

# Centre size and glycemic control: An international study with 504 centres from seven countries

Niels H. Birkebaek<sup>1</sup>, Julia M. Hermann<sup>2</sup>, Lena Hanberger<sup>3</sup>, Dimitrios Charalampopoulos<sup>4</sup>, Reinhard W. Holl<sup>2</sup>, Torild Skrivarhaug<sup>5</sup>, Karin Aakesson<sup>6</sup>, Justin T Warner<sup>7</sup>, Ann K. Drivvoll<sup>5</sup>, Ann-Marie Svensson<sup>8</sup>, Terence Stephenson<sup>4</sup>, Sabine E. Hofer<sup>9</sup>, Siri Fredheim<sup>10</sup>, Siv J. Kummernes<sup>5</sup>, Rakesh Amin<sup>4</sup>, Birgit Rami-Merhar<sup>11</sup>, Anders Johansen<sup>12</sup>, Thomas M. Kapellen<sup>13</sup>, Doerte Hilgard<sup>14</sup>, Knut Dahl-Jørgensen<sup>15</sup>, Elke Froehlich-Reiterer<sup>16</sup>, Maria Fritsch<sup>11</sup>, Ragnar Hanas<sup>17</sup>, Jannet Svensson<sup>10</sup>.

<sup>1</sup> Department of Pediatrics, Aarhus University Hospital, Aarhus, Denmark, <sup>2</sup>Institute of Epidemiology and Medical Biometry, ZIBMT, University of Ulm, Germany and German Center for Diabetes Research, Munich, Neuherberg, Germany, <sup>3</sup>Department of Medicine and Health Sciences, Division of Nursing, Linköping University, Linköping, Sweden, <sup>4</sup>Great Ormond Street Institute of Child Health, University College London, London, United Kingdom, <sup>5</sup>Norwegian Childhood Diabetes Registry, Division of Paediatric and Adolescent Medicine, Oslo University Hospital, Oslo, Norway, <sup>6</sup> Department of Clinical and Experimental Medicine, Linköping University, Linköping, and Department of pediatrics Ryhov County Hospital, Jönköping, Sweden, <sup>7</sup>Department of Pediatric Endocrinology and Diabetes, Children's Hospital for Wales, Cardiff, United Kingdom,<sup>8</sup> Centre of Registres in Region Västra Götaland, Gothenburg, Sweden, <sup>9</sup> Department of Pediatrics, Medical University of Innsbruck, Innsbruck, Austria, <sup>10</sup> Department of Pediatrics Herlev University Hospital, Herley, Denmark, <sup>11</sup>Department of Pediatric and Adolescent Medicine, Medical University of Vienna, Vienna, Austria, <sup>12</sup>Department of Growth and Reproduction, Rigshospitalet, Copenhagen, Denmark, <sup>13</sup> Department of Pediatrics, University Childrens Hospital Leipzig, Leipzig, Germany, <sup>14</sup> Pediatric Diabetologic Practice, Witten, Germany, <sup>15</sup>Oslo University Hospital, and Institute of Clinical Medicine, University of Oslo, Oslo, Norway, <sup>16</sup>Department of Pediatrics, Medical University of Graz, Graz, Austria,<sup>17</sup> NU Hospital Group, Uddevalla, and Institute of Clinical Sciences, University of Gothenburg, Gothenburg, Sweden

# **Corresponding author**

Niels H. Birkebaek, MD, PhD Department of Pediatrics Aarhus University Hospital, Aarhus, Denmark Phone: +4530715409 E-mail: nielbirk@rm.dk The variance in glycemic control between different childhood diabetes centres is not fully understood. Although the ISPAD guidelines from 2014 recommended centre sizes of more than 150 patients (1), it is not thoroughly investigated if glycemic control is associated with centre size (2-4). We have data from more than 500 childhood diabetes centres from seven different countries and thereby a unique opportunity to elaborate further on this association. Therefore, this study aims to investigate the relationship between centre size and glycemic control in children with type 1 diabetes (T1D).

Patient data have been described previously (5). Briefly, the population comprised children with T1D in the age group less than 18 years and diabetes duration of more than three months from seven high-income countries during 2013-2014: Austria, Denmark, England, Germany, Norway, Sweden and Wales. Data were anonymized and obtained from five national registries / audits on children with T1D (Austria and Germany use the same electronic health record, and England and Wales have a common National Pediatric Diabetes Audit, while Denmark, Norway and Sweden have national registries). Mean HbA<sub>1c</sub> was compared between groups after adjusting for gender, age (<6 years, 6 to <12 years, and 12 to 18 years), duration of diabetes (<2 years, 2 to <5 years, and  $\geq 5$  years), minority status (yes/no) (HbA<sub>1c</sub> adj) before and after stratifying for treatment modality (insulin injection/pump). Centre size was defined as the number of diabetes patients reported to be cared for in a centre. Centre size groupings were: 1) < 20; 2) 20 - < 50; 3) 50 - < 100; 4) 100 - < 200; 5)  $\geq$  200 patients.

In total 54,494 children (48% females) with T1D across 504 centres in seven countries were included in the study. The number of centres per country varied between 14 (Wales) and 219 (Germany). Mean (standard deviation) for age was 12.5 (3.9) years, mean age at T1D onset was 7.5

(4.0) years, and mean T1D duration was 5.0 (3.7) years. 21% of patients had minority status, which varied between 5% (Wales) and 28% (Austria). 38.1% of patients were on pump treatment and the percentage varied between 25% (England) and 69% (Denmark). National coverage of T1D patients was above 95% in all countries, apart from Austria with about 80% data coverage. Included patients had 100% data coverage for all variables, gender, age, diabetes duration, minority status and HbA<sub>1c</sub>. Data on treatment modality were not available for 2428 patients (4.5%); of them 2130 were from England and 154 from Sweden.

23.2% of centres had <50 patients (small centres) with T1D, which represented 4.9% of the total patient population. Most children (45.6%) were cared for in diabetes centres with a centre size between 100 and 200 patients. 30.2% of children were cared for in centres with more than 200 patients, representing 12.3 % of all centres. The distribution of small and large centres in the seven countries varied. England and Sweden had few small centres (< 12%) while Austria, Germany and Norway had a higher percentage of small centres (>34%). HbA<sub>1c</sub> adj was significantly higher in the centres with less than 50 patients compared with larger centres (P<0.001), while there was no difference in HbA<sub>1c</sub>adj with increasing centre size above 50 patients (figure). Stratification for treatment modality (insulin injection /pump) revealed that HbA<sub>1c</sub>adj was significantly higher in centres with less than 50 patients compared with centres with more than 50 patients, both in pen users (P<0.001) and pump users (P<0.01). The influence of centre size was more pronounced in pen users, and pen users had higher HbA<sub>1c</sub>adj than pump users for all centre sizes (P<0.02) (figure).

We conclude that the percentage of small and larger centres differed between countries, but in total the small centres (< 50 patients) comprised 23.2 percent of all diabetes centres in the seven countries. In all countries combined, childhood diabetes centres with less than 50 patients had

higher HbA<sub>1c</sub>, This indicates that, where geographically possible, it may be beneficial to reduce the number of small centres and combine them into larger entities. As small centres did better on pump than pen, small remote centres may benefit from encouraging pump use. Diabetes centres with more than 50 patients managed equally well, therefore centralizing to very high-volume diabetes centres may not necessarily be an advantage. Future research should focus on identifying reasons leading to differences in glycemic control in T1D patients cared for in small and large centres, e.g the lack or presence of an updated multidisciplinary diabetes team.

### ACKNOWLEDGEMENT

The authors thank all national pediatric diabetes groups, all participating centres, and all patients.

# Author contribution

NHB contributed to the design of the study and data acquisition, conducted the literature search, researched data and wrote the manuscript. NHB takes full responsibility for the work as a whole, including the study design, and the decision to submit and publish the manuscript, and NHB is the guarantor of the work. JMH was responsible for data management, did the statistical analysis, was as such lead statistician for the project, and contributed to the manuscript; JMH has full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. LH, KAa, TS, AKD contributed to the design of the study, data acquisition and edited the manuscript drafts. RWH contributed to the design of the study, contributed to the manuscript, and leads the DPV registry. DC, TS contributed to the design of the study, and contributed to the manuscript. JS, JTW, RH contributed to the design of the study, data acquisition, and contributed to the manuscript. RA, AMS, SF, KDJ, SJK, BRM, AJ, TMK, DH, EFR, MF contributed to data acquisition and edited the manuscript drafts. SEH contributed to data acquisition, was involved in interpreting the data, and edited the manuscript drafts. All authors provided substantial contributions to data interpretation and critically reviewed and commented on several drafts of the paper.

Duality of interest:

None.

#### Funding

German Diabetes Association (DDG), German Centre for Diabetes Research (DZD, FKZ: 82DZD01402), European Foundation for the Study of Diabetes (EFSD), and the EU-IMI2 consortium INNODIA. University College London Children's Policy Research Unit (CPRU) is funded by the UK Department of Health Policy Research Programme (funding reference 10090001) and supported by the National Institute for Health Research Biomedical Research Centre at Great Ormond Street Hospital for Children NHS Foundation Trust and University College London. The Norwegian Childhood Diabetes Registry (NCDR) is funded by the South-Eastern Norway Regional Health Authority. The Danish National Diabetes Registry (DanDiabKids) is funded by the Health Research Fund of Central Denmark Region. The Swedish Pediatric Diabetes Quality Registry (SWEDIABKIDS) is supported from the Swedish Association of Local Authorities and Regions (SALAR). Funding sources had no role in the study design, data collection, data analysis, data interpretation, or writing of the paper.



### Legend to figure

 $HbA_{1c}$  adj by centre size total and by treatment modality. Pen users had higher  $HbA_{1c}$  adj than pump users for all centre sizes (P<0.02).

References

- 1. Pihoker C, Forsander G, Fantahun B, Virmani A, Luo X, Hallman M, et al. ISPAD Clinical Practice Consensus Guidelines 2014. The delivery of ambulatory diabetes care to children and adolescents with diabetes. Pediatr Diabetes 2014;15 Suppl 20:86-101.
- 2. Charalampopoulos D, Amin R, Warner JT, Muniz-Terrera G, Mazarello P, V, Viner RM, et al. Clinic variation in glycaemic control for children with Type 1 diabetes in England and Wales: a population-based, multilevel analysis. Diabet Med 2017;34:1710-8.
- 3. 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;35:80-6.
- Rosilio M, Cotton JB, Wieliczko MC, Gendrault B, Carel JC, Couvaras O, et al. Factors associated with glycemic control. A cross-sectional nationwide study in 2,579 French children with type 1 diabetes. The French Pediatric Diabetes Group. Diabetes Care 1998;21:1146-53.

 Charalampopoulos D, Hermann JM, Svensson J, Skrivarhaug T, Maahs DM, Akesson K, et al. Exploring Variation in Glycemic Control Across and Within Eight High-Income Countries: A Cross-Sectional Analysis of 64,666 Children and Adolescents With Type 1 Diabetes. Diabetes Care 2018; 41(6):1180-1187.