

International Comparisons in Diabetes Outcomes: Lessons from Abroad

Type 1 Diabetes Exchange 2023 National Meeting

November 15, 2023

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Session Objective:

• At the end of this session, members will be able to identify and summarize health conditions for diabetes populations in Europe, Australia, and the UK.

Outline

- Where are we now?
- What opportunities exist for future collaboration?
- Overview of selected past papers.
- What to do if you are interested?

DOI: 10.1111/pedi.13362

EPIDEMIOLOGY



A collaborative comparison of international pediatric diabetes registries

Stefanie Lanzinger^{1,2} | Anthony Zimmermann³ | Ajenthen G. Ranjan^{4,5} | Osman Gani^{6,7} | Saira Pons Perez⁸ | Karin Akesson^{9,10} | Shideh Majidi¹¹¹⁰ | Michael Witsch¹² | Sabine Hofer¹³ | Stephanie Johnson¹⁴ | Kasper A. Pilgaard^{15,16} | Siv Janne Kummernes^{6,7} | Holly Robinson⁸ | Katarina Eeg-Olofsson^{17,18} | Osagie Ebekozien^{19,20} | Reinhard W. Holl^{1,2} | Jannet Svensson^{15,16} | Torild Skrivarhaug^{21,22} | Justin Warner²³ | Maria E. Craig^{24,25,26} | David Maahs^{27,28} | Australasian Diabetes Data Network (ADDN), Danish Registry of Childhood and Adolescent Diabetes (DanDiabKids), Diabetes prospective follow-up registry (DPV), Norwegian Childhood Diabetes Registry (NCDR), National Paediatric Diabetes Audit (NPDA), Swedish Childhood Diabetes Registry (Swediabkids), T1D Exchange Quality Improvement Collaborative (T1DX-QI), and SWEET initiative







Key Questions

- Do the data exist?
- Can we harmonize/compare the data?
- How can we share the data and perform the analysis?
- Authorship?
- Do we need funding or biostatistical support?
- What are the hypotheses?
- Is it novel?
- How would it advance the field?



ARTICLE

Contrasting the clinical care and outcomes of 2,622 children with type 1 diabetes less than 6 years of age in the United States T1D Exchange and German/Austrian DPV registries

David M. Maahs • Julia M. Hermann • Stephanie N. DuBose • Kellee M. Miller • Bettina Heidtmann • Linda A. DiMeglio • Birgit Rami-Merhar • Roy W. Beck • Edith Schober • William V. Tamborlane • Thomas M. Kapellen • Reinhard W. Holl • for the DPV Initiative and the T1D Exchange Clinic Network

A1c 7.4% DPV 8.2% in T1DX p<0.001



Fig. 3 (a) Percentage with ≥ 1 SH event in past year by HbA_{1c}. (b) Percentage with ≥ 1 DKA event in past year by HbA_{1c}. White bars, mean HbA_{1c} <7.5% (<58 mmol/l); black bars, mean HbA_{1c} 7.5 to <8.5% (58 to <69 mmol/l); grey bars, mean HbA_{1c} $\geq 8.5\%$ (≥ 69 mmol/l). **p=0.004; ***p<0.001; p values unadjusted and testing whether the frequency of SH/DKA differs by HbA_{1c} group, within each registry

SH/100 pt yrs by 1) HbA1c & 2) registry x 20 years



Haynes, Diabetes Care '19

Year

Mean & 95% CI BMIz (Compared to WHO norms)



T1DX Black Bars/DPV White Bars; Dubose, JPeds, '15

e

Use of Adjuvant Pharmacotherapy in Type 1 Diabetes: International Comparison of 49,996 Individuals in the Prospective Diabetes Follow-up and T1D Exchange Registries Diabetes Care 2017;40:e139-e140 | https://doi.org/10.2337/dc17-0403

Nicole C. Foster.4 Birgit M. Rami-Merhar,6

David M. Maahs,¹¹ and

Reinhard W. Holl^{2,3}



Figure 1—Use of adjuvant noninsulin medication by registry, stratified by age range. Solid white bar, metformin; solid black bar, DPP-4 inhibitor; horizontal striped bar, GLP-1 agonist; dotted bar, SGLT2. inhibitor; vertical striped bar, other.

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International Comparison of Smoking and Metabolic Control in Patients With Type 1 Diabetes Diabetes Care 2016;39:e177-e178 | DOI: 10.2337/dc16-0845



Sabine E. Hofer,¹ Kellee Miller,² Julia M. Hermann,^{3,4} Daniel J. DeSalvo,⁵ Michaela Riedl,⁶ Irl B. Hirsch,⁷ Wolfram Karges,⁸ Roy W. Beck,² Reinhard W. Holl,^{3,4} and David M. Maahs,⁹ for the DPV Initiative* and the T1D Exchange Clinic Network*





Prevalence of Celiac Disease in 52,721 Youth With Type 1 Diabetes: International Comparison Across Three Continents Diabetes Care 2017;40:1034-1040 | https://doi.org/10.2337/dc16-2508 Maria E. Craig.^{1,2,3} Nicole Prinz,^{4,5} Claire T. Boyle⁶, Fiona M. Campbell,⁷ Timothy W. Jones,^{8,9} Sobine E. Hofer,¹⁰ Jill H. Simons,¹¹ Naomi Holman,¹² Elaine Tham,¹³ Elke Fröhlich-Reiterer,¹⁴ Stephanie DuBose⁶ Helen Thornton,¹⁵ Bruce King,¹⁶ David M. Maahs,¹⁷ Reinhard W. Holl,⁴⁵ and Justin T. Warner,¹⁸ on behalf of the Australasian Diabetes Data Network (ADDN), the T1D Exchange Clinic Network

(T1DX), the National Paediatric Diabetes Audit (NPDA) and the Royal College of

Paediatrics and Child Health, and the Prospective Diabetes Follow-up Registry

(DPV) initiative*

RESULTS

Biopsy-confirmed CD was present in 1,835 youths (3.5%) and was diagnosed at a median age of 8.1 years (interquartile range 5.3–11.2 years). Diabetes duration at CD diagnosis was <1 year in 37% of youths, >1–2 years in 18% of youths, >3–5 years in 23% of youths, and >5 years in 17% of youths. CD prevalence ranged from 1.9% in the T1DX to 7.7% in the ADDN and was higher ingirls than boys (4.3% vs. 2.7%, P < 0.001). Children with coexisting CD were younger at diabetes diagnosis compared with those with type 1 diabetes only (5.4 vs. 7.0 years of age, P < 0.001) and fewer were non-white (15 vs. 18%, P < 0.001). Height SDS was lower in those with CD (0.36 vs. 0.48, adjusted P < 0.001) and fewer were overweight/obese (34 vs. 37%, adjusted P < 0.001), whereas mean HbA_{1c} values were comparable: 8.3 ± 1.5% (67 ± 17 mmol/mol) versus 8.4 ± 1.6% (68 ± 17 mmol/mol).

CONCLUSIONS

CD is a common comorbidity in youth with type 1 diabetes. Differences in CD prevalence may reflect international variation in screening and diagnostic practices, and/ or CD risk. Although glycemic control was not different, the lower height SDS supports close monitoring of growth and nutrition in this population. Diabetologia (2016) 59:87-91 DOI 10.1007/s00125-015-3790-6

SHORT COMMUNICATION

Use of insulin pump therapy in children and adolescents with type 1 diabetes and its impact on metabolic control: comparison of results from three large, transatlantic paediatric registries

Jennifer L. Sherr¹ · Julia M. Hermann² · Fiona Campbell³ · Nicole C. Foster⁴ · Sabine E. Hofer⁵ · Jeremy Allgrove⁶ · David M. Maahs⁷ · Thomas M. Kapellen⁸ · Naomi Holman⁹ · William V. Tamborlane¹ · Reinhard W. Holl² · Roy W. Beck⁴ · Justin T. Warner¹⁰ · for the T1D Exchange Clinic Network, the DPV Initiative, and the National Paediatric Diabetes Audit and the Royal College of Paediatrics and Child Health registries



CrossMark



Figure 2—Country mean HbA_{1c} before and after adjustment for cross-country differences in the characteristics of children (age, sex, diabetes duration, and minority status) and center effects. Estimates of adjusted country means derived from a two-level model with a random effect for center including data from all eight countries.

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

https://doi.org/10.2337/dc17-2271

Dimitrios Charalampopoulos,¹ Julia M. Hermann,^{2,3} Jannet Svensson,⁴ Torild Skrivarhaug,⁵ David M. Maahs,⁶ Karin Akesson,⁷ Justin T. Warner,⁸ Reinhard W. Holl,^{2,3} Niels H. Birkebæk,⁹ Ann K. Drivvoll,⁵ Kellee M. Miller,¹⁰ Ann-Marie Svensson,¹¹ Terence Stephenson,¹ Sabine E. Hofer,¹² Siri Fredheim,⁴ Siv J. Kummernes,⁵ Nicole Foster,¹⁰ Lena Hanberger,¹³ Rakesh Amin,¹ Birgit Rami-Merhar,¹⁴ Anders Johansen,¹⁵ Knut Dahl-Jørgensen,^{16,17} Mark Clements,^{18,19,20} and Ragnar Hanas^{21,22}



Charalampopoulos, Diabetes Care '18

Received: 30 October 2019 Revised: 24 March 2020 Accepted: 29 March 2020

DOI: 10.1111/pedi.13014

CLINICAL CARE AND TECHNOLOGY



International benchmarking in type 1 diabetes: Large difference in childhood HbA1c between eight high-income countries but similar rise during adolescence—A quality registry study

Johan Anderzén¹ Julia M. Hermann^{2,3} | Ulf Samuelsson⁴ | Dimitrios Charalampopoulos⁵ | Jannet Svensson⁶ | Torild Skrivarhaug⁷ | Elke Fröhlich-Reiterer⁸ | David M. Maahs⁹ | Karin Akesson^{1,10} | Thomas Kapellen¹¹ | Maria Fritsch¹² | Niels H. Birkebæk¹³ | Ann K. Drivvoll⁷ Kellee Miller¹⁴ | Terence Stephenson⁵ | Sabine E. Hofer¹⁵ | Siri Fredheim⁶ | Siv J. Kummernes⁷ | Nicole Foster¹⁴ | Rakesh Amin⁵ | Dörte Hilgard¹⁶ | Birgit Rami-Merhar¹² | Knut Dahl-Jørgensen⁷ | Mark Clements^{17,18,19} | Ragnar Hanas²⁰ | Reinhard W. Holl^{2,3} | Justin T. Warner^{21†}



FIGURE 1 HbA1c by age, including a non-parametric local regression of smoothing = LOESS

Hemoglobin A1c Patterns of Youth With Type 1 Diabetes 10 Years Post Diagnosis From 3 Continents

Jennifer L. Sherr, MD, PhD,^a Anke Schwandt, PhD,^{b,o} Helen Phelan, MPH,^{d,e} Mark A. Clements, MD, PhD,^{f,g} Reinhard W. Holl, MD, PhD,^{b,o} Paul Z. Benitez-Aguirre, MD,^{e,h} Kellee M. Miller, PhD,ⁱ Joachim Woelfle, MD,^j Thomas Dover, MD,^{k,i} David M. Maahs, MD, PhD,^{m,n} Elke Fröhlich-Reiterer, MD,^o Maria E. Craig, MD^{e,h}



FIGURE 1

HbA1c trajectories with 95% confidence intervals among youth with T1D from the time of diagnosis. A, ADDN (N = 7292). B, The German-Austrian-Luxembourgian-Swiss diabetes prospective follow-up (DPV; N = 39226). C, UST1DX (N = 3704). DIABETES TECHNOLOGY & THERAPEUTICS Volume 24, Number 1, 2022 © 2022, Mary Ann Liebert, Inc., publishers https://doi-org.laneproxy.stanford.edu/10.1089/dia.2021.0225



ORIGINAL ARTICLE

Changes in HbA1c Between 2011 and 2017 in Germany/Austria, Sweden, and the United States: A Lifespan Perspective

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A 2011 Data







FIG. 2. Changes in HbA1c Across the Lifespan, All Registries. (A) 2011 Data (B) 2107 Data. German/Austrian data are represented in burgundy (stars), Swedish data are represented in yellow (circles), U.S. data are represented in green (triangles). Circles/triangles/stars express HbA1c for each year of age by registry. The line and shaded area represent the LOESS fit +95% confidence interval.

HbA1c by Age DPV (Germany/Austria) Compared to T1DX (US)



N=51,024 Hermann, Diabetic Medicine '20



Type 1 diabetes in older adults: Comparing treatments and chronic complications in the United States T1D Exchange and the German/Austrian DPV registries

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Fig. 1A – Prevalence of renal disease in the T1D Exchange and DPV registries. Solid white bar = urine albumin 30–300 mg/g Cr (microalbuminuria). Solid black bar = urine albumin > 300 mg/g Cr (macroalbuninuria).



Fig. 1B – Glomerular Filtration Rate in the T1D Exchange and DPV registries. Solid white bar \leq 60 ml/min/1.73². Solid black bar \leq 30 ml/min/1.73². Formula validation limited in those \geq 70 years of age. All DPV participants analyzed as White/Caucasian.



Fig. 1C – Stroke and myocardial infarction in the T1D Exchange and DPV registries. Solid white bar = T1D Exchange registry. Solid black bar = DPV registry.

Undertreatment of cardiovascular risk factors in the type 1 diabetes exchange clinic network (United States) and the prospective diabetes follow-up (Germany/Austria) registries

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FIGURE 1 Percentage of participants meeting glycaemic, blood pressure and lipid goals (A) in the T1DX and DPV registries by age group (B) and sex (C)



FIGURE 2 Frequency of antihypertensive medication use in those with hypertension (A) and use of lipid-lowering medication in those with dyslipidaemia (B) in T1DX and DPV registries by age group and sex

Challenges for T1D Care in the US

Diabetes Technology & Disparities

Age 1to<13 years

Age 13to<18 years



Mean HbA1c level according to race/ethnicity and insulin regimen/method. MDI, multiple daily injections. White bar, non-Hispanic black; black and white striped bar, Hispanic. Willi et al *Pediatrics '15*

Longitudinal Changes in Continuous Glucose Monitoring Use Among Individuals With Type 1 Diabetes: International Comparison in the German and Austrian DPV and U.S. T1D Exchange Registries Diabetes Care 2020;43:e1-e2 | https://doi.org/10.2337/dc19-1214 Check for updiates



es in Continuous Use Among pe 1 Diabetes: arison in the German d U.S. T1D Exchange DIABETES TECHNOLOGY & THERAPEUTICS Volume 24, Number 12, 2022 © 2022, Mary Ann Liebert, Inc., publishers https://doi.org.laneproxy.stanford.edu/10.1089/dia.2022.0248



BRIEF REPORTS

Transatlantic Comparison of Pediatric Continuous Glucose Monitoring Use in the Diabetes-Patienten-Verlaufsdokumentation Initiative and Type 1 Diabetes Exchange Quality Improvement Collaborative

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FIG. 1. (a) Proportion of CGM use from 2017 to 2020 among those <25 years of age. (b) HbA1c (%) in CGM users compared with nonusers. CGM, continuous glucose monitoring; HbA1c, hemoglobin A1c.

DIABETES TECHNOLOGY & THERAPEUTICS Volume 21, Number 2, 2019 © Mary Ann Liebert, Inc. DOI: 10.1089/dia.2018.0384



ORIGINAL ARTICLE

State of Type 1 Diabetes Management and Outcomes from the T1D Exchange in 2016–2018

Nicole C. Foster, MS¹, Roy W. Beck, MD, PhD¹, Kellee M. Miller, PhD¹, Mark A. Clements, MD², Michael R. Rickels, MD, MS³, Linda A. DiMeglio, MD, MPH⁴, David M. Maahs, MD, PhD⁵, William V. Tamborlane, MD⁶, Richard Bergenstal, MD⁷, Elizabeth Smith, BS¹, Beth A. Olson, BAN, RN, CDE⁷, and Satish K. Garg, MD⁸; for the T1D Exchange Clinic Network



FIG. 3. Mean HbA1c by technology use in 2016–2018. Solid black represents injection only. Horizontal stripes represent pump only. Solid white represents injection+CGM. Diagonal stripes represent pump+CGM.



FIG. 2. Average HbA1c by year of age: 2010–2012 versus 2016–2018. Orange line represents 2010–2012 cohort, and blue line represents 2016–2018 cohort. Participants must be contained in both cohorts with at least a 3-year duration for the 2010–2012 collection. $* \ge 80$ years old are pooled.

How to explain increased A1c from 2010-12 to 2016-18?

<u>What is role of</u>: Diabetes technology Income Insurance

Race-ethnicity

DIABETES TECHNOLOGY & THERAPEUTICS Volume 22, Number 9, 2020 © Mary Ann Liebert, Inc. DOI: 10.1089/dia.2019.0393

DTT

ORIGINAL ARTICLE

HbA1c Levels in Type 1 Diabetes from Early Childhood to Older Adults: A Deeper Dive into the Influence of Technology and Socioeconomic Status on HbA1c in the T1D Exchange Clinic Registry Findings

Kellee M. Miller, PhD,¹ Roy W. Beck, MD, PhD,¹ Nicole C. Foster, MS,¹ and David M. Maahs, MD, PhD²; for the T1D Exchange



Higher A1c:

Public Insurance Lower income Hispanic or Black v NHW No CGM **MDI v Pump**

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A Decade of Disparities in Diabetes Technology Use and HbA_{1c} in Pediatric Type 1 Diabetes: A Transatlantic Comparison

Diabetes Care 2021;44:133-140 | https://doi.org/10.2337/dc20-0257



Ananta Addala,¹ Marie Auzanneau,^{2,3} Kellee Miller,⁴ Werner Maier,^{3,5} Nicole Foster,⁴ Thomas Kapellen,⁶ Ashby Walker,⁷ Joachim Rosenbauer,^{3,8} David M. Maahs,^{1,9} and Reinhard W. Holl^{2,3}





Greater gap in US v Germany by SES quintile (low v hi):

- Pump: 39 v 6%
- CGM: 37 v 9%
- A1c: 1.3 v 0.3%

SES Gap widening for US from 2010-12 to 2016-18 for CGM (p=0.038) & A1c (p=0.0005)

Role of Quality Improvement to Improve Outcomes

Longitudinal Comparison of A1c in 3 Pediatric Diabetes Groups (Lal, DTT '22)

T1DX QI, DPV, NPDA

HbA1c by Registry

- Stable and lowest in DPV
- Clinically significant decrease in NPDA
- Clinically significant increase in T1DX



Lal et al, DTT '22

Quality Improvement Efforts – NPDA

 In 2009, the National Clinical Director for Children, Young People and Maternity Services for NPDA commented that "this disappointing situation cannot be allowed to continue". Subsequent QI efforts mandated throughout.



Lal et al, DTT '22

DPV-NPDA-T1DX Longitudinal

- DPV has maintained a population HbA1c < 7.7%
- NPDA has succeeded in reducing the population HbA1c in a clinically meaningful way (>0.7%)
- Further research should focus on how these healthcare systems succeeded
- The United States should consider expanding QI programs nationally to improve HbA1c

The SWEET Map:

Worldwide Pediatric Diabetes Registry 2021



Blue points = new centers in SWEET, submitting data since July 2021

DIABETES TECHNOLOGY & THERAPEUTICS Volume 23, Number 7, 2021 Mary Ann Liebert, Inc. DOI: 10.1089/dia.2020.0618



ORIGINAL ARTICLE

The SWEET Project 10-Year Benchmarking in 19 Countries Worldwide Is Associated with Improved HbA1c and Increased Use of Diabetes Technology in Youth with Type 1 Diabetes

Peter Gerhardsson, MSc,¹ Anke Schwandt, MSc,^{2,3} Michael Witsch, MD,⁴ Olga Kordonouri, MD, PhD,⁵ Jannet Svensson, MD, PhD,^{6,7} Gun Forsander, MD, PhD,⁸ Tadej Battelino, MD, PhD,⁹ Henk Veeze, MD, PhD,¹⁰ and Thomas Danne, MD,^{5,11} on Behalf of the SWEET Study Group



T1DX-QI network has grown!



Improvement in Mean A1c Across the Life Span



Ebekozien, DTT 2023

0.3% improvement from 2016/17→2021/22

	2016 & 2017	2021 & 2022 33070 8.4 (2.1) 8557 (26)	
N	27584		
Mean HbA1c (SD)	8.7 (1.9)		
% with HbA1c <7% [N (%)]	5416 (20)		
% with HBA1c >9% [N (%)]	11811 (43)	10169 (31)	
p-value		p-value <0.01	

	2016 & 2017	2021 & 2022	
N	9579	9579	
Mean HbA1c (SD)	8.5 (1.7)	8.4 (1.9)	
% with HbA1c <7% [N (%)]	2032 (21)	2507 (26)	
% with HBA1c >9% [N (%)]	3524 (37) 3200 (33		
p-value		p-value <0.01	

Demographic, clinical, management and outcome characteristics of 8,004 young children with type 1 diabetes: a vulnerable group in need of specialized healthcare.

In review, Sandy et al, 2023

	ADDN (n= 954)	T1DX-QI (n=1,831)	DPV (n=5,219)	P value
Age at assessment	4.9 ± 1.2	4.4 ± 1.0	4.6 ± 1.2	<0.001
% Insulin Pump	39.2	46.6	86.6	<0.001
% CGM	70.5	57.6	85.1	<0.001
% hybrid closed loop	0.5	3.6	6.9	<0.001
HbA1c [%]	7.7 ± 1.2	8.0 ± 1.4	7.3 ± 0.9	<0.001

Since 2010-12 to now:
DPV 7.4 → 7.3%
T1DX 8.2 → 8.0%





Future Directions

- Desire by other registries for continued collaboration
- Difficult to find funding
- T1DX –QI
 - Process to propose new research topics
 - Biostatistical support
 - Data sharing agreement: future possibility?
- Other ideas?







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SAVE THE DATE

October 16 – 19, 2024 Lisbon, Portugal

Inclusion & Innovation in Pediatric and Adolescent Diabetes

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