Running title: Tubeless Insulin Pump Therapy in Youth with Type 1 Diabetes

Corresponding author:

Thomas Danne, MD

Diabetes Center for Children and Adolescents

Kinder- und Jugendkrankenhaus AUF DER BULT

Janusz-Korczak-Allee 12

30173 Hannover

Germany

Phone: +49- 511-8115-3330

Fax: +49- 511-8115-993344

danne@hka.de

Long-term Study of Tubeless Insulin Pump Therapy Compared to Multiple Daily Injections in Youth with Type 1 Diabetes: Data from the German/Austrian DPV-Registry

Thomas Danne[1], Anke Schwandt[2,9], Torben Biester[1], Bettina Heidtmann[3], Birgit Rami-Merhar[4], Holger Haberland[5], Silvia Müther[6] , Semik Khodaverdi[7], Thomas Haak[8] and Reinhard W. Holl[2,9] for the DPV Initiative[10]

[1]Diabetes Center for Children and Adolescents, AUF DER BULT, Hannover, Germany, [2]Institute for Epidemiology and Medical Biometry, ZIBMT, University of Ulm, Ulm, Germany [3]Catholic Children´s Hospital Wilhelmstift, Hamburg, Germany, [4]Medical University of Vienna, Department of Pediatric and Adolescent Medicine, Vienna, Austria, [5]Sana Klinikum Lichtenberg, Berlin, Germany, [6]DRK-Kinderklinik Westend, Berlin,Germany [7]Klinik für Kinder- und Jugendmedizin, Klinikum Hanau, Hanau, Germany, [8]Diabetes Zentrum Mergentheim, Bad Mergentheim, Germany, [9]German Center for Diabetes Research (DZD), Munich-Neuherberg, Germany
[10]the full list of the participating centers of the DPV Initiative is provided as a Supplement.

Abstract: 249 words, **Text:** 1928 words

Figure: 1, **Tables:** 2

Key words: Type 1 diabetes, pediatric, CSII, MDI, HbA1c

ABSTRACT

Objective: To examine glycemic control in youth with type 1 diabetes (T1D) who switched from multiple daily injections (MDI) to a tubeless insulin pump (Omnipod® Insulin Management System, Insulet Corp., Billerica, MA) compared to patients who continued MDI therapy over a 3-year time period.

Research Design and Methods: This retrospective analysis of the German/Austrian Diabetes Patienten Verlaufsdokumentation (DPV) registry included data from 263 centers and 2529 patients <20 years (n=660 tubeless insulin pump; n=1869 MDI) who initiated treatment on a tubeless insulin pump as of January 1, 2013 and had 1 year of data pre-switch from MDI and 3 years of data post-switch to a tubeless pump. Outcomes included the change in HbA1c, insulin dose and BMI standard deviation score (SDS).

Results: Youth with T1D who switched from MDI therapy to a tubeless insulin pump showed better glycemic control at 1 year compared to patients who continued MDI treatment, adjusted mean±SE: 7.5%±0.03 (58 mmol/mol) vs. 7.7%±0.02 (61 mmol/mol); p<0.001, with no between group difference at 2- and 3-years. Total daily insulin dose was lower (p<0.001) in the tubeless insulin pump group, 0.80±0.01, 0.81±0.01 and 0.85±0.01 U/kg vs. the MDI group 0.89±0.01, 0.94±0.01 and 0.97±0.01 U/kg, at 1-, 2- and 3-years, respectively (all p<0.001). BMI (SDS) increased in both groups and was not different over time.

Conclusions: Treatment with a tubeless insulin pump in youth with T1D was associated with improvements in glycemic control compared to MDI after 1 year and appears to be an effective alternative to MDI.

Key words: Type 1 diabetes, pediatric, CSII, MDI, HbA1c

Abbreviations:

CSII, continuous subcutaneous insulin infusion; BMI, body mass index; DPV, Diabetes Patienten Verlaufsdokumentation; HbA1c, glycated hemoglobin; SDS, Standard Deviation Score; T1D, type 1 diabetes; MDI, multiple daily insulin injections

Introduction

It is well-known that glycemic control tends to be poorer in children and adolescents compared to adults (1,2). This may be attributed to multiple physiologic, behavioral and psychosocial factors including hormonal changes, insulin sensitivity, socialization and increasing self-management over time (3,4). While recent data indicates that continuous subcutaneous insulin infusion (CSII) use is increasing in children and adolescence with type 1 diabetes (T1D), and may be associated with better glycemic control compared to multiple daily injections (MDI) (5,6), most of these patients are not using insulin pump therapy (7-12). In a recent survey of adolescents and young adults the majority reported that they did not want to use an insulin pump due to the constant presence of a catheter, perception that a pump would be unwieldy and the visibility of the insulin pump (13). Differentiated systems such as tubeless insulin pumps have the potential to address barriers to use of traditional CSII therapy.

A recent retrospective study including 276 pediatric and adolescent patients previously treated with MDI demonstrated significant reductions in HbA1c levels at 3 months following treatment initiation of the tubeless Omnipod® Insulin Management System (Insulet Corporation, Billerica, USA) (14). While positive, these results are short-term; little is known about the long-term impact of tubeless insulin pump therapy in pediatric and adolescent patients. To address this gap in knowledge, the present study analyzed data from the German/Austrian Diabetes Patienten Verlaufsdokumentation (DPV) registry to determine the long-term effects of switching from MDI to the Omnipod System.

Research Design and Methods

This retrospective analysis of the German/Austrian DPV registry examined glycemic control in youth with T1D who switched from MDI to treatment with a tubeless insulin pump and compared these patients to those who continued MDI therapy over a 3-year time period.

Out of the 458 centers in the German/Austrian DPV registry database with T1D patients (as of March 2017), data from 263 centers that were identified as having ≥10 tubeless insulin pump patients with T1D were included in the analysis. Patients <20 years of age who initiated treatment on the tubeless insulin pump as of January 1, 2013 and had 1 year of data available on MDI prior to the treatment switch (baseline) and 3 years of follow-up data after the switch were included in the analysis. All MDI patients at the same centers with data available during the same time period as the tubeless insulin pump cohort were included in the analysis as the comparator group. Patients with other forms of diabetes or other therapeutic regimens including previous use of CSII therapy were excluded from this analysis.

Outcome Measures

Outcomes included the change in HbA1c, mathematically standardized to the Diabetes Control and Complications Trial normal range using the multiple of the mean method (2), change in insulin dose (U/kg/24h) and change in body mass index (BMI) standard deviation score (SDS) at 1-, 2- and 3-years post treatment switch from MDI to a tubeless insulin pump. Aggregated data from 1 to 6 visits during each year were analyzed.

Statistical Methods

Results are presented as mean±SE for continuous variables and as proportions for binary variables. Kruskal–Wallis test was used for group comparisons of continuous variables. Non-parametric statistics were used because most outcome measurements were not normally distributed. Chi-squared test was used for the comparison of dichotomous variables.

Multiple regression models were applied for the outcome variables HbA1c, total daily dose of insulin and BMI (SDS) to control for differences in age, sex and diabetes duration between treatment groups. Multiple linear regression analyses were used for continuous variables. Mathematical details of the regression models, as well as the implementation in the SAS software, are described in detail in the literature (15). Two-sided hypotheses were used throughout the analysis. A p-value <0.05 was considered statistically significant. The statistical analysis software package SAS, version 9.4 (SAS Institute, Carey, NC, USA) was used for all analyses.

Results

A total of 2529 patients (n=660 tubeless insulin pump; n=1869 MDI) were included in the analysis. Baseline characteristics are presented in Table 1. The groups were similar at baseline.

HbA1c

A reduction in HbA1c from baseline was observed with tubeless insulin pump use at 1 year of use; whereas an increase in HbA1c was observed in the MDI cohort, resulting in a significant 0.3% between-group difference ($p<0.001$) which remained significant after adjustment for baseline value, age, gender and diabetes duration (Table 2, Figure 1A). HbA1c values increased progressively over years 2 and 3 in both groups with no significant between-group difference.

Insulin Dose

Daily insulin dose was significantly lower ($p<0.001$) in the tubeless insulin pump group compared to the MDI group at years 1, 2 and 3 with no difference in baseline dose after adjustment for demographic and clinical characteristics (Table 2, Figure 1B). Insulin dose remained fairly constant in the tubeless insulin pump group and increased over time in the MDI group.

BMI (SDS)

BMI (SDS) increased over time in both groups with no significant between group differences (Table 2, Figure 1C).

Discussion

In this 3-year, retrospective analysis of the German/Austrian DPV registry youth with T1D who switched from MDI therapy to a tubeless insulin pump showed significantly greater glycemic control and lower daily insulin use at 1 year compared to patients who continued MDI treatment. At 2 and 3 years the total daily insulin dose was also significantly lower in the tubeless insulin pump group compared to the MDI group which continued to increase during the observation period. Both groups showed a slight increase of BMI over time. There was no between-group difference in HbA1c at 2 and 3 years.

Overall, the results of the present study are clinically meaningful: a relatively good level of glycemic control with a lower total daily insulin dose was observed over time with tubeless insulin pump use compared to MDI. A recent analysis of the German/Austrian DPV registry including more than 1,700 tubeless insulin pump users <20 years of age supports this finding with average HbA1c levels ≤7.6% (60 mmol/mol) and daily insulin dose of ≤0.78 U/kg reported (16).

A long-term case-control study from Australia may serve as reference how this compares to changing to tethered pumps from MDI as patchpumps were not available in Australia at this time. Patients switching to tethered pumps with a baseline HbA1c of 8.0% (approximately 0.5% higher than the present study) reported unchanged A1c values at 2 years (8.1%) comparable to the present study with tubeless pumps (17). This improvement was maintained at this level for up to 7 years. However, in the Australian study, the MDI group deteriorated after 2 years considerably leading to a 0.6% difference between MDI and tethered pump over the

7 year observation period. Such a marked decline in the MDI group was not observed in our study with an observation period for up to 3 years.

The results of the present study demonstrating lower HbA1c in the tubeless insulin pump group compared to MDI at 1 year are consistent with recently reported data from a US retrospective study comparing glycemic control at 3 months in youth switching to Omnipod treatment from MDI (14). Cross-sectional results from a pooled analysis of 3 large registries, including the T1D Exchange Clinic Registry, the English/Welsh National Pediatric Diabetes Audit (NPDA) and the German/Austrian DPV registry, also indicate that HbA1c is lower in youth treated with CSII compared to MDI (17). Of the 3 registries, HbA1c was lowest overall in the German/Austrian DPV registry with a mean value of 8.0% (64 mmol/mol), compared to 8.3% (67 mmol/mol) and 8.9% (74 mmol/mol) in the T1D Exchange Clinic Registry and the NPDA, respectively (18).

At 2 and 3 years HbA1c levels increased in both the tubeless insulin pump and MDI groups. This result is consistent with other reports from the German/Austrian DPV registry and the T1D Exchange Clinic Registry which have shown that glycemic control worsens with puberty (18-20). However, while HbA1c levels increased at 2- and 3-years, these HbA1c values still remained lower than the levels reported for the larger German/Austrian DPV cohort and the other registries, potentially due to the cohort selection criteria (19,20). It is also important to note that the differences in HbA1c levels between MDI and pump users in the German/Austrian DPV population were much smaller than observed in these other registries (18). Additionally, the relatively well-controlled HbA1c levels seen in the tubeless insulin pump and MDI groups at baseline in the present study, 7.5% (58 mmol/mol) and 7.7% (61

mmol/mol), respectively, may have limited the potential for a greater difference in HbA1c after treatment switch that might occur in less well-controlled pediatric populations.

There have been controversial publications regarding the dosing accuracy of tubeless insulin pumps (21). Our study results indicate that concerns regarding infusion rate or bolusing accuracy that have been raised particularly with the lower insulin doses commonly used in pediatric patients are not clinically relevant (22). The circumstantial evidence from this large cohort study indicates that the technical robustness of tubeless pumps is efficacious for achieving glycemic targets even in the difficult pediatric population.

Insulin pump use shows large differences between nations which are not readily explained by different health care systems, guidelines or reimbursement modalities (23). Although the pump penetration for pediatric patients with T1D in Germany has increased significantly from year to year, significant differences exist between different regions indicating the importance of care provider preference – and likely level of familiarity with this treatment option (24). CSII is especially prevalent in younger age groups with currently 91% of pediatric patients in Germany choosing this treatment regimen, while adolescents are more reluctant to use this option (25). Visibility of tubing with conventional pumps may be a hindrance particularly in the adolescent age group where peer pressure regarding appearance is common. Indeed the average age of the current cohort was 12 years indicating that the obvious advantages of substituting insulin with a discrete tubeless pump may convince more adolescents to choose CSII over MDI.

Key strengths of the present study include the large sample size of the MDI and tubeless insulin pump users and the robust nature of the German/Austrian DPV registry. Limitations of the study are inherent in a retrospective design including that only associations between treatment modalities and outcomes can be made. Limited data was available on glycemic variability, diabetic ketoacidosis and hypoglycemic episodes, thus these measures of measures could not be evaluated in the present study. Compared to other large cohort studies of pediatric populations the study population was in fairly good glycemic control which may limit the generalizability of our findings.

Conclusions

This large, retrospective analysis of the German/Austrian DPV registry demonstrated that treatment with the Omnipod Insulin Management System in youth with T1D was associated with improvements in glycemic control and lower total daily dose of insulin compared with MDI at 1 year with stability in HbA1c in both groups at 2 and 3 years. Although registry data is unable to show superiority or inferiority of one mode of therapy compared to another, switching to tubeless insulin pump therapy appears as an effective alternative to MDI in youth with T1D.

Acknowledgments:

T.D. conceptualized the study, researched the data and wrote the manuscript. T.B., B.H., B R-M., A.S. and R.W.H reviewed/edited the manuscript and contributed to the discussion. R.W.H., A.S. conceptualized the study and researched data. T.D. is the guarantor of this work and, as such, had 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. Editorial support was provided by Dr. Esther Bollow of the University of Ulm, Jennifer E. Layne, PhD, Insulet Corporation, and Christopher G. Parkin, M.S., CGParkin Communications, Inc.

Funding:

This study was sponsored by Insulet Corporation. The study was financially supported by the Federal Ministry of Education and Research within the German Competence Network for Diabetes mellitus (grant number: 01GI1106) which is integrated in the German Center for Diabetes Research (DZD) as of January 2015. This project has received funding from the Innovative Medicines Initiative 2 Joint Undertaking under grant agreement No 115797 (INNODIA) supported by from the Union's Horizon 2020 research and innovation program and "EFPIA", "JDRF" and "The Leona M. and Harry B. Helmsley Charitable Trust". The German Diabetes Association (DDG) and the European Foundation for the Study of Diabetes (EFSD) provided further financial support. Sponsors were not involved in data acquisition or analysis.

Author Disclosures:

Dr. Danne has received research support or has consulted for Abbott, AstraZeneca, Bayer, Boehringer, DexCom, Insulet Corp., Eli Lilly, Medtronic, NovoNordisk, Roche,

Dr. Rami-Merhar has received research support or has consulted for, Bayer, Boehringer, Eli Lilly, Medtronic, NovoNordisk, Roche, and Sanofi.

Dr. Biester received research support honoraria for lecture and travel support from Medtronic, Ypsomed, NovoNordisk.

Drs. Schwandt, Heidtmann, and Holl have no disclosures.

References:

1. Miller KM, Foster NC, Beck RW, Bergenstal RM, DuBose SN, DiMeglio LA, et al. Current state of type 1 diabetes treatment in the U.S.: Updated data from the t1d exchange clinic registry. *Diabetes Care*. 2015;38:971-978
2. Schwandt A, Hermann JM, Rosenbauer J, Boettcher C, Dunstheimer D, Grulich-Henn J, Kuss O, Rami-Merhar B, Vogel C, Holl RW; DPV Initiative.Longitudinal Trajectories of Metabolic Control From Childhood to Young Adulthood in Type 1 Diabetes From a Large German/Austrian Registry: A Group-Based Modeling Approach. Diabetes Care. 2017;40(3):309-316
3. Moran A, Jacobs DR, Jr., Steinberger J, Hong CP, Prineas R, Luepker R, et al. Insulin resistance during puberty: Results from clamp studies in 357 children. *Diabetes*. 1999;48:2039-2044
4. Cameron F. Teenagers with diabetes--management challenges. *Aust Fam Physician*. 2006;35:386-390
5. Phillip M, Battelino T, Rodriguez H, Danne T, Kaufman F. Use of insulin pump therapy in the pediatric age-group: Consensus statement from the European Society for Paediatric Endocrinology, the Lawson Wilkins Pediatric Endocrine Society, and the International Society for Pediatric and Adolescent Diabetes, endorsed by the American Diabetes Association and the European Association for the Study of Diabetes. *Diabetes Care*. 2007;30:1653-1662
6. Danne T, Bangstad HJ, Deeb L, Jarosz-Chobot P, Mungaie L, Saboo B, et al. ISPAD clinical practice consensus guidelines 2014. Insulin treatment in children and adolescents with diabetes. *Pediatr Diabetes*. 2014;15 (Suppl 20):115-134

7. Dovc K, Telic SS, Lusa L, Bratanic N, Zerjav-Tansek M, Kotnik P, et al. Improved metabolic control in pediatric patients with type 1 diabetes: A nationwide prospective 12-year time trends analysis. *Diabetes Technol Ther*. 2014;16:33-40
8. Thrailkill KM, Moreau CS, Swearingen C, Rettiganti M, Edwards K, Morales AE, et al. Insulin pump therapy started at the time of diagnosis: effects on glycemic control and pancreatic beta-cell function in type 1 diabetes. *Diabetes Technol Ther*. 2011;13:1023-1030
9. Brorsson AL, Viklund G, Ortqvist E, Lindholm Olinder A. Does treatment with an insulin pump improve glycaemic control in children and adolescents with type 1 diabetes? A retrospective case-control study. *Pediatr Diabetes*. 2015;16:546-553
10. Fendler W, Baranowska AI, Mianowska B, Szadkowska A, Mlynarski W. Three-year comparison of subcutaneous insulin pump treatment with multi-daily injections on hba1c, its variability and hospital burden of children with type 1 diabetes. *Acta Diabetol*. 2012;49:363-370
11. Johnson SR, Cooper MN, Jones TW, Davis EA. Long-term outcome of insulin pump therapy in children with type 1 diabetes assessed in a large population-based case-control study. *Diabetologia*. 2013;56:2392-2400
12. Majedah MA, Mousa M, Al-Mahdi M, Al-Sanaa H, Dalia A-A, Al-Kandari H. A comparison of continuous subcutaneous insulin infusion vs. Multiple daily insulin injection in children with type i diabetes in kuwait: Glycemic control, insulin requirement, and bmi. *Oman Med J*. 2015;30:336-343
13. Seereiner S, Neeser K, Weber C, Schreiber K, Habacher W, Rakovac I, et al. Attitudes towards insulin pump therapy among adolescents and young people. *Diabetes Technol Ther*. 2010;12:89-94

14. Layne JE, Parkin CG, Zisser H. Efficacy of the Omnipod insulin management system on glycemic control in patients with type 1 diabetes previously treated with multiple daily injections or continuous subcutaneous insulin infusion. *J Diabetes Sci Technol*. 2016;10:1130-1135
15. Littell RC, Milliken GA, Stroup WW, Wolfinger RS, Schabenberger O. SAS for mixed models. 2nd edn. Cary NC, USA: SAS Press, 2006. isbn:978-1-59047-500-3.
16. Danne T, Bollow E, Schwandt A, Heidtmann B, Kordonouri O, Rami-Merhar B et al. Prevalence of Tubeless Insulin Pump Use in Type 1 and Type 2 Diabetes: Data from 2074 Patients in the German/Austrian DPV Registry. *Diabetes Care*. 2017; 67(Suppl 1): A663.
17. Johnson SR, Cooper MN, Jones TW, Davis EA. Long-term outcome of insulin pump therapy in children with type 1 diabetes assessed in a large population-based case-control study. Diabetologia. 2013;56: 2392-400.
18. Sherr JL, Hermann JM, Campbell F, Foster NC, Hofer SE, Allgrove J, et al. 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. Diabetologia. 2016;59(1):87-91
19. Gerstl EM et al. Metabolic control as reflected by HbA1c in children, adolescents and young adults with type-1 diabetes mellitus: combined longitudinal analysis including 27,035 patients from 207 centers in Germany and Austria during the last decade. *Eur J Pediatr*. 2008;167: 447–453.
20. Hofer SE et al. Tracking of metabolic control from childhood to young adulthood in type 1 diabetes. *J Pediatr*. 2014;165: 956–961

21. Zisser H, Breton M, Dassau E, Markova K, Bevier W, Seborg D, Kovatchev B. Novel methodology to determine the accuracy of the OmniPod insulin pump: a key component of the artificial pancreas system. *J Diabetes Sci Technol*. 2011;5(6):1509-18
22. Jahn LG, Capurro JJ, Levy BL. Comparative dose accuracy of durable and patch insulin infusion pumps. *J Diabetes Sci Technol.* 2013;7(4):1011-20
23. Pozzilli P, Battelino T, Danne T, Hovorka R, Jarosz-Chobot P, Renard E. Continuous subcutaneous insulin infusion in diabetes: patient populations, safety, efficacy, and pharmacoeconomics. *Diabetes Metab Res Rev*. 2016;32(1):21-39.
24. Bohn B, Rosenbauer J, Icks A, Vogel C, Beyer P, Rütschle H, Hermann U, Holterhus PM, Wagner V, von Sengbusch S, Fink K, Holl RW; DPV initiative.Regional Disparities in Diabetes Care for Pediatric Patients with Type 1 Diabetes. A Cross-sectional DPV Multicenter Analysis of 24,928 German Children and Adolescents. *Exp Clin Endocrinol Diabetes*. 2016;124(2):111-9
25. Holl RW, Prinz N; Gesundheitsbericht Diabetes 2017. Medizinische Versorgung von Kindern und Jugendlichen mit Diabetes – Entwicklungen der letzten 21 Jahre http://www.diabetesde.org/system/files/documents/gesundheitsbericht_2017.pdf

Table 1. Baseline Characteristics

	MDI (N=1869)	Tubeless Insulin Pump (N=660)
Male, %	57	49**
Age, yr	12.0±2.8	11.5±5.1**
Diabetes duration, yr	4.1±3.2	3.2±3.7**
HbA1c, % (mmol/mol)	7.6±1.3 (60±14)	7.5±1.2 (58±13)
BMI SDS	0.40±0.90	0.43±0.91
Insulin Dose, U/kg/24h	0.86±0.32	0.79±0.29**

Data are presented as unadjusted mean±SD unless otherwise indicated; **p<0.001

MDI: Multiple daily injections; BMI, SDS: Body mass index standard deviation score

Table 2. Change in HbA1c, Insulin Dose and BMI with Tubeless Insulin Pump Therapy Compared to MDI Over 3 Years

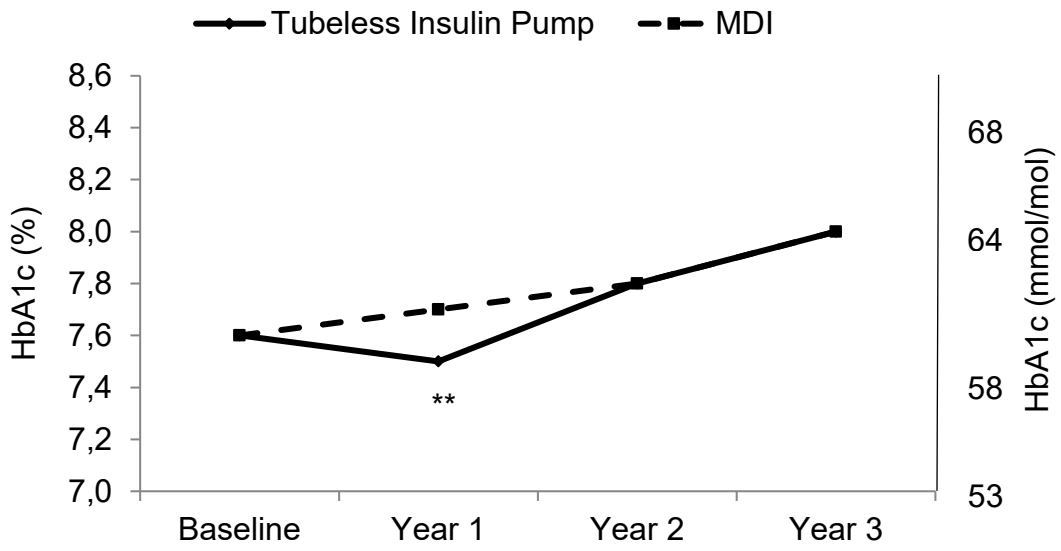
	MDI (N=1869)				Tubeless Insulin Pump (N=660)			
Outcome	Baseline	Year 1	Year 2	Year 3	Baseline	Year 1	Year 2	Year 3
HbA1c, % (mmol/mol)	7.6±0.03 (60)	7.7±0.02 (61)	7.8±0.02 (62)	8.0±0.02 (64)	7.6±0.5 (60)	7.5±0.03** (58)	7.8±0.04 (62)	8.0±0.05 (64)
Insulin Dose (U/kg/24h)	0.84±0.01	0.89±0.01	0.94±0.01	0.97±0.01	0.79±0.01	0.80±0.01**	0.81±0.01**	0.85±0.01**
BMI (SDS)	0.40±0.02	0.46±0.01	0.49±0.01	0.54±0.01	0.43±0.04	0.48±0.02	0.52±0.02	0.58±0.02

Results adjusted for baseline variable value, age, gender, diabetes duration; values are presented as mean±SEM; BMI (SDS), Body Mass Index Standard Deviation Score; **p<0.001

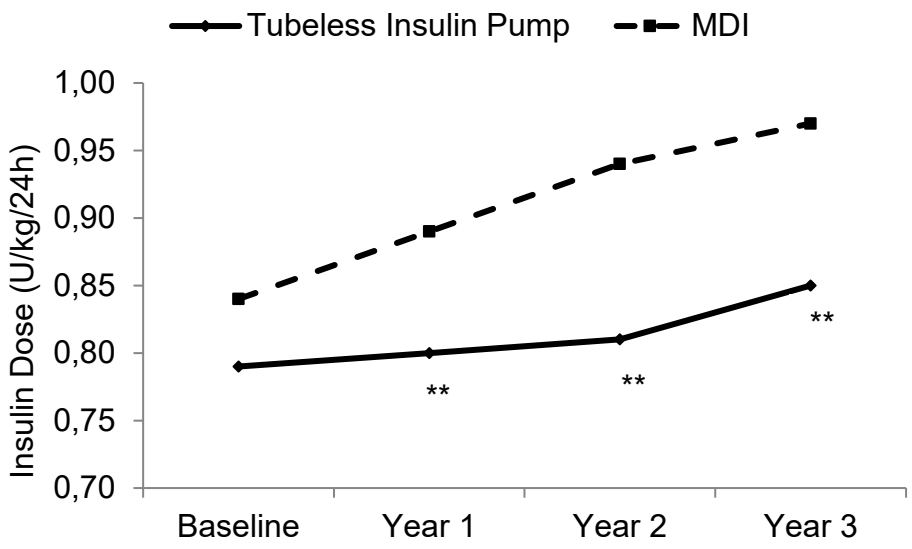
Figure Legend. (A) Mean HbA1c was significantly lower in the tubeless insulin pump group compared to the MDI group at year 1 with no between group difference observed at years 2 and 3. (B) Mean insulin dose was significantly lower in the tubeless insulin pump group compared to MDI at years 1, 2 and 3. (C) Mean Body Mass Index (BMI) Standard Deviation Score (SDS) was not different between groups at any time point. **p<0.001; Results adjusted for baseline variables age, gender, diabetes duration.

Figure 1. Change in HbA1c, Insulin Dose and BMI with Tubeless Insulin Pump Therapy Compared to MDI Over 3 Years

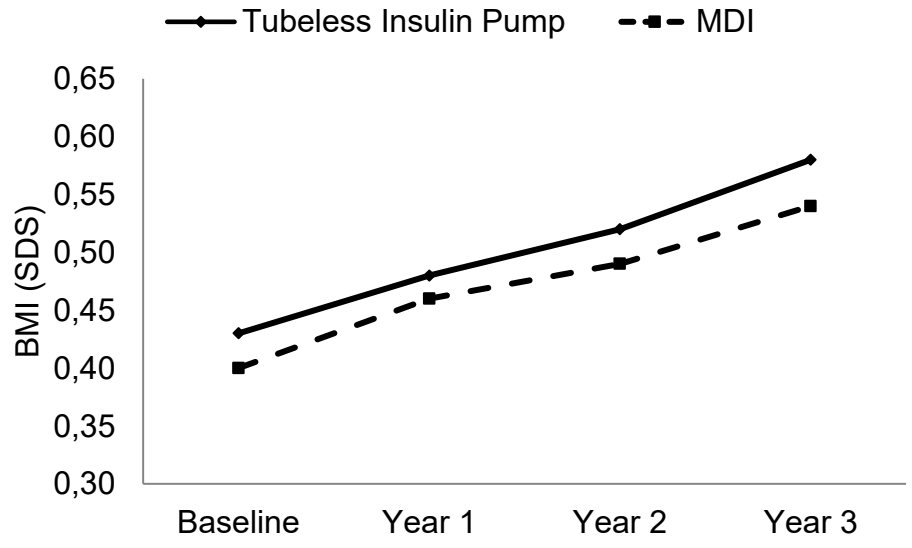
A.



B.


Tubeless Insulin Pump
MDI
Insulin Dose (U/kg/24h)
1,00
0,95
0,90
0,85
0,80
0,75
0,70
**
**
**
Baseline
Year 1
Year 2
Year 3

C.


Tubeless Insulin Pump
MDI
BMI (SDS)
0,65
0,60
0,55
0,50
0,45
0,40
0,35
0,30
Baseline
Year 1
Year 2
Year 3

Supporting Information - Acknowledgements

Centers that have contributed to the German/Austrian Diabetes Patienten Verlaufsdokumentation (DPV) registry analysis

Aachen - Innere RWT H,Aachen - Uni-Kinderklinik RWTH, Aalen Kinderklinik, Ahlen St. Franziskus Kinderklinik, Aidlingen Praxisgemeinschaft, Altötting Zentrum Inn-Salzach, Altötting-Burghausen Innere Medizin, Amberg Kinderklinik St. Marien,vAmstetten Klinikum Mostviertel Kinderklinik, Arnsberg-Hüsten Karolinenhosp. Kinderabteilung, Asbach Kamillus-Klinik Innere, Aue Helios Kinderklink, Augsburg IV. Med. Klinik, Augsburg Josefinum Kinderklinik, Augsburg Kinderklinik Zentralklinikum, Aurich Kinderklinik, Bad Aibling Internist. Praxis, Bad Driburg / Bad Hermannsborn Innere, Bad Hersfeld Innere, Bad Hersfeld Kinderklinik, Bad Kreuznach-St.Marienwörth-Innere, Bad Kreuznach-Viktoriastift, Bad Krozingen Klinik Lazariterhof Park-Klinikum, Bad Kösen Kinder-Rehaklinik, Bad Lauterberg Diabeteszentrum Innere, Bad Mergentheim – Diabetesfachklinik, Bad Mergentheim - Gemeinschaftspraxis DM-dorf Althausen, Bad Oeynhausen Herz-und Diabeteszentrum NRW, Bad Orb Spessart Klinik, Bad Orb Spessart Klinik Reha, Bad Reichenhall Kreisklinik Innere Med,Bad Salzungen Kinderklinik, Bad Säckingen Hochrheinklinik Innere, Bad Waldsee Kinderarztpraxis, Bautzen Oberlausitz KK, Bayreuth Innere Medizin, Berchtesgaden CJD, Berchtesgaden MVZ Innere Med, Berlin DRK-Kliniken Innere, Berlin DRK-Kliniken Pädiatrie, Berlin Endokrinologikum, Berlin Evang. Krankenhaus Königin Elisabeth, Berlin Klinik St. Hedwig Innere, Berlin Lichtenberg – Kinderklinik, Berlin Oskar Zieten Krankenhaus Innere, Berlin Parkklinik Weissensee, Berlin Schlosspark-Klinik Innere, Berlin St. Josephskrankenhaus Innere, Berlin Virchow-Kinderklinik, Berlin Vivantes Hellersdorf Innere, Bern Universitätsklinik InselSpital Innere Medizin, Bielefeld Kinderklinik Gilead, Bocholt Kinderklinik, Bochum Universitäts St. Josef, Bochum Universitätskinderklinik St. Josef, Bonn Uni-Kinderklinik, Bottrop Kinderklinik,Bottrop Knappschaftskrankenhaus Innere, Braunfels-Wetzlar Innere, Braunschweig Kinderarztpraxis,Bremen - Kinderklinik Nord, Bremen - Mitte Innere, Bremen Zentralkrankenhaus Kinderklinik, Bremerhaven Kinderklinik, Bruchweiler Edelsteinklinik Kinder-Reha Böblingen Kinderklinik, Castrop-Rauxel Rochus-Hospital, Celle Klinik für Kinder- und Jugendmedizin, Chemnitz Kinderklinik, Chemnitz-Hartmannsdorf Innere Medizin - DIAKOMED-1, Coburg Innere Medizin, Coburg Kinderklinik, Coesfeld Kinderklinik, Coesfeld/Dülmen Innere Med., Darmstadt Innere Medizin, Darmstadt Kinderklinik Prinz. Margaret, Datteln Vestische Kinderklinik, Deggendorf Gemeinschaftspraxis, Deggendorf Kinderklinik, Deggendorf Medizinische Klinik II, Deggendorf Pädiatrie-Praxis, Delmenhorst Kinderklinik, Dessau Kinderklinik, Detmold Kinderklinik, Dinslaken Kinderklinik, Dornbirn Innere Medizin, Dornbirn Kinderklinik, Dortmund Kinderklinik, Dortmund Knappschaftskrankenhaus Innere, Dortmund Medizinische Kliniken Nord, Dortmund-Hombruch Marienhospital, Dortmund-St. Josefshospital Innere, Dortmund-West Innere, Dresden Neustadt Kinderklinik, Dresden Uni-Kinderklinik, Duisburg Evang. und Johanniter Krhs Innere, Duisburg Malteser Rhein-Ruhr St. Anna Innere, Duisburg Malteser St. Johannes Duisburg Sana Kinderklinik, Duisburg-Huckingen, Duisburg-Huckingen Malteser Rhein-Ruhr ST. Johannes, Duisburg-St.Johannes Helios, Düren-Birkesdorf Kinderklinik, Düsseldorf Uni-Kinderklinik, Eberswalde Klinikum Barnim Werner Forßmann – Innere, Eisleben Lutherstadt Helios-Klinik, Erfurt Kinderklinik, Erlangen Uni Innere Medizin, Erlangen Uni-Kinderklinik, Essen Diabetes-Schwerpunktpraxis, Essen Elisabeth Kinderklinik, Essen Kinderarztpraxis, Essen Uni-Kinderklinik, Esslingen Klinik für Kinder und Jugendliche, Eutin Kinderklinik, Eutin St.-Elisabeth Innere, Feldkirch Kinderklinik, Filderstadt Kinderklinik, Flensburg Diakonissen Kinderklinik, Forchheim

Diabeteszentrum SPP, Frankenthal Kinderarztpraxis, Frankfurt Diabeteszentrum Rhein-Main-Erwachsenendiabetologie (Bürgerhospital), Frankfurt Diabeteszentrum Rhein-Main-pädiat. Diabetologie (Clementine-Hospital), Frankfurt Uni-Kinderklinik, Frankfurt Uni-Klinik Innere, Frankfurt-Sachsenhausen Innere, Freiburg Kinder-MVZ, Freiburg St. Josef Kinderklinik, Freiburg Uni Innere, Freiburg Uni-Kinderklinik, Freudenstadt Kinderklinik Friedberg Innere Klinik, Friedrichshafen Kinderklinik, Fulda Innere Medizin, Fulda Kinderklinik, Fürth Kinderklinik, Gaissach Fachklinik der Deutschen Rentenversicherung Bayern Süd, Garmisch-Partenkirchen Kinderklinik, Geislingen Klinik Helfenstein Innere, Gelnhausen Innere, Gelnhausen Kinderklinik, Gelsenkirchen Kinderklinik Marienhospital, Gera Kinderklinik, Gießen Ev. Krankenhaus Mittelhessen, Gießen Uni-Kinderklinik, Graz Uni-Kinderklinik, Greifswald Uni-Kinderklinik, Göppingen Innere Medizin, Göppingen Kinderklinik am Eichert, Görlitz Städtische Kinderklinik, Göttingen Uni Gastroenterologie, Göttingen Uni-Kinderklinik, Güstrow Innere, Hachenburg Kinderpraxis, Hagen Kinderklinik, Halberstadt Innere Med. AMEOS Klinik, Halberstadt Kinderklinik AMEOS, Halle Uni-Kinderklinik, Halle-Dölau Städtische Kinderklinik, Hamburg Altonaer Kinderklinik, Hamburg Endokrinologikum, Hamburg Kinderklinik Wilhelmstift, Hamburg-Nord Kinder-MVZ, Hameln Kinderklinik Hamm Kinderklinik, Hanau Kinderklinik, Hanau St. Vincenz – Innere, Hannover Henriettenstift – Innere, Hannover Kinderklinik MHH, Hannover Kinderklinik auf der Bult, Haren Kinderarztpraxis, Heide Kinderklinik, Heidelberg St. Josefskrankenhaus, Heidelberg Uni-Kinderklinik, Heidelberg Uniklinik Innere, Heidenheim Arztpraxis Allgemeinmed, Heidenheim Kinderklinik, Heilbronn Innere Klinik, Heilbronn Kinderklinik, Herdecke Kinderklinik, Herford Innere Med I, Herford Kinderarztpraxis, Herford Klinikum Kinder & Jugendliche, Heringsdorf Inselklinik, Hermeskeil Kinderpraxis, Herne Evan. Krankenhaus Innere, Herten St. Elisabeth Innere Medizin, Herzberg Kreiskrankenhaus Innere, Hildesheim GmbH – Innere, Hildesheim Kinderarztpraxis, Hildesheim Kinderklinik, Hinrichsegen-Bruckmühl Diabetikerjugendhaus, Hof Kinderklinik, Homburg Uni-Kinderklinik Saarland, Idar Oberstein Innere, Ingolstadt Klinikum Innere, Innsbruck Uni-Kinderklinik Innsbruck Universitätsklinik Innere, Iserlohn Innere Medizin, Itzehoe Kinderklinik, Jena Uni-Kinderklinik, Kaiserslautern Kinderarztpraxis, Kaiserslautern-Westpfalzklinikum Kinderklinik, Kamen Klinikum Westfalen Hellmig Krankenhaus, Karlsburg Klinik für Diabetes & Stoffwechsel, Karlsruhe Städtische Kinderklinik, Kassel Klinikum Kinder- und Jugendmedizin, Kassel Rot-Kreuz-Krankenhaus Innere, Kassel Städtische Kinderklinik, Kaufbeuren Innere Medizin, Kempen Heilig Geist – Innere, Kempen Heilig Geist-KHS – Innere, Kempten Oberallgäu Kinderklinik, Kiel Städtische Kinderklinik, Kiel Universitäts-Kinderklinik, Kirchen DRK Krankenhaus Kinderklinik, Kirchheim-Nürtingen Innere, Klagenfurt Innere Med I, Kleve Innere Medizin, Koblenz Kemperhof 1. Med. Klinik, Koblenz Kinderklinik Kemperhof, Konstanz Innere Klinik, Konstanz Kinderklinik, Krefeld Alexianer Innere, Krefeld Innere Klinik, Krefeld Kinderklinik, Krefeld-Uerdingen St. Josef Innere, Kreischa-Zscheckwitz Klinik Bavaria, Köln Kinderklinik Amsterdamerstrasse, Köln Uni-Kinderklinik Landau/Annweiler Innere, Landshut Kinderklink, Lappersdorf Kinderarztpraxis, Leer Kreiskrankenhaus - Kinderabt., Leipzig Uni-Kinderklinik, Leoben LKH Kinderklinik, Leverkusen Kinderklinik, Lienz BKH Kinderklinik, Lienz BKH Pädiatrie, Lienz Diabetesschwerpunktpraxis für Kinder und Jugendliche, Lilienthal Diabeteszentrum, Limburg Innere Medizin, Lindenfels Luisenkrankenhaus Innere, Lindenfels Luisenkrankenhaus Innere 2, Lingen Kinderklinik St. Bonifatius, Linz AKH - 2. Med, Linz Krankenhaus Barmherzige Schwestern Kardiologie Abt. Int. II, Linz Krankenhaus der Barmherzigen Schwestern Kinderklinik, Linz Landes-Kinderklinik, Lippstadt Evangelische Kinderklinik, Ludwigsburg Innere Medizin, Ludwigsburg Kinderklinik, Ludwigshafen Kinderklinik St.Anna-Stift, Ludwigshafen diabetol. SPP, Luxembourg - Centre Hospitalier, Lübeck Uni-Kinderklinik,

Lübeck Uni-Klinik Innere Medizin, Lüdenscheid Hilfswerk Kinder & Jugendliche, Lüdenscheid Märkische Kliniken - Kinder & Jugendmedizin, Lünen Klinik am Park, Magdeburg Städtisches Klinikum Innere, Magdeburg Uni-Kinderklinik, Mainz Uni-Kinderklinik Malchower See Rehaklinik, Mannheim Uni-Kinderklinik, Mannheim Uniklinik Innere Medizin, Marburg - UKGM Endokrinologie & Diabetes, Marburg Uni-Kinderklinik, Marktredwitz Innere Medizin, Marpingen-SPP, Mechernich Kinderklinik, Meissen Kinderklinik Elblandklinikum, Memmingen Internistische Praxis, Memmingen Kinderklinik, Merzig Kinderklinik, Minden Kinderklinik, Moers - St. Josefskrankenhaus Innere, Moers Kinderklinik, Murnau am Staffelsee - diabetol. SPP, Mutterstadt Kinderarztpraxis, Mödling Kinderklinik, Mölln Reha-Klinik Hellbachtal, Mönchengladbach Kinderklinik Rheydt Elisabethkrankenhaus, Mühlacker Enzkreiskliniken Innere, Mühldorf am Inn Kinderarztpraxis, München 3. Orden Kinderklinik, München Diabetes-Zentrum Süd, München Kinderarztpraxis diabet. SPP, München Schwerpunktpraxis, München von Haunersche Kinderklinik, München-Gauting Kinderarztzentrum, München-Harlaching Kinderklinik, München-Schwabing Kinderklinik, Münster Clemens-Hospital Innere, Münster Herz Jesu Innere, Münster St. Franziskus Kinderklinik Münster Uni-Kinderklinik, Münster pädiat. Schwerpunktpraxis, Nagold Kreiskrankenhaus Innere, Nauen Havellandklinik, Neuburg Kinderklinik, Neumarkt Innere, Neunkirchen Innere Medizin ,Neunkirchen Marienhausklinik Kohlhof Kinderklinik, Neuruppin Kinderklinik, Neuss Lukaskrankenhaus Kinderklinik, Neuwied Kinderklinik Elisabeth, Neuwied Marienhaus Klinikum St. Elisabeth Innere, Nidda Bad Salzhausen Klinik Rabenstein/Innere-1 Reha, Nidda Bad Salzhausen Klinik Rabenstein/Innere-2 Reha, Nürnberg Cnopfsche Kinderklinik, Nürnberg Med. Klinik 4, Nürnberg Zentrum f Neugeb./Kinder & Jugendl., Oberhausen Innere, Oberhausen Kinderklinik, Oberhausen Kinderpraxis, Oberhausen St.Clemens Hospitale Sterkrade, Oberndorf Gastroenterologische Praxis Schwerpunkt Diabetologie, Offenbach/Main Innere Medizin, Offenbach/Main Kinderklinik, Offenburg Kinderklinik, Oldenburg Kinderklinik, Oldenburg Schwerpunktpraxis, Oschersleben MEDIGREIF Bördekrankenhaus, Osnabrück Christliches Kinderhospital, Osterkappeln Innere, Ottobeuren Kreiskrankenhaus, Oy-Mittelberg Hochgebirgsklinik Kinder-Reha, Paderborn St. Vincenz Kinderklinik Papenburg Marienkrankenhaus Kinderklinik, Passau Kinderarztpraxis, Passau Kinderklinik, Pforzheim Kinderklinik, Pfullendorf Innere Medizin, Pirmasens Städtisches Krankenhaus Innere, Plauen Vogtlandklinikum, Prenzlau Krankenhaus Innere, Rastatt Gemeinschaftspraxis, Rastatt Kreiskrankenhaus Innere, Ravensburg Kinderklink St. Nikolaus, Recklinghausen Dialysezentrum Innere, Regensburg Kinderklinik St. Hedwig, Remscheid Kinderklinik, Rendsburg Kinderklinik, Reutlingen Kinderarztpraxis, Reutlingen Kinderklinik, Reutlingen Klinikum Steinenberg Innere, Rheine Mathiasspital Kinderklinik, Ried Innkreis Barmherzige Schwestern, Rodalben St. Elisabeth, Rosenheim Innere Medizin, Rosenheim Kinderklinik, Rosenheim Schwerpunktpraxis, Rostock Uni-Kinderklinik, Rostock Universität Innere Medizin, Rotenburg/Wümme Agaplesion Diakonieklinikum Kinderabteilung, Rüsselsheim Kinderklinik, Saaldorf-Surheim Diabetespraxis, Saalfeld Thüringenklinik Kinderklinik, Saarbrücken Kinderklinik Winterberg, Saarbrücken Kinderklinik Winterberg 2, Saarlouis Kinderklinik Salzburg Universitäts-Kinderklinik, Scheibbs Landesklinikum, Scheidegg Prinzregent Luitpold, Scheidegg Reha-Kinderklinik Maximilian, Schw. Gmünd Stauferklinik Kinderklinik, Schweinfurt Kinderklinik, Schwerin Innere Medizin, Schwerin Kinderklinik, Schwäbisch Hall Diakonie Innere Medizin, Schwäbisch Hall Diakonie Kinderklinik, Siegen Kinderklinik, Singen - Hegauklinik Kinderklinik, Singen Kinderarztpraxis, Sinsheim Innere, Spaichingen Innere, St. Augustin Kinderklinik, St. Pölten Universitäts-Kinderklinik, St. Pölten Universitätsklinik Innere, Stade Kinderklinik, Stolberg Kinderklinik, Stuttgart Bethesda Agaplesion, Stuttgart Olgahospital

Kinderklinik, Suhl Kinderklinik, Sylt Rehaklinik, Tettnang Innere Medizin, Timmendorfer Strand, Traunstein Kinderklinik, Traunstein diabetol. Schwerpunktpraxis, Trier Kinderklinik der Borromäerinnen, Trostberg Innere, Tübingen Uni-Kinderklinik, Ulm Agaplesion Bethesda-Krankenhaus, Ulm Endokrinologikum Ulm Schwerpunktpraxis Bahnhofsplatz, Ulm Uni Innere Medizin, Ulm Uni-Kinderklinik, Vechta Kinderklinik, Viersen Kinderkrankenhaus St. Nikolaus, Villach Kinderklinik, Villingen-Schwenningen SPP, Villingen-Schwenningen Schwarzwald Baar Klinikum Kinderklinik, Villingen-Schwenningen Schwarzwald-Baar-Klinikum Innere, Waldshut Kinderpraxis, Waldshut-Tiengen Kinderpraxis Biberbau, Wangen Oberschwabenklinik Innere Medizin, Waren-Müritz Kinderklinik, Weiden Kinderklinik, Weingarten Kinderarztpraxis, Weisswasser Kreiskrankenhaus, Wels Innere, Wels Klinikum Pädiatrie, Wernberg-Köblitz SPP, Wetzlar Schwerpunkt-Praxis, Wien 3. Med. Hietzing Innere, Wien Preyersches Kinderspital, Wien Rudolfstiftung, Wien SMZ Ost Donauspital, Wien Uni Innere Med III, Wien Uni-Kinderklinik, Wien Wilhelminenspital 5. Med. Abteilung, Wiesbaden Horst-Schmidt-Kinderkliniken, Wiesbaden Kinderklinik DKD, Wilhelmshaven Reinhard-Nieter-Kinderklinik, Wilhelmshaven St. Willehad Innere, Winnenden Rems-Murr Kinderklinik, Wismar Kinderklinik Wittenberg Innere Medizin, Wittenberg Kinderklinik, Wolgast Innere Medizin, Worms – Weierhof, Worms Kinderklinik, Wuppertal Kinderklinik, Zweibrücken Ev. KH. Innere, Zweibrücken Kinderarztpraxis