreatic diabetes (E13)	103 (12.7)
	Lymphoid leukemia (C91)	35 (4.3)
	Diabetes mellitus in pregnancy, premature rupture of membranes, preterm delivery (O24/O42/O60)	34 (4.2)
	Failure and rejection of transplanted organs and tissues (T86)	30 (3.7)
	Follow-up examination after treatment for conditions other than malignant neoplasms (Z09)	29 (3.6)
	Other interstitial pulmonary diseases (J84)	10 (1.2)
	Acute pancreatitis (K85)	9 (1.1)

Table 3. Median length of hospital stay, stratified by diabetes type, sex, age, residence, and principal diagnosis

		T1D	P-value	T2D	P-value	T3D	P-value
sex	girls	4 (2-8)	0.98	3 (2-6)	0.28	5 (2-12)	0.58
	boys	4 (2-9)		3 (2-6)		5 (3-11)	
Age group	0 -4	8 (3-13)	<0.001	3 (1-8)	0.87	10 (3-23)	0.011
	5 -9	5 (3-10)		3 (2-4)		8 (3-14)	
	10-14	5 (3-8)		3 (2-5)		5 (2-13)	
	15-19	4 (2-7)		3 (2-6)		5 (3-11)	
Residence	West	4 (2-9)	0.78	3 (2-6)	0.42	4 (2-10)	<0.001
	East	5 (2-9)		3 (2-5)		9.5 (3-14)	
Principal diagnosis	Diabetes mellitus type 1 (E10)	6 (3-9)					
	Gastroenteritis (A08/A09)	2 (1-3)					
	Mental and behavioural disorders due to alcohol use (F10)	1 (1-1)					
	Diabetes mellitus type 2 (E11)			4 (3-8)			
	Obesity (E66)			4 (3-6)			
	Abdominal and pelvic pain (R10)			2 (1-3)			
	Cystic fibrosis (E84)					7 (3-14)	
	Other specified DM, incl. pancreatic diabetes (E13)					6 (3-10)	
	Lymphoid leukemia (C91)					8 (2-23)	
Total		**4 (2-9)**		**3 (2-6)**		**5 (3-12)**	

Legend: For each type of diabetes, median number of hospital days (lower – upper quartile). Group differences in the length of stay were assessed using the Wilcoxon-test.