Effect of automated insulin delivery systems on person-reported outcomes in people with diabetes: a systematic review and meta-analysis

Timm Roos,[a,*] Norbert Hermanns,[a,b] Christopher Groß,[b] Bernhard Kulzer,[a,b] Thomas Haak,[a,c] and Dominic Ehrmann[a,b]

[a]Research Institute of the Diabetes Academy Mergentheim (FIDAM), Johann-Hammer-Str. 24, 97980, Bad Mergentheim, Germany
[b]Department of Clinical Psychology and Psychotherapy, Otto-Friedrich-University of Bamberg, Markusplatz 3, 96047, Bamberg, Germany
[c]Diabetes Centre Mergentheim, Diabetes Clinic, Theodor-Klotzbuecher-Str. 12, 97980, Bad Mergentheim, Germany

eClinicalMedicine
2024;76: 102852

Published Online xxx
https://doi.org/10.1016/j.eclinm.2024.102852

Summary

Background Conclusive evidence on the benefits of automated insulin delivery (AID) systems on person-reported outcomes (PROs) is missing.

Methods In this systematic review and meta-analysis, four databases (PubMed, PsycINFO, Cochrane, and GoogleScholar) were searched from inception up to August 7th, 2024. All types of studies were included if studies reported on PROs in people with diabetes using an AID system. All types of control groups in randomised controlled trials (RCT) were included. Summary data were extracted by three reviewers. Main outcomes focused on diabetes distress, fear of hypoglycaemia and quality of life. Meta-analyses were conducted for RCTs and observational studies separately. When five or more studies could be pooled, random-effects meta-analysis was used, otherwise common-effects meta-analysis was used. Risk of bias was evaluated with Cochrane tools. This study was registered with PROSPERO, CRD42022352502.

Findings A total of 62 studies (n = 9253) were included reporting on 45 different questionnaires. Twenty-seven studies were RCTs and 25 were observational studies. RCT meta-analyses showed reduced diabetes distress (standardised mean difference [95% CI]: −0.159 [−0.309, −0.010], I^2 = 23.0%), reduced fear of hypoglycaemia (−0.339 [−0.566, −0.111], I^2 = 42.6%), and improved hypoglycaemia unawareness (−0.231 [−0.424, −0.037], I^2 = 0.0%), quality of life in adults (0.347 [0.134, 0.560], I^2 = 0.0%) and children/adolescents (0.249 [0.050, 0.448], I^2 = 0.0%). Observational meta-analyses corroborated improvements in diabetes distress (−0.217 [−0.403, −0.031], I^2 = 68.5%), fear of hypoglycaemia (−0.445 [−0.540, −0.349], I^2 = 0.0%), hypoglycaemia unawareness (−0.212 [−0.419, −0.004], I^2 = 0.0%), and showed improved sleep quality (−0.158 [−0.255, −0.061], I^2 = 0.0%).

Interpretation We found low to moderate effect sizes indicating that AID therapy is associated with reduced burden and improved well-being in people with diabetes. Evidence comes from both RCTs and observational studies. However, for some PROs only a limited number of studies could be pooled with a large heterogeneity in questionnaires used. More research is needed with a more uniformed assessment of PROs to demonstrate the added value of AID therapy on psychosocial outcomes.

Funding None.

Keywords: Diabetes mellitus; Automated insulin delivery; Person-reported outcomes; Meta-analysis; Systematic review

Introduction

Automated insulin delivery (AID) systems have changed the landscape of management of type 1 diabetes.[1] Hereby, an algorithm calculates the dose of insulin to be administered based on data from a continuous glucose monitoring (CGM) sensor. AID systems have consistently shown that they significantly improve glycaemic control.[2,3] In randomised

*Corresponding author. Research Institute Diabetes Academy Mergentheim (FIDAM), Johann-Hammer-Str. 24, 97980, Bad Mergentheim, Germany.
E-mail address: roos@fidam.de (T. Roos).

Research in context

Evidence before this study

There is convincing evidence from randomised controlled trials (RCTs) as well as real-world observational studies that demonstrates the beneficial effects of automated insulin delivery (AID) systems on glycaemic control including improvements in HbA1c, time in range (% 70–180 mg/dl, 3.9–10 mmol/L), and hypoglycaemia. Recent meta-analysis on glycaemic outcomes corroborated the effectiveness and safety of AID therapy. Qualitative research and experiences from clinical practice suggests additional beneficial effects on psychosocial well-being. Thus, we searched four electronic databases (PubMed, PsycINFO, Cochrane, and GoogleScholar) from inception up to August 7th, 2024 using the search terms "diabetes mellitus", "automated insulin delivery", "closed loop", "hybrid closed loop", "artificial pancreas", "patient reported outcomes", "person reported outcomes", "quality of life", "distress", "well-being", "mental health", "satisfaction", and "fear of hypoglycaemia". In contrast to glycaemic control, conclusive evidence on beneficial effects of AID therapy on person-reported outcomes (PROs) such as quality of life, fear of hypoglycaemia, sleep quality, and diabetes distress was missing as just one systematic review and meta-analysis was found. This systematic review and meta-analysis, however, focused solely on fear of hypoglycaemia and found reduced fear associated with using an AID system. One narrative review summarised the effects of different diabetes technology on PROs and found some evidence for diabetes-specific but not for generic PROs. A comprehensive systematic review and meta-analysis is missing that analyses the effects of AID on different PRO domains. However, such a meta-analysis is needed to fully evaluate the impact of AID therapy on psychosocial dimensions.

Added value of this study

To our knowledge, this is the first systematic review that performed meta-analyses on eight different PRO domains (diabetes distress, fear of hypoglycaemia, impaired awareness of hypoglycaemia, quality of life, paediatric quality of life, sleep quality, treatment satisfaction, and the INSPIRE measure). Furthermore, meta-analysis on RCTs and observational studies were performed. Results from the RCT meta-analyses revealed significant effects of AID on reduced diabetes distress, reduced fear of hypoglycaemia, improved hypoglycaemia awareness, and improved quality of life in adults and children/adolescents. Furthermore, there is additional evidence from observational studies that suggest improved diabetes distress, quality of life, hypoglycaemia awareness, and sleep quality when using an AID system.

Implications of all the available evidence

The results of the meta-analyses offer important data on the added value of AID systems beyond glycaemic endpoints. They also highlight the potential of AID systems to alleviate some of the burden associated with intensified insulin regimen and to improve quality of life of people with type 1 diabetes. These findings can be used by health technology assessment bodies and policy makers to inform reimbursement decisions for AID therapy, and can also help to widen access to this diabetes technology.

controlled trials, AID systems generally increase time in range (% 70–180 mg/dl [3.9–10 mmoL/l]) by 10% compared to, for example, sensor-augmented pump therapy.[2,3] There is also convincing evidence that AID systems can reduce the exposure to hypoglycaemic values.[2,4]

Besides these glycaemic effects, there is the expectation that AID systems at least partly simplify diabetes management and alleviate some of the burden of diabetes self-management.[5–7] Thus, the effects of AID systems on psychosocial aspects are important to consider in order to fully comprehend the effects of AID therapy on diabetes management.[5,8] Recent reviews highlighted the importance of person-reported outcomes (PROs) in evaluating new technological interventions for diabetes and established key domains of PROs such as diabetes distress, sleep quality, fear of hypoglycaemia, and quality of life.[9–12] A narrative review by Speight et al. showed the complexity of analysing effects of AID therapy on PROs. The review showed the multitude of existing PRO measures that are being used in evaluation studies. They did not find conclusive evidence for the effectiveness of AID systems regarding improved psychosocial well-being but highlighted the heterogeneity in the effects on different PROs, for example diabetes-specific vs. generic PROs.[8] A recent systematic review and meta-analysis demonstrated beneficial effects of AID systems on fear of hypoglycaemia.[13] However, this meta-analysis did not analyse effects of AID systems on other important PROs such as diabetes distress, sleep quality, treatment satisfaction, and quality of life. Thus, there is a need for a comprehensive systematic review and meta-analysis on the effects of AID therapy on different dimensions of PROs. By analysing randomised controlled trials and observational trials, we conducted a systematic review and meta-analysis on the effects of AID system on a variety of PRO measures.

Methods

Search strategy and selection criteria

This systematic review and meta-analysis follows the guidelines for Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). The protocol

was registered in PROSPERO in August 2022 (PROSPERO CRD42022352502). Four electronic databases (PubMed, PsycINFO, Cochrane, and GoogleScholar) were searched until August 7th, 2024. A combination of MeSH Terms and/or keywords such as "Pancreas, Artificial", "Patient Outcome Assessment", "automated insulin delivery", "hybrid closed loop", "patient reported outcomes", "quality of life", "distress", "fear of hypoglycaemia", "well-being" combined with Boolean operators "AND" "OR" were used. The full search strategy is reported in Supplementary Table S1. Studies that were published in English or German and either observational studies, case control studies, controlled trials, or randomised controlled trials, were included. For narrative synthesis, also qualitative studies were included. No restriction on population was applied, so that studies could include children, adolescents, adults, or pregnant women with type 1 diabetes or adults with type 2 diabetes. The intervention had to be an AID system consisting of an insulin pump, continuous glucose monitoring system (CGM), and an algorithm that controls insulin delivery based on CGM data. The control group, if included, could either be multiple daily injection (MDI) of insulin, stand-alone insulin pump therapy, or sensor augmented insulin pump therapy but without a control algorithm or with low glucose suspend function only. Studies were included if they reported results of at least one PRO assessed via a validated questionnaire. No restrictions were made on the type of PRO, and all PRO were considered for the systematic review. Studies only reporting glycaemic outcomes were not included.

The systematic review was conducted using the Covidence tool. The literature search and abstract screening was performed by two independent reviewers (T.R. and C.G.). Full-text screening and risk of bias assessment was performed by three independent researchers (T.R., C.G., and D.E.). If necessary, consensus was reached by discussing the respective paper with a fourth reviewer (N.H.). Data extraction was independently performed by T.R. and C.G., and validated by D.E.

Data analysis

Prior to data extraction, an extraction mask was created in Covidence. Duplicate data was resolved by D.E. in the validation process of data extraction. All data for every reported PRO measure was extracted. For randomised controlled trials, baseline and follow-up mean scores and standard deviation (SD) for the intervention and control group were extracted; for observational trials, pre and post scores (mean and SD) were extracted. Median and interquartile range were transformed into mean and SD following the estimation provided by Wan et al.[14] Key PRO included diabetes distress, fear of hypoglycaemia, hypoglycaemia unawareness, quality of life, sleep quality, treatment satisfaction, and the INSPIRE measure. Three questionnaires assessing diabetes distress were considered: Problem Areas in Diabetes (PAID) scale,[15] Diabetes Distress Scale (DDS),[16] and the DDS for type 1 diabetes (T1-DDS).[17] Since they all address diabetes distress, they were combined in the meta-analyses and one meta-analysis was calculated for all diabetes distress measures. For fear of hypoglycaemia, the Hypoglycaemia Fear Survey (HFS-II) with its two subscales for worries (HFS-W) and behaviour (HFS-B) was considered.[18] Two assessment tools for hypoglycaemia unawareness were considered, the Clarke questionnaire[19] and the Gold score.[20] Also here, these two questionnaires were combined in meta-analyses, also to increase the number of studies included in the meta-analyses on hypoglycaemia unawareness. Quality of life measures included the WHO-5 well-being index,[21] and the PEDsQL™ for paediatric health-related quality of life.[22] The Pittsburgh Sleep Quality Index (PSQI) was considered for the assessment of sleep quality.[23] For treatment satisfaction, the Diabetes Treatment Satisfaction Questionnaire (DTSQ)[24] was considered. The INSPIRE measure was considered as an AID-specific assessment tool of user experiences.[25] Data for other PRO were also extracted; however meta-analyses were only conducted when three or more studies could be synthesised. For studies reporting on PROs, glycaemic parameters were extracted when reported: HbA1c, % of glucose values <54 mg/dl (3.0 mmol/L), <70 mg/dl (3.9 mmol/L), between 70 and 180 mg/dl (3.9–10 mmol/L), >180 mg/dl (10 mmol/L) and >250 mg/dl (13.9 mmol/L) as well as coefficient of variation (CV). The following information were also extracted from included articles: funding (industry vs. public vs. both), study design (randomised controlled trial vs. observational study vs. qualitative study), crossover design (yes vs. no), inclusion and exclusion criteria, number of participants, setting, age, sex, type of diabetes, primary outcome, and type of AID system.

Risk of bias of randomised controlled trials was assessed using the revised Cochrane risk-of-bias tool for randomised trials (RoB 2.0) or, when appropriate, the risk-of-bias tool for randomised crossover trials.[26] Cochrane's Risk Of Bias In Non-Randomized Studies–of Interventions (ROBINS-I) tool was used for observational trials.[27] The *robvis* tool was used to create risk-of-bias plots.[28]

Statistical analyses were conducted using R (version 4.3.2) with the meta package (version 6.5–0) and metafor package (version 4.4–0). In general, meta-analyses were calculated separately for randomised controlled trials and observational trials. Standardised mean differences (SMD) using Hedges g with 95% confidence intervals (CIs) were calculated. In case of sufficient studies (>4 studies), random-effects meta-analyses were conducted using the Knapp-Hartung method[29] and the Paule-Mandel method[30–32] for estimating heterogeneity. In case of few studies (<5 studies), heterogeneity cannot be

reliably estimated from random effects models,[33] and thus, the common effects (CE) model is used following the recommendations of Bender et al.[34] and the German Institute for Quality and Efficiency in Health Care (IQWiG).[35] Heterogeneity was assessed using I^2 and τ^2. The values of τ^2, which indicate the extent to which the effect sizes vary across the included studies beyond what would be expected by chance, between 0.1 and 0.5 were considered acceptable, values between 0.5 and 1.0 fairly high, and values above 1.0 extreme.[35] Prediction intervals for a treatment effect in a single new study were provided. Visual inspection of the symmetry in funnel plots and Egger's test were performed to assess publication bias, both in RCTs and non-RCTs.

Subgroup analyses were conducted to analyse the effects of AID in different populations (paediatric/adolescent vs. adults vs. parents), if a sufficient number of studies was available. A leave-one-out sensitivity analysis was conducted for every meta-analysis, separately. To evaluate the impact of different generations of AID system and to take the evolution of AID therapy into account, meta-regression analyses with publication year and generation of device (Hybrid Closed Loop vs. Advanced Hybrid Closed Loop) as predictors were conducted.

Role of the funding source

There was no funding for this systematic review.

Results

A total of 606 studies were retrieved from the systematic search. After import in Covidence, 42 duplicates were eliminated automatically, and screening started. Title and abstract screening resulted in an exclusion of 472 studies, leading to 92 full texts to be assessed. After full text screening, 62 studies were included in this review including 9253 participants (Fig. 1). Out of the 62 included studies, 27 were RCTs,[36–62] 25 were observational pre-post trials,[6,63–86] six were qualitative studies,[87–92] and the remaining four were other trials (e.g. prevalence trial or a cross-sectional web-survey).[93–96] The RCT by Beato-Vibora et al. compared two AID systems without a non-AID control group, and thus, the two AID study arms were extracted as separate pre-post studies.[64] In case of Ng et al. from 2022,[66] only the newer data from 2024 were used.[77]

The included studies are summarised in Table 1. Overall, a variety of 45 different quantitative questionnaires was used (Table 2, Supplementary Table S2). Number of participants ranged from 13 to 2778 with an average of 126.8 (SD = 377.4), the average age of the participants ranged from 3.3 to 67.0 with an overall average age of 25.0 (SD = 15.8). The gender ratio was balanced, overall, 57.4% of all participants were female (56.9% in the intervention groups and 54.7% in the control groups of RCTs). The average diabetes duration ranged from 1.9 to 38.0 years with an overall average of 12.7 years (SD = 9.5). Regarding the funding of the studies, 16.1% did not receive any funding, 17.7% a funding by industry, 41.9% a funding by a public funding (e. g. JDRF, NIH, NICE) and 24.2% by both—industry and public funding. The majority of studies consisted of people with type 1 diabetes, except one observational trial on people with type 2 diabetes[65] and one web-based survey (98.9% type 1 diabetes).[93]

RCTs

Results of the overall meta-analyses of the several PROs in RCTs can be found in the top part of Table 2. Meta analysis of 13 RCTs with 1248 participants examining diabetes distress[38–44,56,57,59,61] found that the usage of an AID system resulted in a significant reduction of diabetes distress (SMD = –0.159; 95% CI [–0.309; –0.010], I^2 = 23.0%, p = 0.0322; Fig. 2). There was no substantial heterogeneity (χ^2 = 15.58, p = 0.21). Subgroup analyses for adults, adolescents, parents, and studies examining mixed groups demonstrate higher effect sizes for the adult (SMD = –0.206; 95% CI [–0.429; 0.017]) and parent (SMD = –0.511; 95% CI [–0.881; –0.140]) population compared to the paediatric/adolescent (SMD = –0.024; 95% CI [–0.236; 0.189]) population (Supplementary Figures S1 and S2).

Also, the fear of hypoglycaemia, assessed by the HFS-II in up to 16 RCTs with 983–1376 participants,[37–39,41–44,46,47,54–56,58,61,62] was found to be reduced in people using an AID system (SMD = –0.339; 95% CI [–0.566; –0.112], I^2 = 42.6%, p = 0.0005; Fig. 3). Subgroup analyses for overall fear of hypoglycaemia found the highest effect sizes in the paediatric/adolescent (SMD = –0.464; 95% CI [–0.696; –0.231]) and parent population (SMD = –0.299; 95% CI [–0.579; –0.018]), with lower but still significant effects in the adult (SMD = –0.238; 95% CI [–0.442; –0.035]) population (Supplementary Figures S3 and S4). Furthermore, also the worry subscale of the HFS-II (HFS-W: SMD = –0.236; 95% CI [–0.355; –0.117], I^2 = 0.0%, p < 0.0001) and the behaviour subscale (HFS-B: SMD = –0.250; 95% CI [–0.435; –0.064], I^2 = 32.1%, p < 0.0001) were significantly lower in people using an AID system compared to the control groups (Table 2, Supplementary Figures S5–S8). Subgroup analyses showed higher effect sizes for the worry subscale in children/adolescents (Supplementary Figure S6) and higher effect sizes for the behaviour subscale in adults (Supplementary Figure S8).

The effect of AID systems on impaired awareness of hypoglycaemia (IAH) was analysed in four RCTs[41,42,54,61] and showed a significant improvement (SMD [CE] = –0.231, 95% CI [–0.424; –0.037], I^2 = 0.0%, p = 0.0193, Table 2, Supplementary Figure S9). People using an AID system reported higher quality of life at follow-up than people in the control group (Table 2). This effect could be found in studies assessing quality of

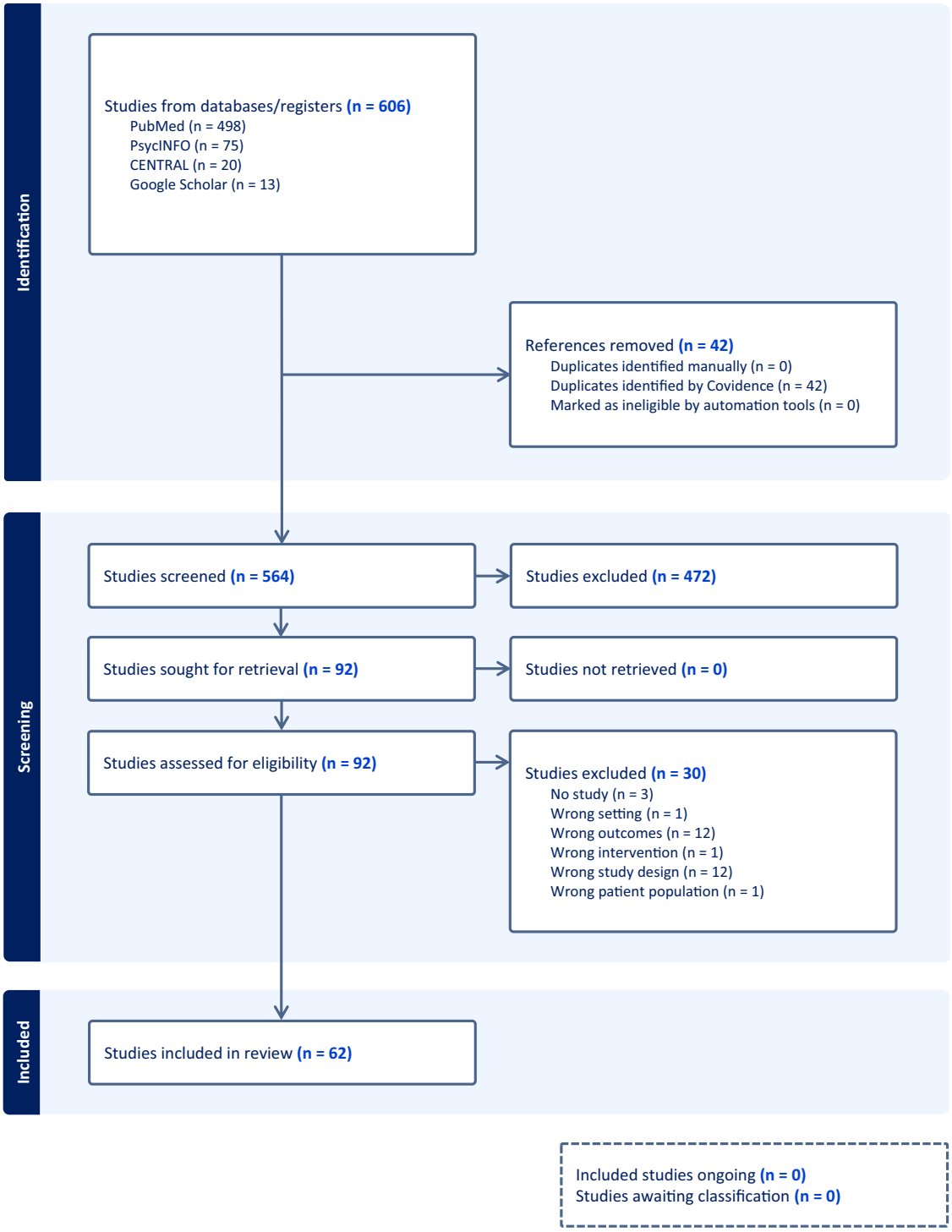

Fig. 1: PRISMA flow chart of analysed studies.

Lead author (year)	RCT	Study design	Sample (mean age)	Manufacturer and model of examined AID	Type of control intervention (only RCTs)	Diabetes duration in years (overall)	PROs	Primary results (significant)	Funding sources
Abraham et al. (2021)[42]	yes	Parallel group, multicentric, randomized	135 children and adolescents, 37 parents (15.3 years)	Medtronic 670G	All but AID	7.7	DTSQ Child & Adult, Gold Score, HFS-II (worry), PAID, PedsQL, STAI Child & Adult	• Improvement in PedsQL and DTSQ • No change in PAID and HFS-II	Public
Adams et al. (2018)[74]	no	Clinical, multicentric, pre-post	15 adolescents, 14 adults (23 years)	Medtronic 670G		14.0 – –	DDS, DTQ, HFS-II	• Improvement in DDS and DTQ • No change in HFS-II	Public
Akiyama et al. (2024)[81]	no	Prospective, single-center observational	22 adults (48.2 years)	Medtronic 770G		15.0	DTSQ, PAID, DTR-QOL	• No change in DTSQ, PAID, DTR-QOL	No funding
Barnard et al. (2017)[52]	yes	Crossover, multicentric, open-label, randomised	32 adults (38.6 years), 26 children and adolescents (12 years)	Other	CGM; Insulin pump	21.1	DTQ, semi structured interviews	• DTQ slightly positive, interviews implicate more satisfaction • Topics: ease of use, alarms and calibrations	Industry and public
Barnard et al. (2015)[51]	yes	Crossover, multicentric, open-label, randomised	22 adults (43 years)	Other	CGM; Insulin pump	29.0	DTQ, semi structured interviews	• No changes in DTQ • Benefits: improved glycaemic control, less worries • Topics: technical issues, alarms, size and weight of the devices	Public
Barnard et al. (2014)[45]	yes	Crossover, mixed methods, monocentric, randomised,	15 adolescents (15.6 years), 13 parents	Other	CGM	7.2	DTQ, HFS-II, semi structured interviews	• Slight improvements of HFS-II in adolescents, slight worsening in parents • Interviews: better sleep quality, less worries in parents • Topics: alarms, calibration, uncomfortable to wear	Public
Beato-Víbora et al. (2023)[64]	yes	Multicentric, head-to-head, randomised	151 adults (39.9 years)	Medtronic 780G & t:slim Control-IQ	Head-to-head comparison	21.6	Clarke Score DDS, DQoL, GMEQ, HFS-II, INSPIRE, PSQI	• Improvements in all PROs (except GMEQ & INSPIRE)	None
Beato-Víbora et al. (2021)[73]	no	Longitudinal, prospective	52 adults (43 years)	Medtronic 780G		27.0	Clarke Score DDS, DQoL, DTSQ, Gold Score, GMEQ, HFS-II, PSQI	• Improvements in Clarke score, DQoL, GMEQ, HFS-II and PSQI • No changes in DTSQ and DDS	None
Beato-Víbora et al. (2020)[71]	no	Longitudinal, multicentric, prospective	36 adults, 22 children and adolescents (overall: 38 years)	Medtronic 670G		15.0	Clarke Score, DDS, DQoL, DTSQ, Gold Score, HFS-II, PSQI	• Improvements in all PROs	None
Benhalima et al. (2024)[61]	yes	Parallel-group, randomised	95 pregnant women (30.5 years)	Medtronic 780G	MDI; Insulin pump	Intervention: 17.0 years; Control: 30.3 years)	HFS-II, Gold Score, PAID-5, SF-36, CES-D, DTSQ	• Improvements in DTSQ and GOLD Score • No changes in other PROs	Industry and public
Bisio et al. (2022)[68]	no	Single arm, two treatment phases	15 adults (68.7 years)	t:slim–Control-IQ		35.2	CES-D, DDS, HFS-II, PSQI	• Improvement of DDS • No changes in other PROs	Industry and public
Bisio et al. (2021)[70]	no	Single arm, two treatment phases	13 children (9.1 years), 13 adults	t:slim–Control-IQ		5.6	CDI-2, CES-D, CSHQ-A, HFS-II, PAID, PSQI, Technology questionnaire for parents	• Improvement in CES-D, HFS-II, PAID and PSQI in parents	Industry and public

(Table 1 continues on next page)

Lead author (year)	RCT	Study design	Sample (mean age)	Manufacturer and model of examined AID	Type of control intervention (only RCTs)	Diabetes duration in years (overall)	PROs	Primary results (significant)	Funding sources
(Continued from previous page)									
Boscari et al. (2022)[67]	no	Field study, monocentric, retrospective	31 adults (38 years)	t:slim–Control-IQ		19.0	DTSQc, DTSQs, HFS-II, PSQI	• Improvements in DTSQ and HFS-II	None
Braune et al. (2021)[93]	no	Web-based cross-sectional	897 adults, children and adolescents (35.6 yers)	Open-source AID		21.4	Questionnaire with 14 fixed-choice questions	• main motivation for usage of an open source AID-system are better glycaemic outcomes and a reduction of short- as well as long-term complications and an increase in the life expectancy	Public
Burckhardt et al. (2021)[54]	yes	Crossover, randomised	17 adults and adolescents (35.8 years)	Medtronic 670G	All but AID	24.2	Clarke Score, DTSQ, Gold Score, HFS-II	• Improvements in Gold score	Public
Choudhary et al. (2022)[37]	yes	Controlled, multi-national, multicentric, prospective, randomised	82 adults (40.6 years)	Medtronic 670G (version 4.0)	CGM; Multiple daily insulin injections (Pen)	Intervention: 18.8; Control: 18.1	DQoL, DTSQ, HFS-II	Improvements in DTSQ and HFS	Industry
Cobry et al. (2020)[75]	no	Field study	37 children and adolescents (13.9 years), 37 parents	Medtronic 670G		6.5	GMSS, HFS-II, PAID-PR, PAID-T, PSQI	• Improvements in GMSS in children and adolescents • No improvements in HFS-II • No improvements in parents' responses	Public
Cobry et al. (2021)[56]	yes	Multicentric, cross-over, randomized	101 children (11.2 years), 101 parents	t:slim–Control-IQ	CGM; Insulin pump	5.2	C-HFS, INSPIRE, P-HFS, PAID, PedsQL, PSQI	• No differences between the groups	Industry and public
Cobry et al. (2022)[94]	no	Secondary analysis of RCT (Cobry et al., 2021; only poor parental sleepers)	49 parents	t:slim–Control-IQ		5.2	Change in PROs only for poor sleepers (PSQI >5)	• Improvements in all PROs of the parents • Improvements in C-HFS	Industry and public
Cobry et al. (2024)[80]	no	Prospective, observational	33 adolescents (11.1 years), 39 parents	t:slim–Control-IQ		2.5	PSQI, PROMIS sleep disturbance, PAID, PedsQL, HFS, DTQ, INSPIRE	• Improvements in parental PSQI • Adolescents: Improvements in worry subscale of HFS • Parents: Improvements in overall HFS and worry subscale	None
De Beaufort et al. (2022)[46]	yes	Multi-national, randomised, crossover	74 adults (parents of 74 children, 5 years)	CamAPS	CGM; Insulin pump	Not reported	ESS, HFS-II, WHO-5	• Improvements in HFS-II in parents • Improvements in WHO-5	Public
DuBose et al. (2021)[72]	no	Field study, multicentric	9 children, 11 adolescents, 60 adults (31.8 years), 20 parents	Medtronic 670G		16.2	HFS-II, INSPIRE	Improvements in HFS-II total score and behaviour subscale only for parents	Public
Edd et al. (2023)[60]	yes	Multicentric, prospective, parallel-group, randomised	82 adults (40.6 years)	Medtronic 780G	CGM; Multiple daily insulin injections (Pen)	Intervention: 18.4; Control: 17.8	DQoL, DTSQc, DTSQs, HFS-II	Improvements in all PROs	Industry
Ekhlaspour et al. (2019)[76]	no	Feasibility study	13 adults (27.9 years)	Other		13.9	T1-DDS, DTSQ, GMSS, HCS, WHO-5, focus groups	• No improvements in PROs	Public

(Table 1 continues on next page)

Lead author (year)	RCT	Study design	Sample (mean age)	Manufacturer and model of examined AID	Type of control intervention (only RCTs)	Diabetes duration in years (overall)	PROs	Primary results (significant)	Funding sources
(Continued from previous page)									
Farrington et al. (2018)[90]	yes	Cross-over, randomised	16 pregnant women (between 18 and 45 years)	Early version of CamAPS	Multiple daily insulin injections (Pen); Insulin pump		Semi structured interviews	• Benefits: inner peace, wonder about new technologies, improved glucose controle • Issues: technical issues, size of the systems, maintenance and logistics	Public
Farrington et al. (2017)[58]	yes	Cross-over, randomized	16 pregnant women (34.1 years)	Early version of CamAPS	Multiple daily insulin injections (Pen); Insulin pump	23.6	DTQ, HFS-II, semi structured interviews	• No improvements in PROs • Benefits: better glycaemic control, improved sleep quality • Issues: thinking more about diabetes, fear of hypoglycaemias remained	Public
Forlenza et al. (2019)[36]	yes	Multicentric, parallel-group, randomised	24 children (9.6 years)	t:slim–Control-IQ	CGM; Insulin pump	Intervention: 4.7; Control:4.4	TAM	• TAM answers mostly positive, satisfied with the system	Industry
Gianini et al. (2022)[96]	no	Mixed-methods, longitudinal	24 children and adolescents (14.5 years)	Medtronic 780G		7.2	C-HFS, PAID, WHO-5, focus groups	• Improvements in all PROs • Focus groups: improved sleep quality in children and parents, improved quality of life and well-being, facilitated diabetes management	Public
Graham et al. (2024)[85]	no	Real-world, observational, prospective	2778 children, adolescents and adults (29.0 years)	t:slim–Control-IQ		Not reported	DIDS, DIDP	• Improvements in DIDS and DIDP	Industry
Hood et al. (2021)[57]	yes	Crossover, multi-national, multicentric, randomized	113 adolescents and young adults (19 years)	Medtronic 780G	Medtronic 670G	12.0	DDS, GMSS, HCS, Technology Attitudes	• Improvements in GMSS	Public
Hood et al. (2022)[39]	yes	Parallel-group, randomised	98 children and adolescents (12.7 years), 98 adults (parents)	CamAPS	Insulin pump	Intervention: 6.3; Control: 6.6 –	CESD, GMSS, HCS, HFS-worry, P-DDS, PAID-T, PedsQL, Technology Attitudes, focus groups	• No improvements in all PROs • Benefits: improved glycaemic control, more freedom and independence for children/adolescents • Issues: unhandiness of the system, connectivity problems	Public
Hood et al. (2024)[62]	yes	Parallel-group, randomised	102 children (4.2 years) with parents	t:slim–Control-IQ	CGM + MDI/ CSII/open loop AID	Intervention: 1.84; Control: 1.96	HFS-II, PedsQL, PSQI, HCS	• Improvements in HFS-II, HCS, PedsQL, and PSQI	Public
Iturralde et al. (2017)[91]	no	Qualitative, retrospective	15 adolescents (16.6 years), 17 adults (28.2 years)	Medtronic 670G		Adolescents: 8.2; Adults: 18.3	Focus groups	• Benefits: better glycaemic control (also overnight), more flexible options for activity • Issues: unexpected new challenges, difficulties in wearing, problems in processing hyperglycaemia	Public

(Table 1 continues on next page)

Lead author (year)	RCT	Study design	Sample (mean age)	Manufacturer and model of examined AID	Type of control intervention (only RCTs)	Diabetes duration in years (overall)	PROs	Primary results (significant)	Funding sources
(Continued from previous page)									
Jalilova et al. (2024)[79]	no	Single-center cohort study	41 children and adolescents (12.5 years)	Medtronic 780G		5.5	PedsQL, SDQ, HFS-C, R-CADS	• No improvements in all PROs	None
Kimbell et al. (2022)[89]	no	Qualitative	33 parents of 30 children (4.9 years)	CamAPS		2.7	Interviews	• Clinical benefits due to the AID, reduced diabetes distress • Parents: Better sleep quality, reduced worries, increased self-confidence • Children: better sleep quality, well-being, concentration, reduced distress	Industry and public
Kropff et al. (2017)[55]	yes	Cross-over, mixed-methods, randomised	32 adults (47 years)	Other	SAP	28.6	AP Acceptance Questionnaire, DTSQc, DTSQs, HFS-II, semi-structured interviews	• No changes in HFS-II and DTSQ • Benefits: trust in the devices, though controlling device's functions • Issues: sleep disorders due to alarms	Public
Kudva et al. (2021)[41]	yes	Multi-centre, randomised	105 adults (25–71 years), 63 adolescents and young adults (14–24 years)	t:slim–Control-IQ	CGM; Insulin pump	Intervention: 17.0; Control:15.0 –	Clarke Score, DDS, HAS, HCS, HFS-II, INSPIRE, SUS, TAS, TES	• Improvements in HFS-II (adults only) • No changes in the other PROs	Industry and public
Lakshman et al. (2024)[92]	no	Qualitative	11 adults (41.5 years)	CamAPS		19.9	Interviews	• Reduced mental load, reduced burden, improved mood • A break from diabetes • Reports on increased snacking	Industry and public
Lee et al. (2023)[38]	yes	Multi-centric, parallel-group, randomised	124 pregnant women (31.1 years)	CamAPS	CGM + MDI	Intervention: 18.0; Control: 16.0	DDS, EQ-5D, HFS-II (worry), INSPIRE, PSQI, interviews	• No improvements in all PROs	Industry and public
Levy et al. (2023)[65]	no	Single-arm, prospective	30 adults	t:slim–Control-IQ			DIDP, DIDS, SUS, PROMIS Sleep Disturbance	• No improvements in PROs	Industry
Marks et al. (2024)[84]	no	Single-arm, prospective, pilot	13 minoritised youth (14.8 years)	t:slim–Control-IQ		8.1	T1DAL, PAID, INSPIRE, DMQ	• Improvements in T1DAL, PAID, and DMQ	Industry
McAuley et al. (2020)[40]	yes	Parallel- groups, randomised	120 adults (44.2 years)	Medtronic 670G	Insulin pump; Multiple daily insulin injections (Pen)	Intervention: 24.0; Control: 24.1	DIDP, DTSQ, PAID, PRMQ, PSQI, W-BQ28	• Improvements in DIDP and W-BQ28	Industry and public
McAuley et al. (2022)[43]	yes	Crossover, randomized, two-stage	30 adults (67 years)	Medtronic 670G	SAP	38.0	Clarke Score, DIDP, GDS, Gold Score, HFS-II, PAID-5, PSQI	• No changes in PROs	Industry and public
Michaels et al. (2024)[78]	no	Prospective, single-arm, dual-centre	17 adults and teens (18.8 years)	Medtronic 780G		9.7	HFS-II, DTSQ, INSPIRE, PSQI, PedsQL	• Improvements in PedsQL and DTSQ	Public

(Table 1 continues on next page)

Lead author (year)	RCT	Study design	Sample (mean age)	Manufacturer and model of examined AID	Type of control intervention (only RCTs)	Diabetes duration in years (overall)	PROs	Primary results (significant)	Funding sources
(Continued from previous page)									
Musolino et al. (2019)[53]	yes	Crossover, multi-national, multicentric, randomised	24 children (5 years), 20 parents	FlorenceM closed loop	Insulin pump	3.1	Closed-loop Experience Questionnaire	• Benefits: reduced burdens in the diabetes management, improved sleep quality, less worries regarding children • Issues: size of the device, battery capacity, connectivity problems	Public
Ng et al. (2022)[66]	no	Real-world, observational, prospective	39 children and adolescents (11.8 years)	t:slim–Control-IQ; CamAPS		3.8	HFS-II, P-HFS	• Improvements in all PROs	Public
Ng et al. (2024)[77]	no	Real-world, observational, prospective	221 children and young people (12.3 years)	t:slim–Control-IQ; CamAPS, Medtronic 780G		6.6	HFS-II, PROMIS sleep disturbance	• Improvements in all PROs	Public
Patel et al. (2022)[95]	no	Prevalence trial, retrospective comparison	184 adults (46 years)	Open-source AID	FSL + CSII	25.0	DDS-2, Gold Score	• No between-group differences in retrospective comparisons	None
Petrovski et al. (2022)[63]	no	Single-arm, monocentric, prospective	34 children and adolescents (12.5 years)	Medtronic 780G		4.3	DTSQ	• Improvements in DTSQ	Public
Pinsker et al. (2021)[6]	no	Retrospective, mixed-methods	1435 adolescents and adults (45.5 years)	t:slim - Control-IQ		25.4	DIDS, TAS, WHO-5, open questions regarding trust and satisfaction	• Improvements in DIDS • Reduction in WHO-5	Industry
Polonsky et al. (2022)[69]	no	Single-arm, prospective, multicentric	115 adults (39.3 years)	Omnipod 5		19.0	DTSQc, HCS, IDSS, PSQI, SUS, T1-DDS, WHO-5	• Improvements in DTSQ, HCS, SUS and T1-DDS	Industry
Pulkkinen et al. (2022)[86]	no	Single-arm, prospective, retrospective registry controls	35 children (4.3 years) and their parents	Medtronic 780G		2.3	PAID-PR	• Improvements in PAID	Industry
Reznik et al. (2024)[83]	no	Multicentric, longitudinal, real-life	55 adolescents (15.1 years), 202 adults (42.4 years)	t:slim–Control-IQ		Adolescents: 7.0; Adults: 24.1	PAID, ADDQOL, PSS, GAD 7, FSS, HFS-II, PSQI, PHQ-9	• Adolescents: Improvements in HFS-II • Adults: Improvements in PAID, ADDQOL, PSS, GAD 7, HFS-II	Industry
Sharifi et al. (2016)[50]	yes	Crossover, prospective, randomized	12 adolescents (15.2 years), 16 adults (42.1 years)	Other	CGM; Insulin pump with low glucose suspend	Adolescents: 6.6; Adults: 26.9	Cogstate, DTSQc, PSQI	• Improvements in DTSQ • Worsening in PSQI in adults	Public
Van Bon et al. (2010)[87]	no	Qualitative	22 adults (42 years)	Hypothetical AP		27.0	Interviews	• Attitudes towards AID therapy mostly positive: better sleep quality, glycaemic control, life quality, less burdens • Issues: necessity to wear 2 subcutaneous devices at the same time and accuracy of the systems	Public
Van Bon et al. (2024)[82]	no	Multicentric, prospective, single-arm, intervention trial	78 adults (47.7 years)	Bihormonal fully closed-loop		26.7	WHO-5, PAID, PSQI, INSPIRE, Gold Score	• Improvements in WHO-5, PAID, PSQI	Industry
Von dem Berge et al. (2022)[48]	yes	Crossover, monocentric, randomised, two-stage	38 children (8.7 years)	Medtronic 670G	Insulin pump with predictive low glucose suspend	4.3	DISABKIDS, HFS-II	• No changes in the PROs	Industry and public

(Table 1 continues on next page)

Lead author (year)	RCT	Study design	Sample (mean age)	Manufacturer and model of examined AID	Type of control intervention (only RCTs)	Diabetes duration in years (overall)	PROs	Primary results (significant)	Funding sources
(Continued from previous page)									
Wang et al. (2021)[88]	no	Qualitative	21 adults (50.0 years)	Medtronic 670G		27.5	Semi structured interviews	• Benefits: reduction of hypoglycaemia, improvement of HbA1c and nocturnal glycaemic control • Issues: frequency of alarms, missing options for individual input, sensor issues and bad processing of hyperglycaemia	None
Weissberg-Benchell et al. (2016)[44]	yes	Crossover, randomised	19 children (9.8 years)	Other	Insulin pump	Not reported	HFS-II, PAID-C	• Improvements in HFS-II	None
Weissberg-Benchell et al. (2017)[59]	yes	Crossover, multicentric, randomised	39 adults (33.3 years)	Dual-hormone AID	CGM + insulin pump	16.9	DTSQc, DTSQs, T1-DDS, WHO-5	• Improvements in all PROs	Public
Wheeler et al. (2022)[47]	yes	Crossover, multicentric, randomised	16 children (7–12 years), 14 adolescents (13–17 years), 29 adults (18–65 years) (23.5 years)	Medtronic 670G	Insulin pump with predictive low glucose suspend	13.2	DTQ, DTSQc, DTSQs, HCS, HFS-II, PSQI, WHO-5	• Improvements in DTSQ in adolescents and adults • Improvements in DTQ in all participants • Improvements in PSQI in participants >16 years	Industry and public
Ziegler et al. (2015)[49]	yes	Multi-national, multicentric, crossover, randomised	20 children (12.3 years), 20 adolescents (15.6 years), 19 adults (31.2 years)	Other	SAP	11.6	AP Satisfaction, C-HFS, HFS-II, TAM-Q	• Improvements in the HFS-II worry subscale • Improvements in TAM-Q • Overall high satisfaction with the AID-system	Industry and public

Abbreviations: Technologies/devices: **AID**, Automated Insulin Delivery; **CGM**, Continous Glucose Monitoring; **CSII**, Continous Subcutaneous Insulin Infusion; **MDI**, Multiple Daily Injections; SAP, Sensor-Augmented Pump, Person-Reported Outcomes; **ADDQoL**, Audit of Diabetes-Dependent Quality Of Life; **AP Acceptance**, Artificial Pancreas Acceptance; CDI-2, Childrens' Depression Inventory 2nd Edition; **CES-D**, Center for Epidemiologic Studies Depression Scale; **C-HFS**, Children Hypoglycemia Fear Survey; CogState, Cognitive functioning task; **CSHQ-A**, Children's Sleep Habit Questionnaire—Abbreviated; DDS, Diabetes Distress Scale; **DIDP**, Diabetes Attitudes, Wishes and Needs Impact of Diabetes Profile; **DIDS**, Diabetes Impact and Devices Satisfaction; DISABKIDS, diabetes treatment satisfaction and burden; **DMQ**, Diabetes Management Questionnaire; **DQoL**, Diabetes Quality of Life; **DTQ**, Diabetes Technology Questionnaire; **DTSQ**, Diabetes Treatment Satisfaction Questionnaire; **DTSQc**, Diabetes Treatment Satisfaction Questionnaire—Change; **DTSQs**, Diabetes Treatment Satisfaction Questionnaire—State; **DTR-QOL**, Diabetes-Therapy-Related Quality Of Life; **EQ-5D**, European Quality of Life 5 Dimensions; **ESS**, Epworth Sleepiness Scale; **FSS**, Fatigue Severity Scale; **GAD-7**, Generalised Anxiety Disorder 7-item; **GDS**, Geriatic Depression Scale; **GMEQ**, Glucose Monitoring Experience Questionnaire; **GMSS**, Glucose Monitoring Satisfaction Survey; **HAS**, Hyperglycemia Avoidance Scale; **HCS**, Hypoglycemia Confidence Scale; **HFS-II**, Hypoglycemia Fear Survey 2nd Edition; **IDSS**, Insulin Delivery Satisfaction; **INSPIRE**, Insulin Delivery Systems: Perceptions, Ideas, Reflections, and Expectations; **PAID**, Problem Areas in Diabetes; **PAID-C**, Problem Areas in Diabetes—Child; **PAID-PR**, Problem Areas in Diabetes-Parent Report; **PAID-T**, Problem Areas in Diabetes—Teen; **P-DDS**, Parent Diabetes Distress Scale; **PedsQL**, Pedriatic Quality of Life Inventory; **P-HFS**, Parent Hypoglycemia Fear Survey; **PHQ-9**, Patient Health Questionnaire-Depression; **PRMQ**, Prospective and Retrospective Memory Questionnaire; **PSQI**, Pittsburgh Sleep Quality Index; **R-CADS**, Revised Child Anxiety and Depression Scale; **SDQ**, Strength and Difficulties Questionnaire; **SF-36**, 36-Item Short Form Health Survey; **STAI**, State-Trait-Anxiety Inventory; **SUS**, System Usability Scale; **T1-DAL**, Type 1 Diabetes And Life; **T1-DDS**, Type 1 Diabetes Distress Scale; **TAM-Q**, Technology Acceptance Model Questionnaire; **TAS**, Technology Acceptance Survey; **TES**, Technology Expectation Survey; **W-BQ28**, Well-Being Questionnaire—diabetes-specified of the W-BQ; **WHO-5**, World Health Organization-5 Well-Being Scale.

Table 1: **Characteristics and narrative summary of included studies.**

life in adults (SMD [CE] = 0.347; 95% CI [0.134; 0.560], I^2 = 0.0%, p = 0.0014; Fig. 4 and Supplementary Figure S10)[46,47,59] as well as paediatric quality of life (SMD = 0.249; 95% CI [0.050; 0.448], I^2 = 0.0%, p = 0.0081; Fig. 5 and Supplementary Figure S11).[39,42,56,62] Regarding sleep quality,[38,40,43,47,50,56,62] treatment satisfaction[40,42,47,54,55,59,61] and the INSPIRE questionnaire,[41] no significant benefit for AID systems compared to the control group could be found in the meta-analyses (Table 2, Supplementary Figures S12–S16). Some evidence for improved sleep quality due to AID use was seen in parents (SMD = –0.549, 95% CI [–0.870; –0.229]; Supplementary Figure S13).

Of the included RCTs that also reported glycaemic effects besides PROs, meta-analyses showed significant improvements of HbA1c (SMD = –0.420, p = 0.0012), time in range (SMD = 1.061, p = <0.0001), % >180 mg/dl (SMD = –0.832, p = 0.0023) and % <54 mg/dl

	Studies and participants		Effect size			Heterogeneity		
	Studies (N)	Observations	SMD	95% CI	p-value	I^2	τ^2	χ^2 (p)
Randomised controlled trials								
Diabetes distress[b]	13	1248	−0.159	−0.309; −0.010	0.0322[a]	23.0%	0.0142	15.58 (0.21)
Fear of hypoglycaemia[b]	14	1085	−0.339	−0.566; −0.111	0.0005[a]	42.6%	0.0860	22.66 (0.046)
Worry subscale[b]	16	1376	−0.236	−0.355; −0.117	<0.0001[a]	0.0%	0.0	5.61 (0.99)
Behaviour subscale[b]	12	983	−0.250	−0.435; −0.064	<0.0001[a]	32.1%	0.0266	16.20 (0.13)
Impaired awareness of hypoglycaemia[b]	4	434	−0.231	−0.424; −0.037	0.0193	0.0%	0.0	0.71 (0.87)
Quality of life[c]	3	344	0.347	0.134; 0.560	0.0014	0.0%	0.0	1.11 (0.57)
Paediatric quality of life[c]	5	529	0.249	0.050; 0.448	0.0081[a]	0.0%	0.0	2.33 (0.68)
Sleep quality[b]	8	577	−0.109	−0.498; 0.280	0.4247[a]	68.4%	0.1396	22.18 (<0.01)
Treatment satisfaction[c]	8	642	0.184	−0.164; 0.532	0.2838[a]	67.2%	0.1162	21.34 (<0.01)
INSPIRE[c]	3	264	0.199	−0.057; 0.456	0.1266[a]	52.5%	0.0555	4.21 (0.12)
Observational, pre-post studies								
Diabetes distress[b]	21	1009	−0.217	−0.403; −0.031	0.0133[a]	68.5%	0.1028	63.42 (<0.01)
Fear of hypoglycaemia[b]	16	1029	−0.445	−0.540; −0.349	<0.0001[a]	0.0%	0.0	9.43 (0.85)
Worry subscale[b]	17	862	−0.423	−0.527; −0.320	<0.0001[a]	0.0%	0.0	12.09 (0.74)
Behaviour subscale[b]	12	622	−0.376	−0.584; −0.168	<0.0001[a]	31.2%	0.0463	15.99 (0.14)
Impaired awareness of hypoglycaemia[b]	5	338	−0.212	−0.419; −0.004	0.0066[a]	0.0%	0.0	3.73 (0.44)
Quality of life[c]	4	1641	−0.049	−0.118; 0.019	0.1584	87.1%	0.1430	23.19 (<0.01)
Sleep quality[b]	15	841	−0.158	−0.255; −0.061	0.0016[a]	0.0%	0.0	12.01 (0.61)
Treatment satisfaction[c]	6	214	0.668	−0.044; 1.381	0.0607	79.6%	0.3855	24.50 (<0.01)
INSPIRE[c]	10	443	−0.028	−0.236; 0.179	0.8189[a]	42.9%	0.0304	15.77 (0.07)

SMD, standardised mean difference; 95% CI, 95% confidence interval; I^2, measure of heterogeneity; τ^2, measure of heterogeneity; χ^2, test statistic for heterogeneity. [a]p-value from hierarchical meta-analysis with study as random, level-2 factor. [b]Negative SMDs indicate improvement. [c]Positive SMDs indicate improvement.

Table 2: **Results of the meta-analyses for person-reported outcomes in randomised controlled trials and observational, pre-post studies.**

(SMD = −0.329, p = 0.0319) (Supplementary Table S3, Supplementary Figures S17–S22).

Observational, pre-post studies

Results of the overall meta-analyses of the several PROs in observational, pre-post studies can be found in the lower part of Table 2. In observational trials, diabetes distress was significantly reduced from baseline to follow-up after AID use (SMD = −0.217; 95% CI [−0.403; −0.031], I^2 = 68.5%, p = 0.0133; Supplementary Figure S23).[64,68–71,73–76,80–84,86] Subgroup analysis revealed a significant effect in studies including adult population (Supplementary Figure S24). Overall fear of hypoglycaemia (HFS-II: SMD = −0.445; 95% CI [−0.540; −0.349], I^2 = 0.0%, p < 0.0001; Supplementary Figure S25) as well as two subscales worry (HFS-W: SMD = −0.423; 95% CI [−0.527; −0.320], I^2 = 0.0%, p < 0.0001; Supplementary Figure S27) and behaviour (HFS-B: SMD = −0.376; 95% CI [−0.584; −0.168], I^2 = 31.2%, p < 0.0001; Supplementary Figure S29) were significantly reduced at follow-up.[64,66–68,70–75,77,78,80,83] Results were consistent across the subgroups

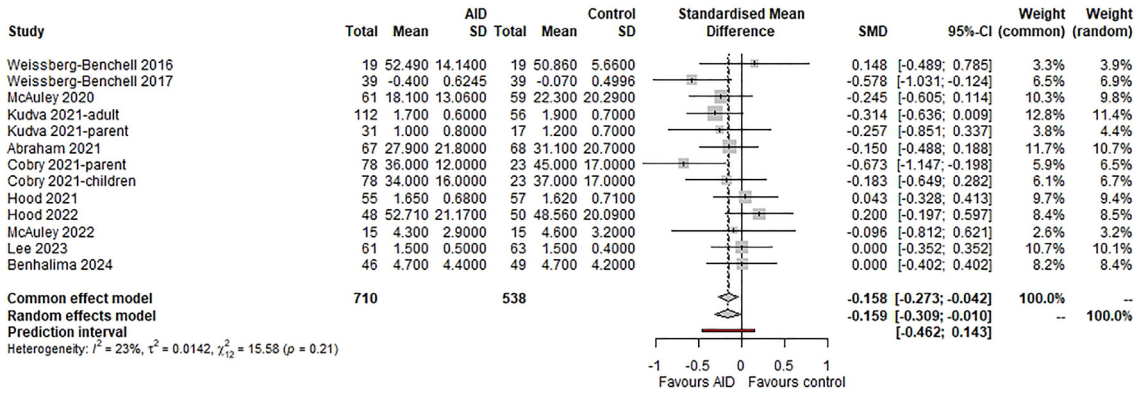

Fig. 2: Forest plot regarding diabetes distress in randomised controlled trials (RCTs).

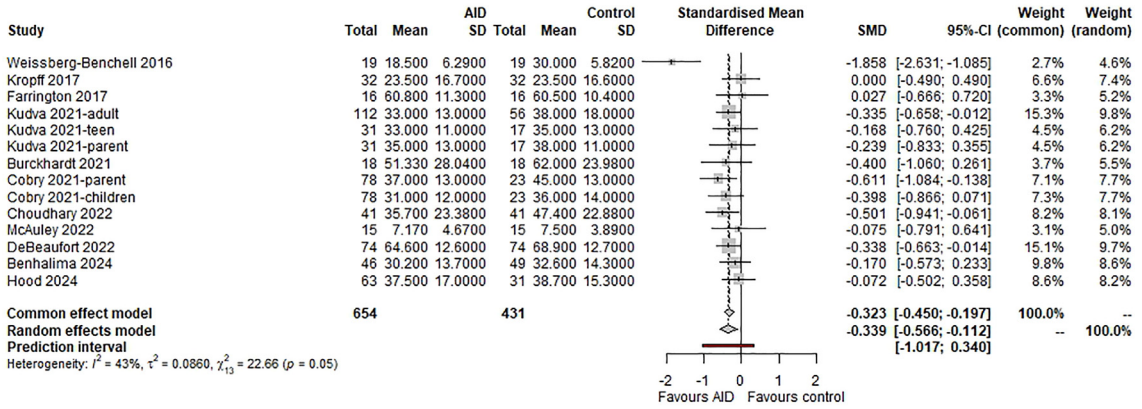

Fig. 3: Forest plot regarding fear of hypogylcaemia in randomised controlled trials (RCTs).

(Supplementary Figures S26, S28, S30). In observational trials, IAH[64,71,73,82] was found to be improved after using an AID system (SMD = –0.212; 95% CI [–0.419; –0.004], I^2 = 0.0%, p = 0.0066; Supplementary Figure S31). There was no significant change in quality of life[6,69,76,82] from baseline to follow-up (SMD [CE] = –0.049; 95% CI [–0.118; 0.019], I^2 = 87.1%, p = 0.1584; Supplementary Figure S32). Sleep quality[64,67–70,73,75,78,80,82,83] improved from baseline to follow-up after using an AID-system (SMD = –0.158; 95% CI [–0.255; –0.061], I^2 = 0.0%, p = 0.0016; Supplementary Figure S33), with the highest effect in the population of parents (Supplementary Figure S34). No significant effects were found for treatment satisfaction[63,67,71,73,78,81] (Supplementary Figure S35) and the INSPIRE measures[64,72,78,80,82,84] (Supplementary Figures S36, S37).

Of the included observational trials that also reported glycaemic effects besides PROs, meta-analyses showed a significant improvement of HbA1c (SMD = –0.747, p < 0.0001), time in range (SMD = 1.157, p = 0.0004), % > 180 mg/dl (SMD = –0.942, p = 0.0025) and % > 250 mg/dl (SMD = –0.743, p = 0.0023) (Supplementary Table S3, Supplementary Figures S38–43).

Qualitative and other results

Qualitative research revealed high expectations but also consistently positive effects of AID therapy of people's life.[87–92] Furthermore, in a cross-sectional web-based survey, Braune et al. found that a majority of people with diabetes (71.6%) and parents of children with diabetes (80.0%) reported a better sleep quality.[93] Also, Kimbell et al. could confirm these findings, as well as less diabetes related distress, less worries of parents of children with diabetes and more normality for them as well as for siblings of the children with diabetes.[89] Cobry et al. identified parents post-hoc as poor-sleepers and found significant improvements in sleep quality and fear of hypoglycaemia in this subpopulation.[94] On the other hand, also aspects like more cognitive and emotional effort due to the AID therapy in people with diabetes with good glycaemic control (HbA1c <7.5%) could be found.[88] Using two items of the DDS and one self-designed item on quality of life, Patel et al. showed evidence for reduced diabetes distress and an extremely positive impact on quality of life with high recommendation of AID therapy.[95] Lastly, Lakshman et al. identified the theme "a break from diabetes" because of AID, and participants reported less mental load, but also increased snacking.[92]

An overview of results for questionnaires for which no meta-analysis (N <3) could be conducted is provided in Supplementary Table S2. An indication for a beneficial effect of AID therapy on diabetes-specific quality of life (DQoL) can be found. Otherwise, results were rather mixed.

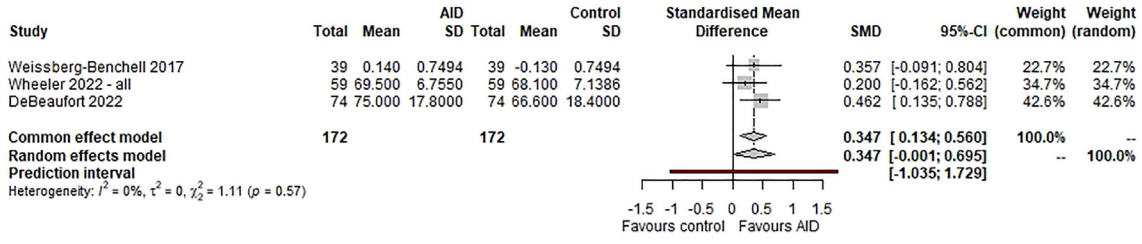

Fig. 4: Forest plot regarding quality of life in randomised controlled trials (RCTs).

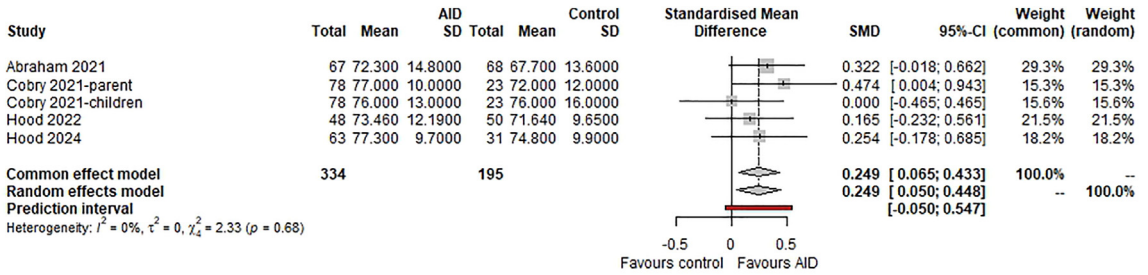

Fig. 5: Forest plot regarding pediatric quality of life in randomised controlled trials (RCTs).

Publication bias

In general, inspection of Funnel plots did not reveal any signs of substantial publication bias in most PROs (Supplementary Figures S44–S62). Egger's tests were negative for all PROs (data not shown) for which an Egger's test could be conducted (k >10).

Sensitivity analyses

Sensitivity analyses revealed that some studies showed a meaningful impact when leaving them out of the analyses (Supplementary Figures S63–S81). In RCTs assessing diabetes distress, mainly two studies[56,59] had some impact on the SMD when leaving them out. For fear of hypoglycaemia, mainly one study showed an impact on the SMD.[44] Regarding quality of life only three studies for adults and five for paediatrics/adolescents were found, therefore, sensitivity analyses emphasized this limitation.

Results of the meta-regression analyses revealed that in RCTs, neither publication year nor generation of device had a significant impact on SMDs. Only in pre-post studies was there a significant association between newer studies and greater benefits for the HFS-II worry subscale ($p = 0.0012$), quality of life ($p < 0.0001$), and the INSPIRE measures ($p = 0.0406$) (Supplementary Table S4). In pre-post studies there was also a significant association between generation of the device and greater benefits for the HFS-II worry subscale ($p = 0.0175$) and the INSPIRE measures ($p = 0.0036$) (Supplementary Table S5).

Risk of bias

Risk of bias assessments for RCTs (Supplementary Figures S82–S85) and observational trials (Supplementary Figures S86–S87) showed in general a low to moderate risk of bias. Only four of 27 RCTs (14.8%) showed a high risk of bias. The main source of bias in RCTs came from the lack of blinding of participants. In observational studies, only one out of 25 studies (4%) showed a serious risk of bias. The main source of bias in observational trials were concerns about confounding factors and bias due to selection of participants.

Discussion

This systematic review and meta-analysis demonstrate the significant benefit of AID systems on different aspects of PROs, both in RCTs and observational studies. In particular, the usage of AID systems in RCTs led to a reduction in diabetes distress and fear of hypoglycaemia as well as to improved quality of life in adults and children/adolescents and hypoglycaemia awareness. Effect sizes were strongest for quality of life, followed by fear of hypoglycaemia, paediatric quality of life, impaired awareness of hypoglycaemia, and diabetes distress. In pre-post studies, significant improvements in diabetes distress, fear of hypoglycaemia, impaired awareness of hypoglycaemia, and sleep qualitywere observed. Effect sizes were strongest for fear of hypoglycaemia, followed by diabetes distress, impaired awareness of hypoglycaemia, and sleep quality.

Most convincing evidence for the beneficial impact of AID systems were found for fear of hypoglycaemia with its two components, worries about hypoglycaemia and avoidance behaviour. This corroborates the recent review by Talbo et al.[13] In our analysis, the effect sizes indicated a reduction in fear of hypoglycaemia of almost half a standard deviation indicating a moderate effect. Interestingly, worries and avoidance behaviour seem to benefit similarly, indicating a psychological as well as behavioural effect of AID systems. As issues with hypoglycaemia can be one of the main sources of diabetes distress,[17] this may explain the beneficial effect of AID on overall diabetes distress found in RCTs and observational trials. Reduced fear of hypoglycaemia and reduced diabetes distress may also play a part in the improvements in quality of life, found in RCTs.[5] In contrast, however, observational studies indicate a slight worsening of quality of life after AID use. However, this effect was rather small (SMD <0.05) and further studies are needed. Interestingly, beneficial effects on sleep quality were not found in RCTs but only in observational studies. This heterogeneity of the effect on sleep quality may be due to the inclusion of all different AID systems. Some AID systems, especially the earlier ones, required multiple calibration and thus, may have had more alarms potentially disturbing sleep and treatment

satisfaction.[50,97] However, evidence of the meta-analysis of RCTs and observational trials indicate a beneficial effect on parents sleep quality. In contrast to previous CGM studies,[98–101] a beneficial effect of AID on impaired awareness of hypoglycaemia was found in meta-analysis in RCTs and observational studies, possibly due to the avoidance of hypoglycaemic values.[102] However, the assessment of impaired awareness of hypoglycaemia may be confounded by CGM-related glucose alarms and warnings.

In general, effect sizes of PROs were low-to-moderate, particularly when compared to the effect sizes found for glycaemic outcomes in this review and the one by Jiao et al.[2] This may be due to the fact that PROs are usually considered as secondary outcomes in AID studies and, thus, studies are often not sufficiently powered to detect a significant effect on PROs.[98] This may also partly explain the finding that for diabetes distress, for example, most of the individual studies included did not yield a significant SMD. Only by combining the studies, the meta-analysis revealed a significant effect of AID on diabetes distress. Also, leave-on-out sensitivity analyses indicated that some effects are mainly driven by single studies. Thus, more sufficiently powered studies with PROs as primary outcome are needed to increase the stability of beneficial effects of AID on psychosocial variables. Also, more mechanistic studies are needed to understand the underlying mechanisms how an AID system affects different PROs.

On the other hand, it's important to emphasise that an AID system is primarily a technology whose main purpose is to improve glycaemic control, and does not constitute a psychosocial intervention. Thus, improvements in certain PRO domains (e.g. depression) are not likely.[8,10] Therefore, the multitude of effects found in this meta-analysis on diabetes-specific and generic PROs must be highlighted. In addition, the beneficial effects of AID on diabetes distress, fear of hypoglycaemia, and impaired awareness of hypoglycaemia were corroborated by both meta-analysis of RCTs and observational trials.

The following limitations of the meta-analysis must be considered. First, a central limitation is the enormous number of different questionnaires used to assess PROs in the included studies. Thus, we focused on the most central PROs for which meta-analysis could be conducted. The variety in PROs used is not only a result of the pluralism of psychosocial aspects in diabetes but is also the result of the lack of a core outcome set for PROs and PROMs in diabetes.[10] As Speight et al. already underlined, this multitude of PROMs leads to a large complexity in analysing the effects of AID therapy on PROs.[8] This meant that most PROs lacked sufficient numbers of trials to do meta-analyses or only a limited number of studies (<4) could be synthesized for e.g. quality of life and impaired awareness of hypoglycaemia. Also, the relevance of PROs in the examined studies seemed to be secondary, since PRO data sometimes was not reported completely or only in the supplementary material. We therefore emphasize the necessity of a core outcome set of PROMs and a standardised reporting allowing meta-analytical approaches. Recently, a consensus statement on PRO domains in diabetes research was published[12] and efforts to offer a Tool Box for the selection of PROMs were made.[9,10] Furthermore, a list of the most commonly used PROs in medical device studies can be found in de Wit et al.[103] Thus, for future trials, we would argue to use these Tool Boxes for the selection of PROMs. The prediction intervals provided in the forest plots of this meta-analysis can be seen as guidance for effect and sample size considerations for each PROM. Second, it must be noted that glycaemic outcomes were not the main aim of the literature search and were only extracted for those studies that reported PROs. Therefore, the meta-analyses of glycaemic outcomes did not include all relevant studies on AID. Third, sensitivity analyses indicate the relative importance of single studies on overall SMDs and shows that the effects should be interpreted with caution. Lastly, the inclusion of different generations of AID systems may have introduced a degree of bias with respect to the observed effects on PROs.

Overall, heterogeneity within PROs was rather low with the highest τ^2 value still below 0.4 and therefore well within an acceptable level.[35] Also, methodological quality of the included studies did not seem to introduce a risk of bias. Taken together, robustness of the effects can be assumed. Regarding quality of life and impaired awareness of hypoglycaemia, further RCTs are needed as the common effects (CE) model and the random effects model yielded different results. Furthermore, there was no evidence that publication year or the generation of the device had a substantial impact on meta-analytic findings, also indicating the robustness of effects. While AID systems certainly evolve over time (e.g. older versions were only activated at night[50]), the impact of different generations of AID systems was rather low. There was some evidence from observational trials that indicate that newer AID generations may improve quality of life,[82] fear of hypoglycaemia, and the INSPIRE measure more strongly. However, with the next generation of AID systems, which promise to enable fully closed-loop therapy,[82] this needs to be further investigated.

In summary, this systematic review and meta-analysis demonstrate that the use of an AID system is associated with an improved psychosocial well-being compared to non-AID therapy. Evidence for reduced distress, fear of hypoglycaemia, as well as improved well-being can be seen from RCTs and observational studies. These quantitative findings also mirror the findings from qualitative research in which people with

diabetes frequently report less burden and improved well-being when using an AID system. However, more research is needed with a core outcome set of PROMs to strengthen the evidence and demonstrate the added value of AID therapy. Furthermore, efficacy and safety of AID therapy in elderly people needs to be further investigated. Taken together, however, the results justify the widening of access to AID therapy as an added valued of AID therapy was demonstrated. This should be taken into account by health technology assessment bodies.

Contributors

T.R., N.H., C.G., and D.E. designed the study. T.R. and C.G. performed the literature search and abstract screening. T.R., C.G., and D.E. performed full-text screening, risk of bias assessment, and data extraction. N.H. supervised the consensus process and helped with the interpretation and discussion of the results. T.R. and D.E. analysed the data and wrote the first draft of the manuscript. N.H., C.G., B.K. and T.H. helped with the discussion of the results and revised the manuscript. All authors read and approved the final version of the manuscript. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication. T.R., N.H., and D.E. have accessed and verified the underlying data.

Data sharing statement

All data of the included studies in this systematic review are available in the referenced articles as listed in the References or by contacting their respective corresponding authors.

Declaration of interests

T.R. reports honoraria for lectures from Berlin-Chemie AG.

N.H. reports Advisory Board member fees from Abbott Diabetes Care and Insulet as well as honoraria for lectures from Berlin Chemie AG, Becton Dickenson, Sanofi Germany, Roche Diabetes Care, and Dexcom Germany.

C.G. reports no conflict of interest.

B.K. reports Advisory Board member fees from Abbott Diabetes Care, Embecta, Roche Diabetes Care, Novo Nordisk, Berlin Chemie AG, and Dexcom Germany as well as honoraria for lectures from Sanofi Germany, Novo Nordisk, Abbott Diabetes Care, Roche Diabetes Care, Berlin Chemie AG, Embecta, Dexcom, and Feen. In addition, he reports support for travel and fees for scientific meetings from Sanofi, Roche Diabetes Care and Berlin Chemie AG as well as unpaid obligations as workshop leader and member of working groups of the German Diabetes Association.

T.H. reports consulting fees from Eli Lilly, NovoNordisk, Sanofi, Boehringer Ingelheim, and Abbott Diabetes Care as well as honoraria for lectures from Abbott Diabetes Care, Sanofi, and Eli Lilly.

D.E. reports Advisory Board member fees from Dexcom Germany and Roche Diabetes Care as well as honoraria for lectures from Berlin Chemie AG, Sanofi-Aventis, Dexcom Germany, Boehringer Ingelheim, and Roche Diabetes Care.

Acknowledgements

None.

Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.eclinm.2024.102852.

References

1 Sherr JL, Heinemann L, Fleming GA, et al. Automated insulin delivery: benefits, challenges, and recommendations. A consensus report of the joint diabetes technology working group of the European association for the study of diabetes and the American diabetes association. *Diabetes Care*. 2022;45(12):3058–3074.
2 Jiao X, Shen Y, Chen Y. Better TIR, HbA1c, and less hypoglycemia in closed-loop insulin system in patients with type 1 diabetes: a meta-analysis. *BMJ Open Diabetes Res Care*. 2022;10(2):e002633.
3 Peacock S, Frizelle I, Hussain S. A systematic review of commercial hybrid closed-loop automated insulin delivery systems. *Diabetes Ther*. 2023;14(5):839–855.
4 Renard E, Joubert M, Villard O, et al. Safety and efficacy of sustained automated insulin delivery compared with sensor and pump therapy in adults with type 1 diabetes at high risk for hypoglycemia: a randomized controlled trial. *Diabetes Care*. 2023;46(12):2180–2187.
5 Nefs G. The psychological implications of automated insulin delivery systems in type 1 diabetes care. *Front Clin Diabetes Healthc*. 2022;3:846162.
6 Pinsker JE, Muller L, Constantin A, et al. Real-world patient-reported outcomes and glycemic results with initiation of control-IQ technology. *Diabetes Technol Ther*. 2021;23(2):120–127.
7 Naranjo D, Suttiratana SC, Iturralde E, et al. What end users and stakeholders want from automated insulin delivery systems. *Diabetes Care*. 2017;40(11):1453–1461.
8 Speight J, Choudhary P, Wilmot EG, et al. Impact of glycaemic technologies on quality of life and related outcomes in adults with type 1 diabetes: a narrative review. *Diabet Med*. 2023;40(1):e14944.
9 Terwee CB, Elders PJM, Blom MT, et al. Patient-reported outcomes for people with diabetes: what and how to measure? A narrative review. *Diabetologia*. 2023;66(8):1357–1377.
10 Hermanns N, Kulzer B, Ehrmann D. Person-reported outcomes in diabetes care: what are they and why are they so important? *Diabetes Obes Metab*. 2024;26(Suppl 1):30–45.
11 Hamilton K, Forde R, Due-Christensen M, et al. Which diabetes specific patient reported outcomes should be measured in routine care? A systematic review to inform a core outcome set for adults with Type 1 and 2 diabetes mellitus: the European Health Outcomes Observatory (H2O) programme. *Patient Educ Couns*. 2023;116:107933.
12 Barnard-Kelly K, Marrero D, de Wit M, et al. Towards the standardisation of adult person-reported outcome domains in diabetes research: a consensus statement development panel. *Diabet Med*. 2024;41(8):e15332.
13 Talbo MK, Katz A, Hill L, Peters TM, Yale J-F, Brazeau A-S. Effect of diabetes technologies on the fear of hypoglycaemia among people living with type 1 diabetes: a systematic review and meta-analysis. *eClinicalMedicine*. 2023;62:102119.
14 Wan X, Wang W, Liu J, Tong T. Estimating the sample mean and standard deviation from the sample size, median, range and/or interquartile range. *BMC Med Res Methodol*. 2014;14:135.
15 Polonsky WH, Anderson BJ, Lohrer PA, et al. Assessment of diabetes-related distress. *Diabetes Care*. 1995;18(6):754–760.
16 Polonsky WH, Fisher L, Earles J, et al. Assessing psychosocial distress in diabetes: development of the diabetes distress scale. *Diabetes Care*. 2005;28(3):626–631.
17 Fisher L, Polonsky WH, Hessler DM, et al. Understanding the sources of diabetes distress in adults with type 1 diabetes. *J Diabetes Complications*. 2015;29(4):572–577.
18 Gonder-Frederick LA, Schmidt KM, Vajda KA, et al. Psychometric properties of the hypoglycemia fear survey-ii for adults with type 1 diabetes. *Diabetes Care*. 2011;34(4):801–806.
19 Clarke WL, Cox DJ, Gonder-Frederick LA, Julian D, Schlundt D, Polonsky W. Reduced awareness of hypoglycemia in adults with IDDM. A prospective study of hypoglycemic frequency and associated symptoms. *Diabetes Care*. 1995;18(4):517–522.
20 Gold AE, MacLeod KM, Frier BM. Frequency of severe hypoglycemia in patients with type I diabetes with impaired awareness of hypoglycemia. *Diabetes Care*. 1994;17(7):697–703.
21 Hajos TR, Pouwer F, Skovlund SE, et al. Psychometric and screening properties of the WHO-5 well-being index in adult outpatients with type 1 or type 2 diabetes mellitus. *Diabet Med*. 2013;30(2):e63–e69.
22 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):631–637.
23 Carpenter JS, Andrykowski MA. Psychometric evaluation of the pittsburgh sleep quality index. *J Psychosom Res*. 1998;45(1):5–13.
24 Bradley C. The diabetes treatment satisfaction questionnaire: DTSQ. *Handb Psychol Diabetes*. 1994;111:132.
25 Weissberg-Benchell J, Shapiro JB, Hood K, et al. Assessing patient-reported outcomes for automated insulin delivery systems: the

psychometric properties of the INSPIRE measures. *Diabet Med*. 2019;36(5):644–652.
26 Jonathan ACS, Jelena S, Matthew JP, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ*. 2019;366:l4898.
27 Jonathan ACS, Miguel AH, Barnaby CR, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. *BMJ*. 2016;355:i4919.
28 McGuinness LA, Higgins JP. Risk-of-bias VISualization (robvis): an R package and Shiny web app for visualizing risk-of-bias assessments. *Res Synth Methods*. 2021;12(1):55–61.
29 Knapp G, Hartung J. Improved tests for a random effects meta-regression with a single covariate. *Stat Med*. 2003;22(17):2693–2710.
30 IntHout J, Ioannidis JPA, Borm GF. The Hartung-Knapp-Sidik-Jonkman method for random effects meta-analysis is straightforward and considerably outperforms the standard DerSimonian-Laird method. *BMC Med Res Methodol*. 2014;14(1):25.
31 Veroniki AA, Jackson D, Bender R, et al. Methods to calculate uncertainty in the estimated overall effect size from a random-effects meta-analysis. *Res Synth Methods*. 2019;10(1):23–43.
32 Langan D, Higgins JPT, Jackson D, et al. A comparison of heterogeneity variance estimators in simulated random-effects meta-analyses. *Res Synth Methods*. 2019;10(1):83–98.
33 Higgins JPT, Thompson SG, Spiegelhalter DJ. A Re-evaluation of random-effects meta-analysis. *J R Stat Soc Ser A Stat Soc*. 2009;172(1):137–159.
34 Bender R, Friede T, Koch A, et al. Methods for evidence synthesis in the case of very few studies. *Res Synth Methods*. 2018;9(3):382–392.
35 German Insitute for Quality and Efficiency in Health Care (IQWiG). General methods version 7.0 of 19 September 202319 September 2023. https://www.iqwig.de/en/about-us/methods/methods-paper/; 2023. Accessed February 18, 2024.
36 Forlenza GP, Ekhlaspour L, Breton M, et al. Successful at-home use of the tandem control-IQ artificial pancreas system in young children during a randomized controlled trial. *Diabetes Technol Ther*. 2019;21(4):159–169.
37 Choudhary P, Kolassa R, Keuthage W, et al. Advanced hybrid closed loop therapy versus conventional treatment in adults with type 1 diabetes (ADAPT): a randomised controlled study. *Lancet Diabetes Endocrinol*. 2022;10(10):720–731.
38 Lee TTM, Collett C, Bergford S, et al. Automated insulin delivery in women with pregnancy complicated by type 1 diabetes. *N Engl J Med*. 2023;389(17):1566–1578.
39 Hood KK, Garcia-Willingham N, Hanes S, et al. Lived experience of CamAPS FX closed loop system in youth with type 1 diabetes and their parents. *Diabetes Obes Metab*. 2022;24(12):2309–2318.
40 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):3024–3033.
41 Kudva YC, Laffel LM, Brown SA, et al. Patient-reported outcomes in a randomized trial of closed-loop control: the pivotal international diabetes closed-loop trial. *Diabetes Technol Ther*. 2021;23(10):673–683.
42 Abraham MB, de Bock M, Smith GJ, et al. Effect of a hybrid closed-loop system on glycemic and psychosocial outcomes in children and adolescents with type 1 diabetes: a randomized clinical trial. *JAMA Pediatr*. 2021;175(12):1227–1235.
43 McAuley SA, Trawley S, Vogrin S, et al. Closed-loop insulin delivery versus sensor-augmented pump therapy in older adults with type 1 diabetes (ORACL): a randomized, crossover trial. *Diabetes Care*. 2022;45(2):381–390.
44 Weissberg-Benchell J, Hessler D, Polonsky WH, Fisher L. Psychosocial impact of the bionic pancreas during summer camp. *J Diabetes Sci Technol*. 2016;10(4):840–844.
45 Barnard KD, Wysocki T, Allen JM, et al. Closing the loop overnight at home setting: psychosocial impact for adolescents with type 1 diabetes and their parents. *BMJ Open Diabetes Res Care*. 2014;2(1):e000025.
46 De Beaufort C, Schierloh U, Thankamony A, et al. Cambridge hybrid closed-loop system in very young children with type 1 diabetes reduces caregivers' fear of hypoglycemia and improves their well-being. *Diabetes Care*. 2022;45(12):3050–3053.
47 Wheeler BJ, Collyns OJ, Meier RA, et al. Improved technology satisfaction and sleep quality with medtronic MiniMed® advanced hybrid closed-loop delivery compared to predictive low glucose suspend in people with type 1 diabetes in a randomized crossover trial. *Acta Diabetol*. 2022;59(1):31–37.
48 von dem Berge T, Remus K, Biester S, et al. In-home use of a hybrid closed loop achieves time-in-range targets in preschoolers and school children: results from a randomized, controlled, crossover trial. *Diabetes Obes Metab*. 2022;24(7):1319–1327.
49 Ziegler C, Liberman A, Nimri R, et al. Reduced worries of hypoglycaemia, high satisfaction, and increased perceived ease of use after experiencing four nights of MD-logic artificial pancreas at home (DREAM4). *J Diabetes Res*. 2015;2015:590308.
50 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(12):772–783.
51 Barnard KD, Wysocki T, Thabit H, et al. Psychosocial aspects of closed- and open-loop insulin delivery: closing the loop in adults with Type 1 diabetes in the home setting. *Diabet Med*. 2015;32(5):601–608.
52 Barnard KD, Wysocki T, Ully V, et al. Closing the loop in adults, children and adolescents with suboptimally controlled type 1 diabetes under free living conditions: a psychosocial substudy. *J Diabetes Sci Technol*. 2017;11(6):1080–1088.
53 Musolino G, Dovc K, Boughton CK, et al. Reduced burden of diabetes and improved quality of life: experiences from unrestricted day-and-night hybrid closed-loop use in very young children with type 1 diabetes. *Pediatr Diabetes*. 2019;20(6):794–799.
54 Burckhardt MA, Abraham MB, Dart J, et al. Impact of hybrid closed loop therapy on hypoglycemia awareness in individuals with type 1 diabetes and impaired hypoglycemia awareness. *Diabetes Technol Ther*. 2021;23(7):482–490.
55 Kropff J, DeJong J, Del Favero S, et al. Psychological outcomes of evening and night closed-loop insulin delivery under free living conditions in people with Type 1 diabetes: a 2-month randomized crossover trial. *Diabet Med*. 2017;34(2):262–271.
56 Cobry EC, Kanapka LG, Cengiz E, et al. Health-related quality of life and treatment satisfaction in parents and children with type 1 diabetes using closed-loop control. *Diabetes Technol Ther*. 2021;23(6):401–409.
57 Hood KK, Laffel LM, Danne T, et al. Lived experience of advanced hybrid closed-loop versus hybrid closed-loop: patient-reported outcomes and perspectives. *Diabetes Technol Ther*. 2021;23(12):857–861.
58 Farrington C, Stewart ZA, Barnard K, Hovorka R, Murphy HR. Experiences of closed-loop insulin delivery among pregnant women with Type 1 diabetes. *Diabet Med*. 2017;34(10):1461–1469.
59 Weissberg-Benchell J, Hessler D, Fisher L, Russell SJ, Polonsky WH. Impact of an automated bihormonal delivery system on psychosocial outcomes in adults with type 1 diabetes. *Diabetes Technol Ther*. 2017;19(12):723–729.
60 Edd SN, Castañeda J, Choudhary P, et al. Twelve-month results of the ADAPT randomized controlled trial: reproducibility and sustainability of advanced hybrid closed-loop therapy outcomes versus conventional therapy in adults with type 1 diabetes. *Diabetes Obes Metab*. 2023;25(11):3212–3222.
61 Benhalima K, Beunen K, Van Wilder N, et al. Comparing advanced hybrid closed loop therapy and standard insulin therapy in pregnant women with type 1 diabetes (CRISTAL): a parallel-group, open-label, randomised controlled trial. *Lancet Diabetes Endocrinol*. 2024;12(6):390–403.
62 Hood KK, Schneider-Utaka AK, Reed ZW, et al. Patient reported outcomes (PROs) and user experiences of young children with type 1 diabetes using t:slim X2 insulin pump with control-IQ technology. *Diabetes Res Clin Pract*. 2024;208:111114.
63 Petrovski G, Al Khalaf F, Campbell J, et al. Glycemic outcomes of advanced hybrid closed loop system in children and adolescents with type 1 diabetes, previously treated with multiple daily injections (MiniMed 780G system in T1D individuals, previously treated with MDI). *BMC Endocr Disord*. 2022;22(1):1–10.
64 Beato-Víbora PI, Chico A, Moreno-Fernandez J, et al. A multicenter prospective evaluation of the benefits of two advanced hybrid closed-loop systems in glucose control and patient-reported outcomes in a real-world setting. *Diabetes Care*. 2023;47(2):216–224.
65 Levy CJ, Raghinaru D, Kudva YC, et al. Beneficial effects of control-IQ automated insulin delivery in basal-bolus and basal-only insulin users with type 2 diabetes. *Clin Diabetes*. 2024;42(1):116–124.

66 Ng SM, Katkat N, Day H, Hubbard R, Quinn M, Finnigan L. Real-world prospective observational single-centre study: hybrid closed loop improves HbA1c, time-in-range and quality of life for children, young people and their carers. *Diabet Med*. 2022;39(7):e14863.
67 Boscari F, Ferretto S, Cavallin F, Bruttomesso D. Switching from predictive low glucose suspend to advanced hybrid closed loop control: effects on glucose control and patient reported outcomes. *Diabetes Res Clin Pract*. 2022;185:109784.
68 Bisio A, Gonder-Frederick L, McFadden R, et al. The impact of a recently approved automated insulin delivery system on glycemic, sleep, and psychosocial outcomes in older adults with type 1 diabetes: a pilot study. *J Diabetes Sci Technol*. 2022;16(3):663–669.
69 Polonsky WH, Hood KK, Levy CJ, et al. How introduction of automated insulin delivery systems may influence psychosocial outcomes in adults with type 1 diabetes: findings from the first investigation with the Omnipod® 5 System. *Diabetes Res Clin Pract*. 2022;190:109998.
70 Bisio A, Brown SA, McFadden R, et al. Sleep and diabetes-specific psycho-behavioral outcomes of a new automated insulin delivery system in young children with type 1 diabetes and their parents. *Pediatr Diabetes*. 2021;22(3):495–502.
71 Beato-Víbora PI, Gallego-Gamero F, Lázaro-Martín L, Romero-Pérez MDM, Arroyo-Díez FJ. Prospective analysis of the impact of commercialized hybrid closed-loop system on glycemic control, glycemic variability, and patient-related outcomes in children and adults: a focus on superiority over predictive low-glucose suspend technology. *Diabetes Technol Ther*. 2020;22(12):912–919.
72 DuBose SN, Bauza C, Verdejo A, Beck RW, Bergenstal RM, Sherr J. Real-world, patient-reported and clinic data from individuals with type 1 diabetes using the MiniMed 670G hybrid closed-loop system. *Diabetes Technol Ther*. 2021;23(12):791–798.
73 Beato-Víbora PI, Gallego-Gamero F, Ambrojo-López A, Gil-Poch E, Martín-Romo I, Arroyo-Díez FJ. Amelioration of user experiences and glycaemic outcomes with an advanced hybrid closed loop system in a real-world clinical setting. *Diabetes Res Clin Pract*. 2021;178:108986.
74 Adams RN, Tanenbaum ML, Hanes SJ, et al. Psychosocial and human factors during a trial of a hybrid closed loop system for type 1 diabetes management. *Diabetes Technol Ther*. 2018;20(10):648–653.
75 Cobry EC, Hamburger E, Jaser SS. Impact of the hybrid closed-loop system on sleep and quality of life in youth with type 1 diabetes and their parents. *Diabetes Technol Ther*. 2020;22(11):794–800.
76 Ekhlaspour L, Nally LM, El-Khatib FH, et al. Feasibility studies of an insulin-only bionic pancreas in a home-use setting. *J Diabetes Sci Technol*. 2019;13(6):1001–1007.
77 Ng SM, Wright NP, Yardley D, et al. Long-term assessment of the NHS hybrid closed-loop real-world study on glycaemic outcomes, time-in-range, and quality of life in children and young people with type 1 diabetes. *BMC Med*. 2024;22(1):175.
78 Michaels VR, Boucsein A, Watson AS, et al. Glucose and psychosocial outcomes 12 Months following transition from multiple daily injections to advanced hybrid closed loop in youth with type 1 diabetes and suboptimal glycemia. *Diabetes Technol Ther*. 2024;26(1):40–48.
79 Jalilova A, Pilan B, Demir G, et al. The psychosocial outcomes of advanced hybrid closed-loop system in children and adolescents with type 1 diabetes. *Eur J Pediatr*. 2024;183(7):3095–3103.
80 Cobry EC, Pyle L, Karami AJ, et al. Impact of 6-months of an advanced hybrid closed-loop system on sleep and psychosocial outcomes in youth with type 1 diabetes and their parents. *Diabetes Res Clin Pract*. 2024;207:111087.
81 Akiyama T, Yamakawa T, Orime K, et al. Effects of hybrid closed-loop system on glycemic control and psychological aspects in persons with type 1 diabetes treated with sensor-augmented pump: a prospective single-center observational study. *J Diabetes Investig*. 2024;15(2):219–226.
82 van Bon AC, Blauw H, Jansen TJP, et al. Bihormonal fully closed-loop system for the treatment of type 1 diabetes: a real-world multicentre, prospective, single-arm trial in The Netherlands. *Lancet Digit Health*. 2024;6(4):e272–e280.
83 Reznik Y, Bonnemaison E, Fagherazzi G, et al. The use of an automated insulin delivery system is associated with a reduction in diabetes distress and improvement in quality of life in people with type 1 diabetes. *Diabetes Obes Metab*. 2024;26(5):1962–1966.
84 Marks BE, Grundman JB, Meighan S, Monaghan M, Streisand R, Perkins A. Hybrid closed loop systems improve glycemic control and quality of life in historically minoritized youth with diabetes. *Diabetes Technol Ther*. 2024;26(3):167–175.
85 Graham R, Mueller L, Manning M, et al. Real-world use of control-IQ technology is associated with a lower rate of severe hypoglycemia and diabetic ketoacidosis than historical data: results of the control-IQ observational (CLIO) prospective study. *Diabetes Technol Ther*. 2024;26(1):24–32.
86 Pulkkinen M-A, Varimo TJ, Hakonen ET, et al. MiniMed 780G™ in 2- to 6-year-old children: safety and clinical outcomes after the first 12 weeks. *Diabetes Technol Ther*. 2022;25(2):100–107.
87 van Bon AC, Kohinor MJ, Hoekstra JB, von Basum G, deVries JH. Patients' perception and future acceptance of an artificial pancreas. *J Diabetes Sci Technol*. 2010;4(3):596–602.
88 Wang LR, Malcolm J, Arnaout A, Humphrey-Murto S, LaDonna KA. Real-world patient experience of long-term hybrid closed-loop insulin pump use. *Can J Diabetes*. 2021;45(8):750–756.e3.
89 Kimbell B, Rankin D, Hart RI, et al. Parents' experiences of using a hybrid closed-loop system (CamAPS FX) to care for a very young child with type 1 diabetes: qualitative study. *Diabetes Res Clin Pract*. 2022;187:109877.
90 Farrington C, Stewart Z, Hovorka R, Murphy H. Women's experiences of day-and-night closed-loop insulin delivery during type 1 diabetes pregnancy. *J Diabetes Sci Technol*. 2018;12(6):1125–1131.
91 Iturralde E, Tanenbaum ML, Hanes SJ, et al. Expectations and Attitudes of individuals with type 1 diabetes after using a hybrid closed loop system. *Diabetes Educ*. 2017;43(2):223–232.
92 Lakshman R, Hartnell S, Ware J, et al. Lived experience of fully closed-loop insulin delivery in adults with type 1 diabetes. *Diabetes Technol Ther*. 2024;26(4):211–221.
93 Braune K, Gajewska KA, Thieffry A, et al. Why #WeAreNotWaiting-Motivations and self-reported outcomes among users of open-source automated insulin delivery systems: multinational survey. *J Med Internet Res*. 2021;23(6):e25409.
94 Cobry EC, Bisio A, Wadwa RP, Breton MD. Improvements in parental sleep, fear of hypoglycemia, and diabetes distress with use of an advanced hybrid closed-loop system. *Diabetes Care*. 2022;45(5):1292–1295.
95 Patel R, Crabtree TSJ, Taylor N, et al. Safety and effectiveness of do-it-yourself artificial pancreas system compared with continuous subcutaneous insulin infusions in combination with free style libre in people with type 1 diabetes. *Diabet Med*. 2022;39(5):e14793.
96 Gianini A, Suklan J, Skela-Savič B, et al. Patient reported outcome measures in children and adolescents with type 1 diabetes using advanced hybrid closed loop insulin delivery. *Front Endocrinol*. 2022;13:967725.
97 Lal RA, Basina M, Maahs DM, Hood K, Buckingham B, Wilson DM. One year clinical experience of the first commercial hybrid closed-loop system. *Diabetes Care*. 2019;42(12):2190–2196.
98 Ehrmann D, Heinemann L, Freckmann G, Waldenmaier D, Faber-Heinemann G, Hermanns N. The effects and effect sizes of real-time continuous glucose monitoring on patient-reported outcomes: a secondary analysis of the HypoDE study. *Diabetes Technol Ther*. 2019;21(2):86–93.
99 Polonsky WH, Hessler D, Ruedy KJ, Beck RW, Group DS. The impact of continuous glucose monitoring on markers of quality of life in adults with type 1 diabetes: further findings from the DIAMOND randomized clinical trial. *Diabetes Care*. 2017;40(6):736–741.
100 van Beers CA, DeVries JH, Kleijer SJ, et al. Continuous glucose monitoring for patients with type 1 diabetes and impaired awareness of hypoglycaemia (IN CONTROL): a randomised, open-label, crossover trial. *Lancet Diabetes Endocrinol*. 2016;4(11):893–902.
101 Hermanns N, Heinemann L, Freckmann G, Waldenmaier D, Ehrmann D. Impact of CGM on the management of hypoglycemia problems: overview and secondary analysis of the HypoDE study. *J Diabetes Sci Technol*. 2019;13(4):636–644.
102 Cryer PE. Mechanisms of hypoglycemia-associated autonomic failure in diabetes. *N Engl J Med*. 2013;369(4):362–372.
103 de Wit M, van Luik S, Marrero D, Barnard-Kelly K, Snoek FJ. Person-reported outcomes in registered randomised diabetes trials: a mapping review of constructs. *Diabet Med*. 2024;41(9):e15385.