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Clinical and quality of life outcomes in children and adolescents with type 1 diabetes using different insulin therapy types: a cross-sectional observational study

Gianluca Tornese^{1,2}, Antonietta Robino^{1*}, Roberto Franceschi³, Enza Mozzillo⁴, Luana Aldegheri¹, Francesca Di Candia⁴, Gianluca Tamaro¹, Camilla Morosini⁵, Antonietta Chianese⁶, Giorgia Ippolito⁶, Riccardo Bonfanti⁵, Ivana Rabbone⁷, Dario Iafusco⁶ and Eulalia Catamo¹

Abstract

Background Type 1 diabetes (T1D) requires lifelong insulin therapy. Although multiple daily injections (MDI) remain widely used, advanced technologies, such as continuous subcutaneous insulin infusion (CSII) and automated insulin delivery (AID) system have demonstrated benefits in glycemic control and quality of life (QoL). However, comparative data on these modalities in pediatric population are still limited. This study examined the associations between therapy type, clinical outcomes, and health-related QoL (HRQoL) in children and adolescents with T1D.

Methods Demographic, anthropometric, and clinical data were collected from 262 children and adolescents with T1D. HRQoL was assessed using the Pediatric Quality of Life Inventory (PedsQL) 3.2 Diabetes Module.

Results Among participants, 62% were treated with MDI, 11% with CSII, and 27% with AID, without significant differences between children and adolescents.

In adolescents, MDI users showed significantly higher mean HbA1c values and suboptimal glycemic control (p-value < 0.001), higher daily insulin requirements (p-value = 0.003), and lower estimated glomerular filtration rate (eGFR) (p-value < 0.001) compared with CSII and AID users. While, in children only eGFR was associated with therapy type (p-value < 0.001).

Only female adolescents reported better QoL when treated with CSII, with therapy type associated with HRQoL domains related to Worry (p-value = 0.031), Management (p-value = 0.050), and total HRQoL (p-value = 0.034).

Overall, adolescent females also showed poorer HRQoL than males, particularly in domains related to worry about diabetes complications (p-value = 0.002), and communication difficulties (p-value < 0.001).

Conclusions The use of modern insulin delivery technologies was associated with improved clinical outcomes, including early renal markers. However, HRQoL were limited and predominantly observed in female adolescents,

*Correspondence:
Antonietta Robino
antonietta.robino@burlo.trieste.it

Full list of author information is available at the end of the article



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who nevertheless reported lower overall QoL than their male peers. These findings suggest that while technological advances can enhance clinical outcomes, they may not fully address the psychosocial challenges of living with T1D, especially during female adolescence, a period of heightened emotional vulnerability. Integrating gender- and age-sensitive psychosocial support alongside technological innovations may be crucial to achieving holistic diabetes care.

Keywords Clinical outcome, Health-related quality of life, Therapy, Type 1 diabetes

Introduction

Type 1 diabetes (T1D) is characterized by autoimmune destruction of pancreatic β -cells, leading to absolute insulin deficiency and the lifelong need for exogenous insulin therapy [1].

Insulin administration remains the cornerstone of treatment, essential for achieving glycemic control and preventing both acute and chronic complications. In addition, stable glycemic control has shown to improve quality of life (QoL) by alleviating some of the psychological burden associated with daily diabetes management [2–4].

Several insulin delivery methods are currently available. Multiple Daily Injections (MDI) remain the conventional first-line therapy, yet many patients do not achieve recommended HbA1c targets with this approach [5]. Continuous Subcutaneous Insulin Infusion (CSII) provides greater flexibility and reduce the burden of repeated injections [6]. More recently, Automated Insulin Delivery (AID) systems have emerged as the most advanced option, continuously adjusting insulin delivery to optimize glucose control and minimize hypoglycemia [7, 8]. The introduction of Continuous Glucose Monitoring (CGM), either as a stand-alone technology or integrated with these therapies, has further contributed to improve glycemic outcomes and increased time in range (TIR) [6, 9].

Comparative studies have shown that CSII can improve long-term HbA1c levels compared to MDI in pediatric T1D [10, 11], while AID systems consistently outperform both MDI and CSII, particularly in reducing HbA1c and enhancing TIR [7, 8, 10–13]. Accordingly, international guidelines increasingly recommend AID as the preferred therapeutic option when available and affordable [14].

Beyond glycemic metrics, insulin therapy also impacts QoL. Evidence suggests that CSII and especially AID are associated with improved QoL compared with MDI [15–17]. However, psychosocial factors complicate these evaluations: the benefits of advanced technologies are not always immediately reflected in QoL, as adaptation to new devices may require time and support [17, 18]. Adolescence represents an especially vulnerable period for diabetes management, due to physiological changes such as puberty-associated insulin resistance and psychological challenges including treatment fatigue, peer influence and the desire for autonomy. These factors often contribute to suboptimal adherence [19].

In this context, modern technologies such as CSII and AID may not only facilitate improved glycemic control, but also help reduce the daily burden of disease management, ultimately supporting both metabolic outcomes and enhanced quality of life.

Despite growing evidence, most studies assessing the impact of different insulin therapies on diabetes management and QoL have been conducted in adults and typically over relatively short follow-up periods. Direct comparisons between MDI, CSII, and AID in pediatric populations remain scarce.

To address this gap, the present study analyzed a comprehensive clinical database of children and adolescent with T1D who had been treated with their current insulin delivery regimen (MDI, CSII, or AID) for at least one year, with the aim of evaluating the association between the therapy type, clinical characteristics, and Health-Related QoL (HRQoL).

Methods

Study participants

A total of 262 European children and adolescents with T1D were recruited between May 2022 to July 2024 at Diabetes Units of IRCCS Burlo Garofolo (Trieste, Italy), Santa Chiara Hospital (Trento, Italy), IRCCS San Raffaele (Milano, Italy), A.O.U. Luigi Vanvitelli (Naples, Italy), A.O.U. Federico II (Naples, Italy), and A.O.U. Maggiore della Carità (Novara, Italy).

Only subjects with T1D for at least one year since diabetes diagnosis and aged 6–18 years were included in the study.

Participants were categorized into three groups based on the insulin regimen used maintained for at least one year: MDI ($n = 164$), CSII ($n = 28$), and AID ($n = 70$). All participants used CGM, regardless of the insulin therapy type.

Children and adolescents were defined according to pubertal maturation assessed by Tanner staging. Those who were prepubertal (Tanner stage I) were classified as children, whereas participants who had reached entered puberty (Tanner stage II–V) were classified as adolescents [20].

Data related to diabetes onset were also collected, including: age at diabetes onset, presence of ketoacidosis (DKA; defined as a venous pH < 7.3 and/or a bicarbonate < 18 mmol/L [21]).

Table 1 Characteristics of the type 1 diabetes children and adolescents

	T1D (n = 262)	MDI (n = 164)	CSII (n = 28)	AID (n = 70)	p-value
Age (years), median (IQR)	14.0 (4.17)	14.0 (4.03)	14.7 (3.31)	13.9 (4.80)	$p > 0.05$
Sex, % (n) Female	55% (145)	50% (82)	57% (18)	67% (47)	MDI vs. CSII = 0.62 MDI vs. AID = 0.023* CSII vs. AID = 0.48
Age at onset (years), median (IQR)	7.65 (5.16)	8.24 (5.39)	6.47 (4.45)	7.22 (4.95)	MDI vs. CSII = 0.011* MDI vs. AID = 0.025* CSII vs. AID = 0.20
DKA at onset[†], % (n) yes	33% (62)	33% (37)	18% (4)	38% (34)	$p > 0.05$
Disease Duration (years), median (IQR)	6.04 (6.39)	5.48 (5.80)	8.60 (4.28)	6.80 (5.87)	MDI vs. CSII = 0.002* MDI vs. AID = 0.055 CSII vs. AID = 0.048
IDAA1c ≤ 9, % (n) yes	11% (28)	5.5% (9)	11% (3)	23% (16)	MDI vs. CSII = 0.40 MDI vs. AID < 0.001* CSII vs. AID = 0.26
BMI-SDS, median (IQR)	0.16 (1.26)	0.23 (1.36)	0.03 (0.93)	0.26 (0.96)	$p > 0.05$
Celiac Disease, % (n) yes	10% (26)	5.5% (9)	18% (5)	17% (12)	MDI vs. CSII = 0.037* MDI vs. AID = 0.010* CSII vs. AID = 1
Thyroiditis, % (n) yes	13% (34)	10% (17)	4% (1)	23% (16)	MDI vs. CSII = 0.48 MDI vs. AID = 0.023* CSII vs. AID = 0.035*
Physical Activity, % (n) yes	63% (164)	57% (94)	68% (19)	73% (51)	MDI vs. CSII = 0.40 MDI vs. AID = 0.036* CSII vs. AID = 0.80
	T1D children (n = 47)	MDI children (n = 28)	CSII children (n = 3)	AID children (n = 16)	p-value
Age (years), median (IQR)	10.2 (2.28)	10.1 (2.01)	11.4 (0.98)	10.3 (2.76)	$p > 0.05$
Sex, % (n) Female	47% (22)	46% (16)	0%	56% (6)	$p > 0.05$
Age at onset (years), median (IQR)	5.68 (3.29)	6.25 (2.53)	6.08 (1.34)	4.89 (3.89)	$p > 0.05$
DKA at onset, % (n) yes	35% (10)	35% (4)	0%	43% (6)	$p > 0.05$
Disease Duration (years), median (IQR)	4.03 (3.34)	3.86 (2.64)	5.27 (2.32)	5.09 (4.15)	$p > 0.05$
IDAA1c ≤ 9, % (n) yes	15% (7)	3.5% (1)	0% (0)	37.5% (6)	MDI vs. CSII = 1 MDI vs. AID = 0.006* CSII vs. AID = 0.52
BMI-SDS, median (IQR)	0.00 (0.84)	-0.35 (0.91)	0.34 (0.56)	0.15 (0.74)	$p > 0.05$
Celiac Disease, % (n) yes	11% (5)	0%	33% (1)	25% (4)	$p > 0.05$
Thyroiditis, % (n) yes	4% (2)	0%	0%	12.5% (2)	$p > 0.05$
Physical Activity, % (n) yes	64% (30)	53.5% (15)	67% (2)	81% (13)	$p > 0.05$
	T1D adolescents (n = 215)	MDI adolescents (n = 136)	CSII adolescents (n = 25)	AID adolescents (n = 54)	p-value
Age (years), median (IQR)	14.9 (3.17)	14.8 (3.23)	15.3 (2.92)	15.1 (3.44)	$p > 0.05$
Sex, % (n) Female	57% (123)	51% (69)	64% (16)	70% (38)	MDI vs. CSII = 0.32 MDI vs. AID = 0.022* CSII vs. AID = 0.76

Table 1 (continued)

	T1D (n = 262)	MDI (n = 164)	CSII (n = 28)	AID (n = 70)	p-value
Age at onset (years), median (IQR)	7.96 (5.65)	9.07 (5.84)	6.49 (4.82)	7.59 (4.68)	MDI vs. CSII = 0.006* MDI vs. AID = 0.048 CSII vs. AID = 0.12 <i>p</i> > 0.05
DKA at onset, % (n) yes	32% (49)	33% (30)	21% (4)	37% (15)	
Disease Duration (years), median (IQR)	6.78 (6.29)	5.88 (6.33)	9.05 (4.30)	7.85 (5.34)	MDI vs. CSII = 0.006* MDI vs. AID = 0.034 CSII vs. AID = 0.15
IDAA1c ≤ 9, % (n) yes	10% (21)	6% (8)	12% (3)	18.5% (10)	MDI vs. CSII = 0.39 MDI vs. AID = 0.013* CSII vs. AID = 0.53
BMI-SDS, median(IQR)	0.21 (1.33)	0.27 (1.38)	0.02 (0.88)	0.18 (1.13)	<i>p</i> > 0.05
Celiac Disease, % (n) yes	10% (21)	7% (9)	16% (4)	15% (8)	<i>p</i> > 0.05
Thyroiditis, % (n) yes	15% (32)	13% (17)	4% (1)	26% (14)	MDI vs. CSII = 0.31 MDI vs. AID = 0.046* CSII vs. AID = 0.029*
Physical Activity, % (n) yes	62% (134)	58% (79)	68% (17)	70% (38)	<i>p</i> > 0.05

Data are shown as median and interquartile range (IQR) or %

T1D=Type 1 Diabetes; MDI=Multiple Daily Injection; CSII=Continuous Subcutaneous Insulin; AID=Automated Insulin Delivery; DKA=Diabetic ketoacidosis; IDAA1c=Lower Insulin-Dose Adjusted A1c; BMI-SDS=Body Mass Index Standard Deviation Scores

[†] data available for 188 T1D subjects

Differences among T1D subjects were computed by Kruskal-Wallis test followed by Dunn test for continuous variables, and χ^2 test or Fisher's exact test for categorical variables

* indicates significant p values. Statistical significance was set at a p-value ≤ 0.05 and p-value ≤ 0.025 for post-hoc Dunn test

At recruitment, demographic, anthropometric, personal, and clinical data were recorded, including: age, sex, height, weight, sports activity (yes/no), insulin requirements (U/kg/day), HbA1c at recruitment and over the past year, presence of other autoimmune diseases (e.g. celiac disease, autoimmune thyroiditis).

Body mass index standard deviation scores (BMI-SDS) were calculated using WHO reference charts [22] through the Growth Calculator 4 software (<http://www.wboriented.it/gh4/>).

HbA1c and insulin requirements at recruitment were used to calculate IDAA1c (Insulin-Dose Adjusted A1c) using the formula: HbA1c (%) + 4 x insulin dose (units/kg/day). Participants were then subdivided into two groups using IDAA1c ≤ 9 as cut-off to indicate partial remission [23].

Participants were also categorized according to their median HbA1c over the previous year, with ≥ 7% (≥ 53 mmol/mol) defined as inadequate control, in line with ISPAD (International Society for Pediatric and Adolescent Diabetes) guidelines [24].

Systolic and diastolic blood pressure percentiles (SBPP and DBPP) were calculated with sex- and age-specific clinical calculators (www.msdmanuals.com) [25].

Laboratory data from the most recent screening included fasting lipid profile (total cholesterol [TC]; LDL

cholesterol [LDL-C]; HDL cholesterol [HDL-C]; triglycerides [TG]) and serum creatinine. Estimated glomerular filtration rate (eGFR) was calculated with the Schwartz's equation: 0.413 x height (cm)/serum creatinine mg/dL [26].

Written informed consent was obtained from all participants, or their parents/guardians for minors. The study was approved by the ethics committee (CEUR-2018-Em-323-Burlo).

Pediatric quality of life inventory (PedsQL) 3.2 diabetes module

HRQoL was assessed using the PedsQL 3.2 Diabetes Module, a validated diabetes-specific with 33 items across 5 domains: Diabetes symptoms (15 items); Treatment I (or treatment barriers, intended as obstacles or problems during treatment; 5 items); Treatment II (or treatment adherence, 6 items); Worry (3 items); Communication (4 items). Additionally, two composite scales were also calculated: Management (sum of Treatment I, Treatment II, Worry and Communication) and Total (all items) [27].

Items were scored over the past month on a 5-point Likert scale (0 = never a problem; 1 = seldom a problem; 2 = sometimes a problem; 3 = often a problem; 4 = almost always a problem). Scores were reverse transformed to a

0–100 scale (0 = 100, 1 = 75, 2 = 50, 3 = 25, 4 = 0), with higher scores reflecting better HRQoL. Summary scores were obtained as the mean of all answered items [27].

Statistical analysis

Demographic, anthropometric, and clinical data were summarized in contingency table. Continuous variables were tested for normality using the Kolmogorov-Smirnov test. Non-normally distributed data were expressed as median and interquartile range (IQR), whereas categorical variables were reported as frequencies and percentages (%).

Between-group comparisons of continuous variables were performed using the non-parametric Kruskal-Wallis test, followed by Dunn's post-hoc test for pairwise comparisons between independent groups. The χ^2 test or Fisher's exact test, as appropriate, was used for categorical variables.

The association of therapy type with clinical outcomes, in the overall T1D cohort and separately in children and adolescents, was investigated using analysis of variance (ANOVA) adjusted for age, sex, disease duration, and study center and IDA1c ≤ 9 as covariates. When examining the association between therapy type and eGFR, HbA1c levels were also included as a covariate. Pairwise differences were assessed using Tukey honestly significant difference (HSD) post-hoc test.

The association between therapy type and HRQoL was analyzed using ANOVA followed by the Tukey HSD post-hoc test. Analyses were performed both in the overall T1D cohort and stratified by age group (children and adolescents), using sex, age, disease duration, and study center included as covariates. Additional analyses were conducted separately for adolescents females and males, adjusting for age, disease duration, and study center.

Differences in HRQoL scores between female and male were evaluated using the independent samples t-test.

Multivariate regression analyses adjusted for age, sex, disease duration, and study center were performed to explore associations between clinical outcomes and HRQoL.

Statistical significance was set at a p -value ≤ 0.05 and for Dunn's test at a p -value ≤ 0.025 . All analyses were conducted using R software (v 4.3.2; R Foundation for Statistical Computing, Vienna, Austria; www.r-project.org).

Results

T1D individuals' characteristics

Participants' characteristics, stratified by therapy type and pubertal status, are summarized in Table 1.

The study included 262 individuals with T1D (median age 14.0 years), of whom 145 (55%) were female.

At enrolment, 18% were children and 82% were adolescents. For at least 1 year prior to enrolment, 62% had

been treated with MDI, 11% with CSII, and 27% with AID therapy.

Sex distribution differed across treatment groups: females were more frequently on AID compared with MDI (67% vs. 50%).

Additionally, MDI users were older at diagnosis than CSII and AID. They also had a shorter disease duration, approximately 1.4 years less than those on AID and nearly 3 years less than CSII.

Moreover, the prevalence of celiac disease was higher in CSII and AID compared with MDI users (18% and 17% vs. 5.5%, p -value = 0.037 and p -value = 0.010, respectively). Similarly, thyroiditis was more frequent in AID users compared with both MDI (23% vs. 10%, p -value = 0.023) and CSII (23% vs. 4%, p -value = 0.035). In addition, AID users were more physically active than MDI users (73% vs. 57%, p -value = 0.036).

Among children, 60% used MDI, 6% CSII, and 34% AID; while, among adolescents, about 63% used MDI, 12% CSII, and 25% AID, with no significant differences.

Insulin therapies and clinical outcomes

Results of the association analysis between therapy type and clinical outcomes are shown in Table 2 (ANOVA test) and Supplementary Table 1 (pairwise differences assessed by Tukey HSD post-hoc test).

HbA1c differed significantly across therapy type groups (p -value < 0.001, F -value = 12.7): MDI users had the highest mean HbA1c over the prior year (7.7%, 61 mmol/mol) compared with CSII (7.2%, 55 mmol/mol, p -value = 0.007) and AID (7.0%, 53 mmol/mol, p -value < 0.001). Similarly, the proportion of individuals with HbA1c $\geq 7\%$ also varied by therapy type (p -value < 0.001, F -value = 15.3): 75% in MDI users, 50% in CSII users, and 43% in AID (MDI vs. CSII, p -value = 0.011; MDI vs. AID, p -value < 0.001). Insulin requirements were associated with therapy type (p -value < 0.001, F -value = 8.22): insulin requirements were highest in MDI (0.89 U/kg/day) compared with CSII (0.74 U/kg/day, p -value = 0.004) and AID users (0.78 U/kg/day, p -value = 0.002). eGFR also differed by therapy type (p -value < 0.001, F -value = 18.0): MDI users had lower eGFR (102.8 mL/min/1.73m²) than CSII (113.8 mL/min/1.73m²) and AID users (120.9 mL/min/1.73m²), with significance only for MDI vs. AID (p -value = 0.004).

In children, only eGFR was associated with therapy type (p -value < 0.001, F -value = 15.8), and eGFR was < 100 mL/min/1.73m² in MDI users compared with values > 130 mL/min/1.73m² in CSII (p -value = 0.024) and AID (p -value = 0.010).

In adolescents, all outcomes were associated with therapy type, with CSII and particularly AID, showing more favorable profiles than MDI. Mean HbA1c of 7.7% (61 mmol/mol) in MDI compared with 7.2% (55 mmol/mol) in CSII (p -value = 0.010), and 7.0% (53

Table 2 Association between insulin therapy and clinical outcomes

Explanatory variables	HbA1c (%)	HbA1c ≥ 7%	Insulin requirements (U/kg/day)	eGFR (mL/min/1.73m ²)
T1D all				
Therapy type	<0.001 (12.7)	<0.001 (15.3)	<0.001 (8.22)	<0.001 (18.0)
Age (years)	0.56 (0.34)	0.91 (0.01)	0.006 (7.64)	<0.001 (14.4)
Sex	0.31 (1.06)	0.92 (0.01)	0.96 (0.01)	0.38 (0.78)
Disease duration (years)	<0.001 (14.7)	0.015 (6.01)	<0.001 (19.1)	0.035 (4.52)
Center	0.012 (6.31)	0.028 (4.90)	0.06 (3.72)	<0.001 (13.4)
IDAA1c ≤ 9	<0.001 (29.3)	<0.001 (45.4)	<0.001 (47.3)	0.26 (1.26)
HbA1c (%)	-	-	-	0.90 (0.02)
T1D children				
Therapy type	0.20 (1.65)	0.18 (1.80)	0.11 (2.39)	<0.001 (15.8)
Age (years)	0.11 (2.71)	0.06 (3.74)	0.19 (1.81)	0.52 (0.43)
Sex	0.77 (0.09)	0.23 (1.51)	0.79 (0.07)	0.43 (0.63)
Disease duration (years)	0.26 (1.29)	0.36 (0.84)	0.26 (1.32)	0.78 (0.08)
Center	0.07 (3.37)	0.77 (0.09)	0.72 (0.13)	0.051 (4.38)
IDAA1c ≤ 9	0.009 (7.62)	0.002 (11.0)	0.038 (4.64)	0.37 (0.82)
HbA1c (%)	-	-	-	0.87 (0.03)
T1D adolescents				
Therapy type	<0.001 (10.9)	<0.001 (13.8)	0.003 (5.85)	<0.001 (8.60)
Age (years)	0.48 (0.50)	0.35 (0.90)	0.002 (10.0)	<0.001 (20.6)
Sex	0.24 (1.38)	0.54 (0.37)	0.72 (0.13)	0.40 (0.70)
Disease duration (years)	<0.001 (12.6)	0.030 (4.78)	<0.001 (20.5)	0.07 (3.38)
Center	0.051 (3.86)	0.024 (5.18)	0.008 (7.10)	0.003 (9.06)

Table 2 (continued)

Explanatory variables	HbA1c (%)	HbA1c ≥ 7%	Insulin requirements (U/kg/day)	eGFR (mL/min/1.73m ²)
IDAA1c ≤ 9	<0.001 (21.4)	<0.001 (32.4)	<0.001 (43.7)	0.31 (1.02)
HbA1c (%)	-	-	-	0.67 (0.18)

T1D=Type 1 Diabetes; IDAA1c=Lower Insulin-Dose Adjusted A1c; eGFR=Estimated Glomerular Filtration Rate

The association between therapy types and clinical outcomes (HbA1c %, HbA1c ≤ 7%, insulin requirement) was assessed by ANOVA test adjusted for the covariates age, sex, disease duration, and study center and IDAA1c ≤ 9. For the association between eGFR and therapy, HbA1c % was also added as a covariate. For the non-quantitative sex variable, the reference category is female.

Results are presented as p-value and F-value (in brackets). Significant results were indicated in bold (p-values ≤ 0.05).

mmol/mol) in AID (p-value < 0.001). Inadequate glycemic control (HbA1c ≥ 7%) occurred in 75% of MDI compared with 48% of CSII (p-value = 0.009) and 41% of AID (p-value < 0.001). Insulin requirement was higher in MDI (0.88 U/kg/day) than in CSII (0.76 U/kg/day, p-value = 0.008) and AID (0.79 U/kg/day, p-value = 0.008). eGFR was lower in MDI (103.7 mL/min/1.73m²) than in CSII (110.6 mL/min/1.73m²) and AID (117.5 mL/min/1.73m²), with significance only for MDI vs. AID (p-value = 0.027).

Insulin therapies and health-related quality of life

The association between therapy type and HRQoL was also evaluated. Across the seven scores of the PedsQL 3.2 Diabetes Module, no significant differences were observed among MDI, CSII, and AID users (Table 3). In adolescents, however, therapy type was associated with the total HRQoL score (p-value = 0.046, F-value = 3.11), with CSII scoring modestly higher than MDI (77.0 vs. 70.7, p-value = 0.049), as detailed in Supplementary Table 2, where QoL scores by therapy are fully reported, and higher scores indicate better HRQoL. No significant associations were found in children.

In adolescents, a strong association of HRQoL with sex emerged and stratified analyses by sex showed that, while among males HRQoL did not differ by therapy type, in females therapy type was associated with Worry (p-value = 0.031, F-value = 3.58), Diabetes Management (p-value = 0.050, F-value = 2.96), and Total HRQoL scores (p-value = 0.034, F-value = 3.48) (Supplementary Table 3). Specifically, female AID had higher Worry scores than female MDI users (61.0 vs. 47.5, p-value = 0.036), and female CSII users had higher Diabetes Management and Total HRQoL scores than female MDI users (80.6 vs. 70.4, p-value = 0.050 and 75.5 vs. 66.5, p-value = 0.031, respectively) (Supplementary Table 4). Also, females reported lower HRQoL than males across most scales (p-value < 0.01) (Supplementary Table 4).

Table 3 Associations between insulin therapy and health-related quality of life

PedsQL 3.2 Diabetes Module							
Explanatory variables	Diabetes Symptoms	Treatment Barriers	Treatment Adherence	Worry	Communication	Management	Total
T1D							
Therapy type	0.43 (0.84)	0.23 (2.10)	0.37 (0.39)	0.12 (2.14)	0.63 (0.27)	0.15 (1.89)	0.17 (1.77)
Age, (years)	0.47 (0.52)	0.63 (0.24)	0.68 (0.17)	0.051 (3.84)	0.51 (0.44)	0.53 (0.40)	0.46 (0.54)
Sex	0.008 (7.04)	0.27 (1.23)	0.36 (0.83)	0.013 (6.31)	<0.001 (13.0)	0.010 (6.82)	0.002 (9.55)
Disease duration, (years)	0.61 (0.26)	0.58 (0.31)	0.11 (2.63)	0.78 (0.08)	0.45 (0.57)	0.83 (0.04)	0.70 (0.15)
Center	0.23 (1.48)	0.57 (0.33)	0.58 (0.31)	0.64 (0.22)	0.29 (1.11)	0.54 (0.38)	0.31 (1.04)
T1D children							
Therapy type	0.55 (0.61)	0.92 (0.09)	0.74 (0.30)	0.77 (0.27)	0.70 (0.36)	0.33 (0.72)	0.86 (0.15)
Age, (years)	0.06 (3.59)	0.19 (1.77)	0.12 (2.41)	0.13 (2.46)	0.50 (0.46)	0.07 (3.35)	0.030 (5.05)
Sex	0.31 (1.06)	0.69 (0.15)	0.14 (2.22)	0.51 (0.44)	0.90 (0.02)	0.35 (0.90)	0.23 (1.46)
Disease duration (years)	0.040 (4.50)	0.17 (1.94)	0.63 (0.23)	0.289(1.15)	0.13 (2.39)	0.16 (2.03)	0.039 (4.57)
Center	0.40 (0.72)	0.97 (0.01)	0.55 (0.37)	0.13 (2.46)	0.38 (0.79)	0.39 (0.75)	0.24 (1.42)
T1D adolescents							
Therapy type	0.15 (1.92)	0.14 (2.19)	0.17 (1.76)	0.08 (2.62)	0.38 (0.97)	0.07 (2.65)	0.046 (3.11)
Age, (years)	0.63 (0.23)	0.50 (0.46)	0.85 (0.03)	0.49 (0.48)	0.08 (3.01)	0.40 (0.70)	0.75 (0.10)
Sex	0.001 (11.1)	0.20 (1.62)	0.08 (3.12)	0.003 (9.40)	<0.001 (14.3)	0.001 (10.4)	<0.001 (14.5)
Disease duration (years)	0.39 (0.73)	0.88 (0.02)	0.07 (3.33)	0.55 (0.36)	0.72 (0.12)	0.52 (0.41)	0.40 (0.71)
Center	0.12 (2.40)	0.52 (0.43)	0.37 (0.79)	0.86 (0.03)	0.12 (2.42)	0.29 (1.12)	0.13 (2.29)

T1D=Type 1 Diabetes

The association between therapy types and health-related quality of life was assessed by ANOVA test adjusted for the covariates age, sex, disease duration, and study center

For the non-quantitative sex variable, the reference category is female

Results are presented as p-value and F-value (in brackets). Significant results were indicated in bold (p-values ≤ 0.05). Corresponding QoL scores (mean $\pm$ SD) by insulin therapy are reported in Supplementary Table 2

From the analysis of the individual items, it was observed that in some cases adolescents present poor QoL than children, regardless of the therapy type (Supplementary Table 5). Especially in the items relating to the symptoms linked to diabetes, such as headache (67.8 vs. 77.1, p-value=0.023), nausea (83.8 vs. 92.0, p-value=0.009) and dizziness (73.5 vs. 84.0, p-value=0.005). But the greatest differences were found among adolescents stratified by sex, in which females had lower values in several items, both in the Diabetes Symptoms (stomach-ache, headache, nausea, tiredness, weakness, irritability), Treatment Adherence (difficulty playing sports and carrying fast-acting carbohydrates), Worry (worry about having hypoglycemia and long-term diabetes complications) and Communication scores (having difficulty asking doctors and nurses questions and explaining the disease to other people, and being embarrassed about having diabetes) (Supplementary Table 5).

Clinical outcome and health-related quality of life

Associations between clinical parameters and HRQoL are reported in Table 4. In overall cohort, HbA1c was

inversely associated with total HRQoL (p-value = 0.050, β = -1.42, 95% C.I.: -2.86 to -0.01); insulin requirements with Treatment Barriers (p-value=0.024, β = -9.10, 95% C.I.: -16.9 to -1.24) and Worry scores (p-value=0.029, β = -13.6, 95% C.I.: -25.8 to -1.44).

While in children no significant associations were observed, in adolescents HbA1c was inversely associated with Diabetes Symptoms (p-value=0.037, β -1.82, 95% C.I.: -3.53 to -0.11) and total HRQoL score (p-value=0.046, β -1.60, 95% C.I.: -3.18 to -0.03). Additionally, insulin requirements were inversely associated with Treatment Barriers (p-value=0.046, β -10.2, 95% C.I.: -20.1 to -0.20), and Worry scores (p-value=0.019, β -18.0, 95% C.I.: -32.9 to -3.04) (Table 4).

Discussion

This study compared clinical characteristics and HRQoL in children and adolescents with T1D across three therapy types (MDI, CSII, and AID). The distribution of therapies in our cohort (62% MDI, 11% CSII, and 27% AID) is consistent with that reported in prior Italian studies [28,

Table 4 Association between clinical outcomes and health-related quality of life

PedsQL 3.2 Diabetes Module							
Clinical outcomes	Diabetes Symptoms	Treatment Barriers	Treatment Adherence	Worry	Communication	Management	Total
T1D							
HbA1c (%)	0.10 (-1.30)	0.60 (-0.54)	0.15 (-1.37)	0.14 (-2.32)	0.09 (-2.39)	0.09 (-1.54)	0.050 (-1.42)
HbA1c ≥ 7%	0.32 (-1.63)	0.95 (0.15)	0.42 (-1.60)	0.08 (-5.89)	0.72 (-1.06)	0.36 (-1.79)	0.28 (-1.66)
Insulin Requirements (U/kg/day)	0.64 (-1.46)	0.024 (-9.10)	0.38 (-3.31)	0.029 (-13.6)	0.50 (-3.76)	0.06 (-6.80)	0.13 (-4.36)
eGFR (mL/min/1.73 m ²)	0.82 (-0.01)	0.09 (-0.09)	0.58 (-0.03)	0.69 (-0.03)	0.17 (-0.11)	0.28 (-0.05)	0.36 (-0.04)
T1D children							
HbA1c (%)	0.18 (2.06)	0.43 (-2.04)	0.91 (0.31)	0.09 (-7.65)	0.21 (-4.41)	0.22 (-2.89)	0.74 (-0.53)
HbA1c ≥ 7%	0.26 (3.26)	0.75 (1.54)	0.23 (5.77)	0.44 (-6.47)	0.36 (6.02)	0.66 (1.94)	0.33 (2.83)
Insulin requirements (U/kg/day)	0.17 (-5.25)	0.20 (-8.06)	0.82 (-1.46)	0.29 (-11.4)	0.26 (-9.45)	0.24 (-6.79)	0.11 (-6.06)
eGFR (mL/min/1.73 m ²)	0.10 (-0.13)	0.98 (-0.01)	0.57 (0.06)	0.99 (0.01)	0.63 (-0.09)	0.79 (0.03)	0.41 (-0.06)
T1D adolescents							
HbA1c (%)	0.037 (-1.82)	0.74 (-0.39)	0.09 (-1.68)	0.32 (-1.68)	0.16 (-2.15)	0.15 (-1.42)	0.046 (-1.60)
HbA1c ≥ 7%	0.15 (-2.73)	0.88 (-0.38)	0.14 (-3.27)	0.08 (-6.37)	0.41 (-2.74)	0.19 (-2.85)	0.11 (-2.77)
Insulin requirements (U/kg/day)	0.69 (-1.59)	0.046 (-10.2)	0.24 (-5.51)	0.019 (-18.0)	0.73 (-2.40)	0.07 (-8.14)	0.16 (-5.18)
eGFR (mL/min/1.73 m ²)	0.59 (0.03)	0.13 (-0.10)	0.66 (-0.03)	0.93 (0.01)	0.43 (-0.07)	0.47 (-0.04)	0.82 (-0.01)

T1D = Type 1 Diabetes; eGFR = Estimated Glomerular Filtration Rate

The association was assessed by multivariate regression analysis. For all analyses, age, sex, disease duration and study center were used as covariates

Results are presented as p-value and beta (in brackets). Significant results were indicated in bold (p-values ≤ 0.05)

29], although a slightly higher proportion of MDI users was observed.

These findings reflect the still limited real-world adoption of pump-based therapy [14], despite current guideline recommendations favoring the use of insulin pumps, particularly AID systems, for pediatric subjects with T1D.

Insulin therapies and clinical outcomes

Our findings confirm that MDI users exhibited less favorable clinical parameters than those using CSII and AID, consistent with prior evidence supporting the benefits of advanced insulin technologies on HbA1c and insulin requirements [13, 29–31]. A key novelty of this work is the observed association between therapy type and markers linked to long-term T1D complications. Notably, to our knowledge, this is the first study to examine differences in eGFR by therapy type as an indicator of early renal dysfunction. Individuals on MDI, both children and adolescents, had lower eGFR than those on CSII or AID. This observation may indicate a potential association with early renal changes, highlighting the importance of

longitudinal monitoring [32]. Of note, 22% of MDI users had eGFR < 90 mL/min/1.73m², the threshold for early-stage renal dysfunction [33], compared with 12% of CSII and 14% of AID users.

A peculiarity of the study is the finding that, at the age-stratified analysis, the association between therapy type and clinical outcomes were more evident in adolescents than in children. Since all models were adjusted for disease duration, the differences observed between children and adolescents cannot be attributed to a longer diabetes duration. Rather, they likely reflect age-related physiological and behavioral factors, such as pubertal insulin resistance, self-management skills, and differences in therapeutic approach. The lack of significant associations in the children subgroup should be interpreted with caution, as the smaller sample size ($n = 47$) markedly reduced statistical power. The direction of the associations, however, was consistent with that observed in adolescents, suggesting that similar effects might exist but could not be detected due to limited sample size.

Interestingly, in our analysis, eGFR showed the strongest association with therapy type among adolescents,

whereas this relationship was less pronounced in children. This finding agrees with recent data from the Taiwan Diabetes Registry, showing that individuals with T1D onset during puberty or early adulthood had a significantly higher risk of diabetic nephropathy than those with prepubertal onset, independently of diabetes duration and HbA1c [34]. Thus, the lower eGFR observed in adolescents treated with MDI may be indicative of a potential association with early renal vulnerability in the context of pubertal physiology rather than longer disease duration or poorer glycemic control, highlighting the need for possible close renal monitoring during this critical developmental stage. However, it should be acknowledged that during adolescence eGFR values may be influenced by physiological variability, including pubertal hemodynamic changes and hyperfiltration dynamics, suggesting that renal function variability likely reflects the combined effects of pubertal hormonal changes, insulin resistance, and metabolic demands.

In the present cohort, no significant differences emerged between CSII and AID users for the clinical parameters assessed. This contrasts with prior studies reporting HbA1c improvement, absence of DKA events, and reduced severe hypoglycemia in AID users compared to CSII [12], as well as benefits for AID compared with a combined MDI/CSII reference group [13]. Direct comparison is challenging because those studies primarily evaluated short-term outcomes within the first six months after AID initiation, whereas our analyses included participants on a stable therapy type for at least one year. Moreover, glycemic control with CSII tends to improve over time, as shown in retrospective and prospective studies [35, 36], which may attenuate differences relative to AID in longer-term comparisons.

Finally, our sample size, particularly within subgroups, may have limited statistical power to detect small between-group differences, especially between CSII and AID. Future studies with larger and more balanced samples, standardized follow-up windows, and harmonized outcome definitions are needed to clarify these relationships.

Insulin therapies and health-related quality of life

The study also assessed HRQoL using the PedsQL 3.2 Diabetes Module, founding no significant overall differences among therapy groups. These finding contrasts with previous reports showing HRQoL improvements after six months of AID in youth [30] and better HRQoL with CSII in adults in a randomized controlled trial (RCT) [37]. A possible explanation lies in the longer therapy exposure in our cohort compared with those studies. It has been suggested that the initial “novelty effect” of new technologies may wane over time, leading to a plateau in perceived benefit beyond the first months of use

[10]. Methodological differences may also contribute: RCTs typically include highly selected participants and ensure structured follow-up under controlled conditions, thus increasing the likelihood of detecting short-term improvements. In contrast, real-world studies such as ours reflect routine clinical practice, where adherence variability, clinical heterogeneity, and longer exposure may dilute between-group differences in HRQoL.

This study also underscores the importance of considering sex in assessing QoL, particularly during adolescence, a period of heightened vulnerability. The developmental and psychosocial challenges that accompany this stage in youth with T1D, including greater autonomy in disease management, increased self-awareness, and social pressures, may negatively impact perceived QoL, potentially offsetting the gains of advanced therapies, especially in females [19]. In our cohort, females reported lower HRQoL scores than males, particularly in domains related to worries about diabetes complications and communication, for instance, explaining their condition to others or feeling embarrassed about it. These findings are consistent with previous studies reporting poorer HRQoL in females, likely reflecting a greater emotional burden and social stressors associated with diabetes self-management [38, 39]. Altogether, these observations highlight the need for psychosocial support tailored to gender and development stage, alongside therapeutic decisions.

Clinical outcome and health-related quality of life

Since optimal diabetes management influences both clinical outcomes and HRQoL, we examined their relationship. In the overall cohort, HbA1c was inversely associated with total HRQoL score, indicating that lower HbA1c corresponded to better HRQoL. However, the magnitude of these associations was relatively modest, suggesting that while glycemic control contributes to HRQoL, it represents only one of several factors influencing QoL perceived by patients. This aligns with large-scale evidence, most notably the Global TEENs Study of nearly 6,000 youth with T1D, showing a linear association between HbA1c and HRQoL, with lower HbA1c linked with higher HRQoL scores [40].

In our analyses, associations between clinical outcomes (HbA1c and insulin requirement) and HRQoL emerged only in adolescents. In particular, the associations involving insulin requirements and specific HRQoL domains, such as Treatment Barriers and Worry, showed a greater magnitude, suggesting that treatment burden may have a more direct impact on daily experience of diabetes.

This pattern reinforces the view that adolescence is a critical period of psychosocial vulnerability in T1D: increased responsibility for self-management, broader social comparisons, body-image concerns, peer

influence, and emotional/psychological stress can all erode perceived QoL and, in turn, compromise diabetes management and control, further worsening QoL [19, 41].

Furthermore, our findings support prior evidence that HRQoL scores may help predict future metabolic control in adolescents with T1D [40], underscoring the importance of personalized, age- and sex-sensitive psychosocial and educational interventions to support both glycemic and psychological outcomes during this developmental stage.

In contrast, no significant associations were observed in children. This finding may reflect developmental differences in disease perception and self-management involvement, as younger patients typically rely on parental supervision and have limited awareness of diabetes-related risks. Moreover, the PedsQL™ 3.2 Diabetes Module includes age-specific versions with simplified items and response scales for younger children, which may reduce the sensitivity to variations in metabolic control [42]. Similar age-related patterns have been described in previous research, showing that associations between HbA1c and HRQoL tend to emerge predominantly in adolescents and young adults, whereas HRQoL in younger children is more closely related to parental support and family functioning rather than to clinical parameters [43, 44].

Limitations and strengths

The study has some limitations that should be considered when interpreting results. First, baseline clinical and QoL data prior to initiation of CSII and AID were not available, limiting inference about within-person changes attributable to therapy type. Furthermore, no additional information that could have influenced the decision to initiate CSII and AID therapy, such as baseline metabolic control, socioeconomic status, or adherence patterns, was available. Second, hypoglycemic events and DKA during follow-up were not collected, precluding comparisons on acute safety outcomes and their impact on QoL. Third, although the PedsQL 3.2 Diabetes Module is a validated measure of diabetes-related HRQoL, it primarily captures the impact of diabetes management on daily life and does not assess satisfaction or the device-specific burdens/benefits of different insulin delivery methods.

Finally, the relatively small sample size of the CSII group and the pediatric subgroup may have limited statistical power, increasing the risk of type II error. Therefore, non-significant findings, particularly in subgroup analyses, should be interpreted cautiously, as they may reflect underpowering rather than true absence of associations.

Despite these limitations, the study has notable strengths. Unlike most prior reports that focus on the first six months after technology initiation, we assessed

clinical and HRQoL outcomes after one year of stable therapy, an interval that may better reflect sustained, real-world effects. In addition, this is among the few pediatric studies to examine key clinical parameters linked to long-term complications (e.g., eGFR) in relation to therapy type. Finally, the study highlights age-related differences in HRQoL, reinforcing the need for a personalized approach to diabetes care; recognizing that adolescents with T1D experience a greater psychosocial burden can inform tailored support strategies aimed at improving both metabolic and psychological outcomes.

Conclusion

This study suggests that modern insulin technologies (CSII and AID) are associated with more favorable clinical outcomes, while exerting limited impact on HRQoL after at least 1 year of treatment. Notably, to our knowledge, this is the first pediatric real-world study to identify associations between therapy type and early predictors of complications, such as renal markers. These findings should be considered exploratory and generating hypothesis, suggesting a potential role of AID systems that warrants future investigation in longitudinal studies, in line with ISPAD guidelines [14].

The findings also highlight female adolescence as a period of heightened psychosocial vulnerability, during which the potential benefits of new technologies may be attenuated by developmental and emotional challenges. Targeted, sex- and age-sensitive interventions tailored to girls with T1D are therefore essential to optimize both clinical and QoL outcomes in this high-risk group.

Abbreviations

AID	Automated insulin delivery
BMI-SDS	Body mass index standard deviation scores
CGM	Continuous glucose monitoring
CSII	Continuous subcutaneous insulin infusion
DBPP	Diastolic blood pressure percentile
DKA	Ketoacidosis
eGFR	Estimated glomerular filtration rate
HbA1c	Hemoglobin A1c
HDL	High-density lipoprotein cholesterol
HRQoL	Health-related quality of life
IDAA1c	Insulin-dose adjusted A1c
IQR	Interquartile range
ISPAD	International society for pediatric and adolescent diabetes
LDL-C	Low-density lipoprotein-cholesterol
MDI	Multiple daily injections
PedsQL	Pediatric quality of life inventory
QoL	Quality of life
RCTs	Randomized controlled trials
SBPP	Systolic blood pressure percentile
TC	Total cholesterol
TG	Triglycerides
T1D	Type 1 diabetes
TIR	Time in range

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s13098-026-02180-6>.

Supplementary material 1.

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Author contributions

G.To., A.R., E.C.: conception, design and data analysis; R.F., L.A., F.D.C., G.Ta., C.M., A.C., I.R.: data acquisition; G.To., A.R., R.F., E.M., R.B., I.R., D.I., E.C.: data interpretation. All authors critically reviewed drafts of the manuscript and approved it for submission.

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Data availability

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Comitato Unico Regionale Friuli Venezia Giulia (CEUR-2018-Em-323-Burlo). Written informed consent was obtained from all participants and, in the case of minors, from their parents.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Author details

¹Institute for Maternal and Child Health – IRCCS Burlo Garofolo, via dell'Istria 65/1, Trieste 34137, Italy

²Department of Medicine, Surgery and Health Sciences, University of Trieste, Trieste, Italy

³Division of Pediatrics, S. Chiara General Hospital, APSS, Trento, Italy

⁴Department of Translational Medical Science, Section of Pediatrics, Università degli Studi di Napoli Federico II, Naples, Italy

⁵Diabetes Research Institute, Department of Pediatrics, IRCCS San Raffaele Hospital, Milano, Italy

⁶Department of Woman, Child and of General and Specialized Surgery, University of Campania “Luigi Vanvitelli”, Naples, Italy

⁷Division of Pediatrics, Department of Health Sciences, University of Eastern Piedmont, Novara, Italy

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References

- Rodrigues Oliveira SM, Rebocho A, Ahmadpour E, et al. Type 1 Diabetes Mellitus: a review on advances and challenges in creating insulin producing devices. *Micromachines* (Basel). 2023;14(1):151. <https://doi.org/10.3390/mi14010151>.
- Diabetes Control and Complications Trial Research Group, Nathan DM, Genuth S, et al. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *N Engl J Med*. 1993;329(14):977–86. <https://doi.org/10.1056/NEJM199309303291401>.
- Nathan DM, DCCCT/EDIC Research Group. The diabetes control and complications trial/epidemiology of diabetes interventions and complications study at 30 years: overview. *Diabetes Care*. 2014;37(1):9–16. <https://doi.org/10.2337/dc13-2112>.
- Diabetes Control and Complications Trial (DCCT)/Epidemiology of Diabetes Interventions and Complications (EDIC) Study Research Group. Intensive diabetes treatment and cardiovascular outcomes in type 1 diabetes: the DCCT/EDIC study 30-year follow-up. *Diabetes Care*. 2016;39(5):686–93. <https://doi.org/10.2337/dc15-1990>.
- McKnight JA, Wild SH, Lamb MJ, et al. Glycaemic control of type 1 diabetes in clinical practice early in the 21st century: an international comparison. *Diabet Med*. 2015;32(8):1036–50. <https://doi.org/10.1111/dme.12676>.
- Burckhardt M-A, Smith GJ, Cooper MN, et al. Real-world outcomes of insulin pump compared to injection therapy in a population-based sample of children with type 1 diabetes. *Pediatr Diabetes*. 2018;19(8):1459–66. <https://doi.org/10.1111/pedi.12754>.
- Sharifi A, De Bock MI, Jayawardene D, et al. Glycemia, treatment satisfaction, cognition, and sleep quality in adults and adolescents with type 1 diabetes when using a closed-loop system overnight versus sensor-augmented pump with low-glucose suspend function: a randomized crossover study. *Diabetes Technol Ther*. 2016;18:772–83. <https://doi.org/10.1089/dia.2016.0288>.
- Tauschmann M, Thabit H, Bally L, et al. Closed-loop insulin delivery in suboptimally controlled type 1 diabetes: a multicentre, 12-week randomised trial. *Lancet*. 2018;392:1321–9. [https://doi.org/10.1016/S0140-6736\(18\)31947-0](https://doi.org/10.1016/S0140-6736(18)31947-0).
- Almurashi AM, Rodriguez E, Garg SK. Emerging diabetes technologies: continuous glucose monitors/artificial pancreases. *J Indian Inst Sci*. 2023;28:1–26. <https://doi.org/10.1007/s41745-022-00348-3>.
- Hu S, Yang H, Chen Z, et al. Clinical outcome and cost-effectiveness analysis of CSII versus MDI in children and adolescent with type 1 diabetes mellitus in a public health care system of China. *Front Endocrinol (Lausanne)*. 2021;12:604028. <https://doi.org/10.3389/fendo.2021.604028>.
- Qin Y, Yang L-H, Huang X-L, et al. Efficacy and safety of continuous subcutaneous insulin infusion vs. multiple daily injections on type 1 diabetes children: a meta-analysis of randomized control trials. *J Clin Res Pediatr Endocrinol*. 2018;10(4):316–23. <https://doi.org/10.4274/jcrpe.0053>.
- Garg SK, Grunberger G, Weinstock R, et al. Improved glycemia with hybrid closed-loop versus continuous subcutaneous insulin infusion therapy: results from a randomized controlled trial. *Diabetes Technol Ther*. 2023;25(1):1–12. <https://doi.org/10.1089/dia.2022.0421>.
- McAuley SA, Lee MH, Paldus B, et al. Six months of hybrid closed-loop versus manual insulin delivery with fingerprick blood glucose monitoring in adults with type 1 diabetes: a randomized, controlled trial. *Diabetes Care*. 2020;43(12):302433. <https://doi.org/10.2337/dc20-1447>.
- Biester T, Berget C, Boughton C, et al. International Society for Pediatric and Adolescent Diabetes clinical practice consensus guidelines 2024: Diabetes technologies – insulin delivery. *Horm Res Paediatr*. 2024;97(6):636–62. <https://doi.org/10.1159/000543034>.
- Al Shaikh A, Al Zahrani AM, Qari YH, et al. Quality of life in children with diabetes treated with insulin pump compared with multiple daily injections in tertiary care center. *Clin Med Insights Endocrinol Diabetes*. 2020;28(13):1179551420959077. <https://doi.org/10.1177/1179551420959077>.
- Crabtree TSJ, Griffin TP, Yap YW, et al. Hybrid closed-loop therapy in adults with type 1 diabetes and above-target HbA1c: a real-world observational study. *Diabetes Care*. 2023;46(10):1831–8. <https://doi.org/10.2337/dc23-0635>.
- Farrington C. Psychosocial impacts of hybrid close-loop systems in the management of diabetes: a review. *Diabet Med*. 2018;35(4):436–49. <https://doi.org/10.1111/dme.13567>.
- Eldib A, Dhaver S, Kibaa K, et al. Evaluation of hybrid closed-loop insulin delivery system in type 1 diabetes in real-world clinical practice: one-year observational study. *World J Diabetes*. 2024;15(3):455–62. <https://doi.org/10.4239/wjdv15i3.455>.
- Bombaci B, Torre A, Longo A, et al. Psychological and clinical challenges in the management of type 1 diabetes during adolescence: a narrative review. *Child (Basel)*. 2024;11(9):1085. <https://doi.org/10.3390/children11091085>.
- Tanner JM, Whitehouse RH. Clinical longitudinal standards for height, weight, height velocity, weight velocity, and stages of puberty. *Arch Dis Child*. 1976;51(3):170–9. <https://doi.org/10.1136/adc.51.3.170>.
- Glaser N, Fritsch M, Priyambada L, et al. ISPAD clinical practice consensus guidelines 2022: Diabetic ketoacidosis and hyperglycemic hyperosmolar state. *Pediatr Diabetes*. 2022;23(7):835–56. <https://doi.org/10.1111/pedi.13406>.
- WHO Multicentre Growth Reference Study Group. WHO Child Growth Standards based on length/height, weight and age. *Acta Paediatr Suppl*. 2006 Apr;450:76–85. <https://doi.org/10.1111/j.1651-2227.2006.tb02378.x>

23. Mortensen HB, Hougaard P, Swift P, et al. New definition for the partial remission period in children and adolescents with type 1 diabetes. *Diabetes Care*. 2009;32(8):1384–90. <https://doi.org/10.2337/dc08-1987>.
24. De Bock M, Codner E, Craig ME, ISPAD Clinical Practice Consensus Guidelines. 2022: Glycemic targets and glucose monitoring for children, adolescents, and young people with diabetes. *Pediatr Diabetes* 2022;23(8):1270–6. <https://doi.org/10.1111/pedi.13455>
25. National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents. The fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. *Pediatrics*. 2004;114:555–76.
26. Schwartz GJ, Muñoz A, Schneider MF, et al. New equations to estimate GFR in children with CKD. *J Am Soc Nephrol*. 2009;20(3):629–37. <https://doi.org/10.1681/ASN.2008030287>.
27. Varni JW, Delamater AM, Hood KK, et al. PedsQL 3.2 diabetes module for children, adolescent, and young adults: reliability and validity in type 1 diabetes. *Diabetes Care*. 2018;41(10):2064–71. <https://doi.org/10.2337/dc17-2707>.
28. Cherubini V, Zucchini S, Bonfanti R, Rabbone I, Scaramuzza A. Which treatment modalities are being used by Italian children and adolescents with type 1 diabetes? *Diabetes Technol Ther*. 2024;26(4):283–85. <https://doi.org/10.1089/dia.2023.0510>.
29. Cherubini V, Fargalli A, Arnaldi C, et al. Glucometrics and device satisfaction in children and adolescents with type 1 diabetes using different treatment modalities: A multicenter real-world observational study. *Diabetes Res Clin Pract*. 2024;210:111621. <https://doi.org/10.1016/j.diabres.2024.111621>.
30. Abraham MB, de Bock M, Smith GJ, et al. Effect of a hybrid closed-loop system on glycemic and psychosocial outcomes in children and adolescent with type 1 diabetes: a randomized clinical trial. *JAMA Pediatr*. 2021;175(12):1227–35. <https://doi.org/10.1001/jamapediatrics.2021.3965>.
31. Matejko B, Juza A, Kieć-Wilk B, et al. Transitioning of people with type 1 diabetes from multiple daily injections and self-monitoring of blood glucose directly to MiniMed 780G advanced hybrid closed-loop system: a two-center, randomized, controlled study. *Diabetes Care*. 2022;45(11):2628–35. <https://doi.org/10.2337/dc22-0470>.
32. Di Bonito P, Mozzillo E, Rosanio FM, et al. Albuminuric and non-albuminuric reduced eGFR phenotypes in youth with type 1 diabetes: Factors associated with cardiometabolic risk. *Nutr Metab Cardiovasc Dis*. 2021;31(7):2033–41. <https://doi.org/10.1016/j.numecd.2021.03.019>.
33. Levey AS, Eckardt K-U, Dorman NM, et al. Nomenclature for kidney function and disease: report of a kidney disease: Improving Global Outcomes (KDIGO) Consensus Conference. *Kidney Int* 2020;97(6):1117–29. <https://doi.org/10.1016/j.kint.2020.02.010>
34. Lin YB, Taiwan Diabetes Registry Study Group, Chang TJ. Age at onset of type 1 diabetes between puberty and 30 years old is associated with increased diabetic nephropathy risk. *Sci Rep*. 2024;14(1):3611. <https://doi.org/10.1038/s41598-024-54137-2>.
35. Schiaffini R, Ciampalini P, Spera S, et al. An observational study comparing continuous subcutaneous insulin infusion (CSII) and insulin glargine in children with type 1 diabetes. *Diabetes Metab Res Rev*. 2005;21:347–52. <https://doi.org/10.1002/dmrr.520>.
36. Johnson SR, Cooper MN, Jones TW, et al. 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. <https://doi.org/10.1007/s00125-013-3007-9>.
37. Hoogma RPLM, Hammond PJ, Gomis R, et al. Comparison of the effects of continuous subcutaneous insulin infusion (CSII) and NPH-based multiple daily insulin injections (MDI) on glycaemic control and quality of life: results of the 5-nations trial. *Diabet Med*. 2006;23(2):141–47. <https://doi.org/10.1111/j.1464-5491.2005.01738.x>.
38. Dłuzniak-Golaska K, Szostak-Wegierek D, Pancyk M, et al. May gender influence the quality of life in children and adolescent with type 1 diabetes? *Patient Prefer Adherence*. 2019;13:1589–97. <https://doi.org/10.2147/PPA.S206969>.
39. Williams C. Doing health, doing gender: teenagers, diabetes and asthma. *Soc Sci Med*. 2000;50(3):387–96. [https://doi.org/10.1016/s0277-9536\(99\)00340-8](https://doi.org/10.1016/s0277-9536(99)00340-8).
40. Anderson BJ, Laffel LM, Domenger C, et al. Factors associated with diabetes-specific health-related quality of life in youth with type 1 diabetes: The Global TEENS Study. *Diabetes Care*. 2017;40(8):1002–9. <https://doi.org/10.2337/dc16-1990>.
41. Hilliard ME, Mann KA, Peugh JL, et al. How poorer quality of life in adolescence predicts subsequent type 1 diabetes management and control. *Patient Educ Couns*. 2013;91(1):120–5. <https://doi.org/10.1016/j.pec.2012.10.014>.
42. Varni JW, Burwinkle TM, Jacobs JR, Gottschalk M, Kaufman F, Jones KL. The PedsQL in type 1 and type 2 diabetes: reliability and validity of the Pediatric Quality of Life Inventory Generic Core Scales and type 1 Diabetes Module. *Diabetes Care*. 2003;26(3):631–37. <https://doi.org/10.2337/diacare.26.3.631>.
43. Fischer KI, Fischer FH, Barthel D, et al. Trajectories of Health-Related Quality of life and HbA1c values of children and adolescents with diabetes mellitus type 1 over 6 months: a longitudinal observational study. *Front Pediatr*. 2020;7:566. <https://doi.org/10.3389/fped.2019.00566>.
44. Abdul-Rasoul M, AlOtaibi F, Abdulla A, Rahme Z, AlShawaf F. Quality of life of children and adolescents with type 1 diabetes in Kuwait. *Med Princ Pract*. 2013;22(4):379–84. <https://doi.org/10.1159/000347052>.

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