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DIABETIC Medicine

SYSTEMATIC REVIEW

A systematic review on the impact of commercially available hybrid closed loop systems on psychological outcomes in youths with type 1 diabetes and their parents

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Abstract

Aim: To systematically assess the impact of commercially available hybrid closed loop (HCL) systems on psychological outcomes in youths with type 1 diabetes and their parents.

Methods: We performed a systematic review including studies published in the last 10 years. PICOS framework was used in the selection process, and evidence was assessed using the GRADE system.

Results: A total of 215 studies were identified after duplicate removal, and 31 studies were included in this systematic review: 20 on first-generation HCL and 11 on second-generation HCL systems. According to studies with moderate- to high-level quality of evidence, HCL systems led to better, or in some studies, unchanged psychological outcomes such as distress and burden related to diabetes management, fear of hypoglycemia, quality of life, satisfaction; instead, quality of sleep was perceived as improved, although results were not confirmed in studies using actigraphy. From semi-structured interviews, answers were more homogeneous, and participants reported a positive experience and attitude towards HCL technology, which was felt to be easy to use and apt to achieve glycemic targets.

Conclusions: Evidence confirms the importance of evaluating the psychosocial needs of youths with diabetes and their families when starting HCL systems and during follow-up, and to set realistic expectations of what can be achieved along with awareness of the limitations of the systems, and educate and motivate families to overcome barriers.

KEYWORDS

adolescent, child, HCL, psychological outcomes, type 1 diabetes

1 | INTRODUCTION

Hybrid closed loop (HCL) systems, adjust insulin delivery in response to continuous glucose monitoring (CGM) data using specific control algorithms, but still, require user-initiated prandial insulin doses.[1]

Clear benefits of HCL on glycaemic outcomes have been reported for children and adolescents with type 1 diabetes (T1D),[2,3] although the impact of these systems on psychosocial outcomes in youth and their families is less studied, and primarily explored as secondary outcomes in studies testing HCL efficacy and safety. This might reflect underestimation of the importance of psychological outcomes or difficulties in assessing qualitative outcomes, which require validated questionnaires and/or semi-structured interviews to explore this complex and sometimes ambivalent area.[4–6]

Recently, there has been growing interest in including psychosocial assessments and Person-reported Outcomes (PROs) when evaluating new technologies.[1,7] The impact of HCL systems on children's burden and emotional well-being, fear of hypoglycemia, quality of life (QoL) and satisfaction are key PROs to consider,[8] given that the success of new diabetes technologies depend on their appropriate use and identification of related burden and barriers to avoid HCL discontinuation, which among youths has been reported in up to 30%.[9,10]

The impact of HCL systems on psychological outcomes has been summarized by two previous systematic reviews analyzing studies published during the first years following the availability of first-generation HCL, but not including any studies on second-generation HCL.[5,11] In 2015, Barnard et al[11] reviewed 92 publications and only 9 studies met inclusion criteria for analysis and only 3 were related to HCL systems in children or adults.[6,12,13] Farrington et al[5] critically reviewed three studies on psychological outcomes in children and adults using HCL. More recently, Papadakis et al.[4] systematically reviewed 686 abstracts on diabetes technology and among the included 56 studies, only 7 explored the psychological benefits of HCL in youths.

The aim of this systematic literature review is to provide an up-to-date summary of the impact of HCL on psychological outcomes in youths with T1D and their parents.

What's new?

- The impact of commercially available first-generation hybrid closed loop (HCL) systems on Person-reported Outcomes (PROs) in youths with T1D and their parents have been assessed in a few studies, reporting either positive findings or no changes.
- Studies on first- and second-generation HCL systems led to better, or in some studies, unchanged PROs, and this systematic review reports both benefits and burdens. However, there are inconsistencies among studies in terms of PROs related to differences in study design and population as well as the questionnaires used.
- It is important to appropriately educate youths with T1D and their families, set realistic expectations from the system, and provide support to overcome barriers. There is a clear need for future larger studies using consistently validated methods to better assess the impact of current and future HCL on PROs in youths with T1D and their families.

2 | MATERIALS AND METHODS

2.1 | Search strategy

We searched electronic databases (Pubmed, EMBASE, The Cochrane Library, Web of Science, Clinicaltrial.gov, International Clinical Trials Registry Platform) for studies published between 1 November 2012 and 1 November 2022. Search terms or "MESH" (MEdical Subject Headings) for this systematic review included different combinations: "artificial pancreas" or "AP" or "automated insulin delivery" or "AID" or "hybrid closed loop" or "closed loop" or "HCL" or "AHCL" AND "distress" or "burden" or "anxiety" or "psychol*" or "sleep" or "quality of life" or "QoL" or "well-being" or "fear" or "worr*" or "satisfaction."

2.2 | Criteria for study selection

We conducted a systematic search of the literature according to the PICOS model (Population, Intervention, Comparison, Results and Study design):

Population	Paediatric study participants (1–18 years old) with T1D and their parents
Intervention	Use of commercially available HCL systems
Comparison	Multiple daily injections (MDI), continuous subcutaneous insulin infusion (CSII), sensor-augmented pump (SAP) with Low Glucose Suspend (LGS) or Predictive Low Glucose Suspend (PLGS) system or Before and after HCL system application
Results	Changes in diabetes distress/burden, anxiety, fear of hypoglycaemia, sleep quality, QoL, well-being, satisfaction
Study design	Randomized clinical trials (RCTs), observational studies, prospective studies, cross-sectional studies, exploratory studies, a mix of qualitative and quantitative studies

Inclusion criteria were (i) study population: children and adolescents (aged 1–18 years) with T1D; (ii) study type: observational studies (cohort, cross-sectional studies), exploratory studies, a mix of qualitative and quantitative studies; review articles were excluded, but their reference lists were screened to identify potentially eligible studies; only published full papers were included, whereas abstracts only were not included; (iii) data on intervention: use of commercially available HCL systems and at least one psychological outcome analyzed; (iv) publication date: last 10 years (2012–2022).

Exclusion criteria were (i) data available only for adults ≥18 years, (ii) case reports, (iii) studies with less than 10 pediatric participants, (iv) full paper not available, (v) study not yet published, (vi) studies not reporting psychological outcomes, we excluded also studies assessing expectations from HCL systems in participants who had not yet used these systems, (vii) languages other than English were not 'a priori' exclusion criteria.

2.3 | Data extraction and management

Two independent investigators (EM and RF) screened for inclusion in the title and abstract of all the studies identified, using the search strategy. Any discrepancies between them were resolved by consensus or by consultation with a third investigator (MLM). After abstract selection, four investigators conducted the full paper analysis (LL, MG, FMR and FDC).

The following characteristics were evaluated for each study in the full paper: (i) reference details: authorship(s), published or unpublished, year of publication, year in which the study was conducted, other relevant cited papers; (ii) study characteristics: design, topic, setting, treatment period, follow-up duration; (iii) population characteristics: number of participants using HCL, age, type of insulin therapy in the control group, HbA1c; (iv) methodology: use of validated questionnaires and/or semi-structured interviews, primary and secondary outcomes, comparator (CSII, MDI or AP systems before and after its implementation), type of HCL system and (vii) main results: psychological outcomes.

In the grading process of the selected studies, three main criteria were used to assess the precision of the psychological outcomes: (i) at least 15 study participants (less than 15 was reported as 'small cohort'); (ii) psychological outcomes evaluated at least 3 months after starting HCL systems, to allow time for the technology to be embedded in everyday life (study duration less than 3 months was considered 'short follow-up') and (iii) the use of validated questionnaires accompanied by semi-structured interviews, where indicated.

2.4 | Assessment of the certainty of the evidence

We used the GRADE approach (Grading of Recommendations Assessment, Development and Evaluation) to rank the quality of evidence (www.gradeworkinggroup.org) for the included studies. Two authors (EM and RF) independently assessed the certainty of the evidence for each of the outcomes. In the case of risk bias in the study design, imprecision of estimates, inconsistency across studies, indirectness of the evidence and publication bias, the recommended option of decreasing the level of certainty by one or two levels according to the GRADE guidelines was applied.[14] The GRADE approach results in an assessment of the certainty of a body of evidence and allocation to one of the four grades:

High	Further research is very unlikely to change confidence in the estimate of the effect
Moderate	Further research is likely to have an important impact on confidence in the estimate of the effect and may change the estimate
Low	Further research is very likely to have an important impact
Very low	Any estimate of the effect is very uncertain

3 | RESULTS

A total of 215 studies were identified following the literature review after duplicates were removed. After reviewing titles and abstracts, 140 additional records were excluded: 15 review articles, 17 studies including only participants older than 18 years, 104 studies reporting outcomes different from those of interest, 1 study not available as a full paper and 3 studies with publication period before 2012.

A total of 75 full-text manuscripts were assessed for eligibility: after full-text examination, 44 studies were excluded, leaving 29 studies, among which 18 on first-generation HCL and 11 on second-generation HCL, to be included in this systematic review. The PRISMA flow diagram (Figure 1) summarizes the publications screening process. A detailed description of outcomes and related measures used in the studies is reported in Table 1.[12,13,15–48] A summary of the studies included in this systematic review along with the grading of evidence are reported in Table S1 and Table 2.[6,8,40,41,48,51–74]

Studies including 15 or more participants, with a follow-up duration of at least 3 months and using a validated questionnaire ± semi-structured interviews were assigned a high-moderate grade of evidence.

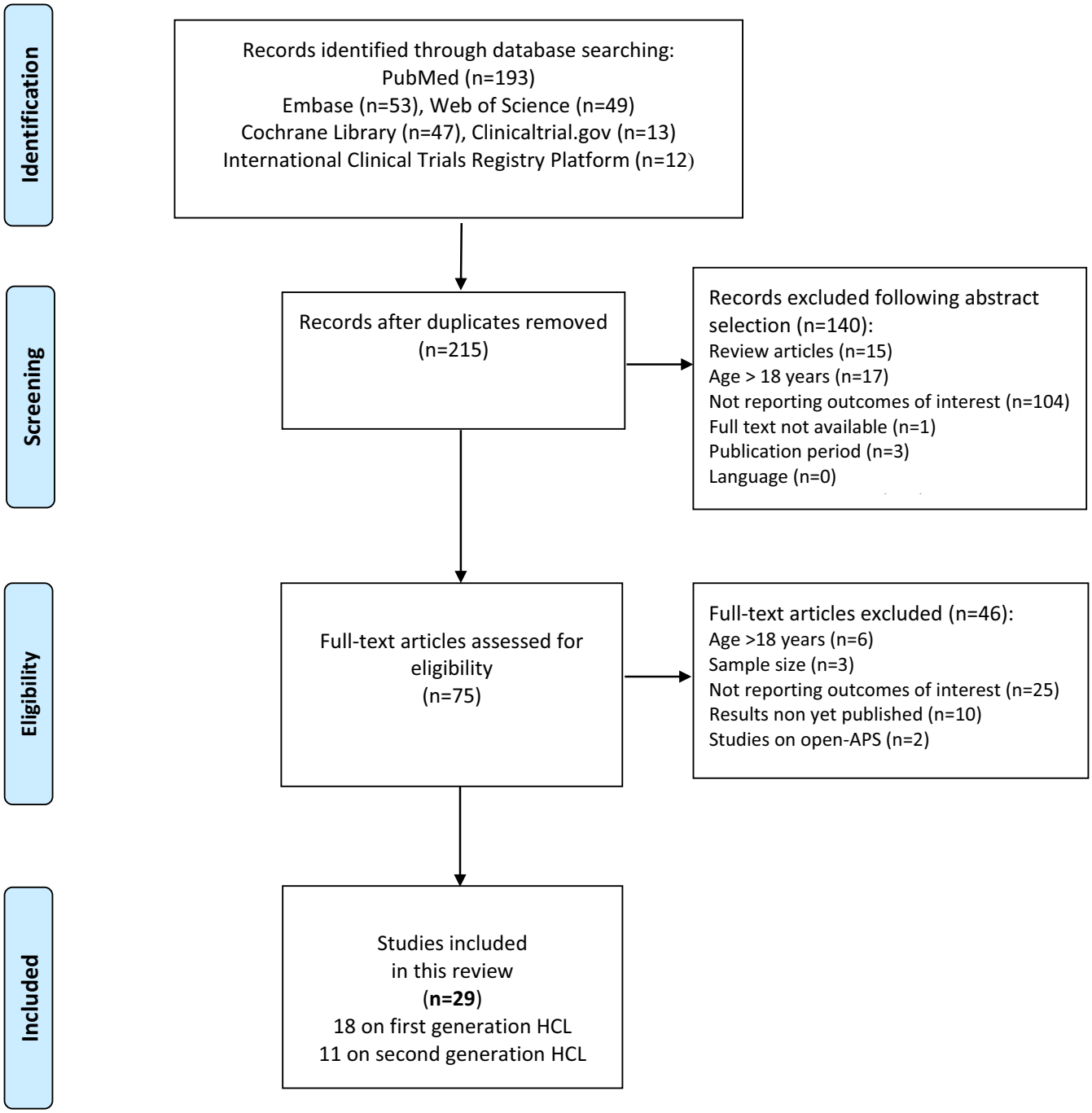

FIGURE 1 Publication selection process summarized by the PRISMA flowchart.

Studies on HCL systems with a number of participants less than 15, or with follow-up less than 3 months or not using validated questionnaires, were classified as being at risk of bias in the study design and/or at risk of imprecision for the estimation of psychological outcomes, and therefore the level of certainty was considered 'low'.

Below we report the results on psychological outcomes based on the 13 studies that were graded as moderate to high quality-level studies, 7 on first-generation HCL and 6 on second-generation HCL; 9 studies were RCTs and 4 prospective observational. In two studies, PROs were explored as primary outcomes,[57,70] in two other studies, there was no clear separation between glycaemic and psychological parameters for the definition of primary/secondary outcomes,[58,72] and in 3 studies, psychological outcomes were included as secondary outcomes, whereas the primary outcome was represented by glycaemic metrics.

In the studies on first-generation HCL, comparisons were primarily made between before and after the implementation of the system (2 studies)[57,58] or with SAP without LGS (4 studies).[8,62,63,73,74] In the studies on second-generation HCL, the comparator was SAP without LGS

TABLE 1 Summary of Psychological Measures used in previous studies in children and adolescents.

Construct	Measure	Self-Report or Proxy-Report	Number of Items	Score Range	Interpretation: ↑ score indicates	References
Diabetes Burden	Problem Areas in Diabetes Survey-Pediatric (PAID-Peds) Problem Areas in Diabetes survey-Parent Revised (PAID-PR)	Youth self-report Parent self-report	20 18	0–100	↑ burden	[15,16]
	The Diabetes Distress Scale (T1-DDS)	Parent self-report	28	Average of all 28 items, each rated on a 1–6 scale		[17]
Depressive Symptoms	Center for Epidemiologic Studies Depression Scale for Children (CES-DC) Center for Epidemiologic Studies Depression Scale (CES-D)	Youth self-report Parent self-report	20	0–60	↑ depressive symptoms	[18,19]
	The Children's Depression Inventory (CDI)	Youth self-report	27	0–54		[20]
State Anxiety, Trait Anxiety	Spielberger State–Trait Anxiety Inventory (STAI)	Youth self-report Parent self-report	20 (state) 20 (trait)	20–60	↑ anxiety	[21,22]
Fear of Hypoglycemia	Hypoglycaemia Fear Survey – Worry Scale (HFS)	Youth self-report (C-HFS) Parent self-report (P-HFS)	15	0–100	↑ fear of hypoglycemia	[23]
	The Hypoglycemia Confidence Scale (HCS)	Parent	9	0–36		[24]
	Hypoglycemia Fear Survey for young adults (HFS-II)	Adult	33	0–132		[25]
Sleep quality	The Pittsburgh Sleep Quality Index (PSQI)	Parent	19	0–21	↑ poor sleep quality	[26]
	The Sleep Disturbance Scale for Children (SDSC)	Child	27	27–135		[27]
	Stanford Sleepiness Scale (SSS)	Adult Child	7	1–7		[28]
	Children's Sleep Habit Questionnaire-Abbreviated (CSHQ-A)	Parent	45	45–135		[29]
Youth QoL	Pediatric Quality of Life Inventory (PedsQL) – Generic and Diabetes-specific	Youth self-report Parent proxy-report	23 (generic) 28 (diabetes)	0–100	↑ quality of life	[30,31]
	The WHO Five Well-Being Index (WHO-5)	Youth self-report Parent proxy-report	5	0–25		[32]
	The Diabetes-Specific Quality of Life Scale (DSQOLS)	Parent proxy-report	64	0–320		[33,34]
	The Diabetes Quality of Life Clinical Trial Questionnaire-Revised (DQLCTQ-R)	Parent proxy-report	57	0–100		[35]
Satisfaction with the CGM system	The CGM Satisfaction Scale (CGM-SAT)	Youth self-report Parent self-report	44	44–220	↑ satisfaction with CGM use	[36]
	The Glucose Monitoring Survey (GMS)	Youth self-report Parent self-report	22	44–154		[36]
	The Blood Glucose Monitoring Communication Questionnaire (BGMC)	Youth self-report Parent self-report	8	8–24		[37]

(Continues)

TABLE 1 (Continued)

Construct	Measure	Self-Report or Proxy-Report	Number of Items	Score Range	Interpretation: ↑ score indicates	References
Diabetes Treatment Satisfaction	The Diabetes Treatment Satisfaction Questionnaire status (DTSQs)	Youth self-report Parent self-report	8	0–48	↑ treatment satisfaction	[38]
	DISABKIDS, items for diabetes	Child Adolescent	28	28–140		[39]
Technology Satisfaction	Technology expectations questionnaire (TEQ)	Child Adolescent	38	38–190	↑ technology satisfaction	[40]
	Technology acceptance questionnaire (TAQ)	Child	38	38–190		[41]
	Diabetes-specific Technology attitude (DSAT)	Adolescent Parent	6	6–30		[42]
	Diabetes Technology Questionnaire (DTQ)	Adult Adolescent Child	30	30–150		[43]
	System usability scale (SUS)	Adult	10	0–100 (> 68: positive response)		[44]
	Insulin delivery System's Perception, Ideas, Reflections and Expectations (INSPIRE)	Adult Adolescent Parent	22 17 21	0–100		[45]
Artificial pancreas satisfaction	Artificial pancreas (AP) acceptance questionnaire based on the Technology acceptance model (TAM)	Adult Adult Adult Adult/ Children	34 15 38 15	34–100 0–90 0–266 0–90	↑ artificial pancreas satisfaction	[12,13,46,47]
	Closed Loop Experience Questionnaire (not validated)	Parent	6	6–30		[48]

(n 2)[67,69] or with PLGS (n 2),[68,70] whereas in one study, it was MDI (n 1),[71] and in another one, there was a comparison between pre- and post-second-generation HCL implementation (n 1).[72]

Study duration varied from 3 to 7 months; study participants were older than 6 years old in most studies; only two studies included participants as young as 2–6 years old along with their parents.[72,74]

The study setting was the participants' home for all studies, and the HCL devices were available on the market at the time of the study.

4 | DISTRESS/DIABETES BURDEN

In most paediatric participants, the use of HCL systems for 3 up to 7 months was not associated with any significant changes in diabetes-related distress and burden compared to SAP with or without PLGS[63,68,73] or comparing outcomes before and after 3–6 months' HCL use.[57,58] Diabetes-related burden was reduced in two studies comparing HCL vs SAP use with or without PLGS for 3–4 months.[8,70]

The use of HCL for 6–7 months did not affect parents' distress and burden in four studies,[58,67,68,73] whereas one study showed a positive impact of HCL use compared to SAP without LGS in parents who were poor sleepers.[69]

Only one study of the moderate quality level of evidence analyzed the effect of HCL on depression and found no differences between children and adolescents using second-generation HCL compared to CSII with or without CGM.[73] Similar findings were reported for their parents.[73]

5 | FEAR OF HYPOGLYCAEMIA (FOH)

The use of HCL systems did not have any significant impact on youths' FOH compared to SAP (with or without PLGS) use for 6–7 months,[63,68,73] or in studies comparing this outcome before and 3–6 months after HCL implementation.[57,58] Similarly, in parents, there was no significant effect of HCL use for 6–7 months on psychological outcomes in all studies,[58,68,73] whereas FOH improved in one study.[74]

In contrast, some recent studies on second-generation HCL reported reduced FOH compared to the use of SAP (with or without PLGS) for 4–7 months[69,70] as well as comparing this outcome before and post-second-generation HCL application (3–7 months).[67,72] Improved FOH was also reported in parents of children using second-generation HCL vs SAP without LGS for 4–7 months[69] and pre–post application.[67] The hypoglycaemia survey

TABLE 2 Summary of the evidence: HCL impact on psychological outcomes in children and adolescents (C) and parents/caregivers (P).

Reference	Device	Distress and burden	Depression	Fear/worry of hypoglycaemia	Sleep quality	QoL/ well-being	Satisfaction	Technology acceptance questionnaires	Level of evidence (GRADE)
Barnard KD et al. 2017[8]	Dana R + FreeStyle Navigator II (12 weeks)	↓ (C)			↑ (C)	↑ (C)	↑ (C)		M
Cobry EC et al. 2020[57]	670G (3 months)	— (C)		— (C)	— (C, P)		↑ (C)		M
Berget G et al. 2020[58]	670G (6 months)	— (C + P)		— (C + P)					M
Taushmann M et al. 2018[62]	Medtronic 640G pump + Enlite 3 sensor, predictive control algorithm (Cambridge) vs SAP (12 weeks)					— (C + P)			M
Abraham MB et al. 2021[63]	670G vs. SAP (6 months)	— (C)		— (C)		↑ (C)	↑ (C)		M
Kudva YC et al. 2021[67]	CIQ vs. SAP (6 months)	— (P)		↓ (C + P)				Positive future expectations	H
Cobry EC et al. 2021[68]	CIQ vs SAP (7 months)	— (C + P)		— (C + P)	— (C + P)	— (C + P)			M
Cobry EC et al. 2022[69]	CIQ vs SAP (7 months)	↓ (P poor sleepers)		↓ (C + P poor sleeper)	↑ (P poor sleeper)				M
Gianini A et al. 2022[70]	780G vs SAP (4 months)	↓ (C)		↓ (C)	↑ (C + P)	↑ (C)			M
Petrovski G et al. 2022[71]	780G (G3) vs MDI (3 months)						↑ (C + P)		M
Ng SM et al. 2022[72]	CIQ pre-post (3 months)			↓ (C + P)					M
Hood KK et al. 2022[73]	Cambridge HCL vs CSII (6 months)	— (C + P)	— (C + P)	— (C + P)		— (C + P)			M
De Beaufort C et al. 2022[74]	Cambridge HCL vs SAP (4 months)			↓ (P)	— (P)	↑ (P)			M
Barnard KD et al. 2014[6]	Dana R + FreeStyle Navigator vs SAP (21 days)			↑↓ (C + P)			↑ (C + P)		L
Weissberg-Benchell J et al. 2016[40]	Bionic pancreas vs SAP (5 ays)	↓ (C)		↓ (C)			↑ (C)		L
Troncone A et al. 2016[52]	Dexcom G4, Roche Combo, DiAs (7 days)						↑ (P)	Easy to use, trust	L
Iturralde E et al. 2017[53]	670G (4 days)	↓ (C)				↑ (C)			L
Adams RN et al. 2018[54]	670G (4–5 days)	↓ (C)		— (C)				Positive attitude	L
Lal RA et al. 2019[55]	670G (1 year)							61% dropped automode	L
Renard E et al. 2019[56]	t:AP Tandem + Dexcom G4, DiAS (2d)			— (C + P)				AP acceptance improved	L
Musolino G et al. 2019[48]	Modified 640G with Cambridge Florence M system (21 days)	↓ (P)		↓ (P)	↑ (P)		↑ (P)		L
Bisio A et al. 2020[65]	CIQ vs SAP (1 months)	↓ (P)	↓ (P)	↓ (P)	↓ — (P)			Perceived benefits by parents	L
Messer LH et al. 2020[59]	670G (6 months)	— (C discontinuers)		— (discontinuers)					L
Sharifi A et al. 2016[60]	Veo + Enlite + Amdroid APS HCL (4 days)				— (C)				L
Taushmann M et al. 2016[61]	Dana Diabecare R pump + FreeStyle Navigator II and FlorenceD2A algorithm vs SAP (21 days)	↓ (C)			↑ (C)				L
Forlenza GP et al. 2019[41]	CIQ vs SAP (3 days)							Perceived benefits	L
Wheeler BJ et al. 2021[66]	780G vs 640G (1 months)			—	↑ (C)		↑ (C)	Positive expectations	L
Von dem Berge T et al. 2022[64]	670G vs SAP with PLGS (2 months)	— (C)		— (C)			— (C)	High scores of acceptance	L

Note: ↓, reduced; ↑, increased; —, no variation; ↑↓, heterogeneity in the response, mixed results.

behaviour and worry subscales improved using second-generation HCL, the users trust the automated system to protect them from hypoglycemia.[65,68,72]

6 | SLEEP QUALITY

Sleep quality, evaluated by questionnaires, improved in a few studies after 3–4 months of use of HCL systems compared to SAP with or without PLGS, in children and adolescents[8,70] but it did not change in youths and parents in another two studies after 4–7 months.[68,74] In a group of poor sleeper parents, second-generation HCL compared to SAP without LGS for 7 months improves the reported quality of sleep.[69] The use of actigraphy revealed no change in sleep quality in two studies evaluating HCL systems after 3 months in youths and their parents,[57] while a reduction in the number of parental overnight awakenings was reported after 2 months in a study with a low level of evidence.[65]

7 | QUALITY OF LIFE, WELL-BEING

QoL improved in a few studies comparing HCL to SAP with or without PLGS in youths after 3 to 6 months,[8,63,70,74] whereas it was unchanged in other studies comparing second-generation HCL to SAP with or without PLGS for 6–7 months.[62,68,73] In the latter studies, scores remained unchanged in all the PedsQL subscales: diabetes symptoms, treatment barriers, treatment adherence, worry and communication.[68,73]

8 | SATISFACTION

Youths' satisfaction improved with HCL systems compared to SAP without LGS after 3–6 months in two studies,[8,63] whereas no changes were found in a study comparing pre- and 3-month post-HCL application,[57] and in another study comparing second-generation HCL with MDI + CGM in youth and parents after 3 months.[71]

Diabetes technology acceptance and attitudes were high for HCL systems compared to SAP without LGS after 6 months of use.[67] Reported barriers were having to carry the devices, the size of the equipment,[8] technical difficulties with CGM connectivity, alarms, and calibration.[8]

From the semi-structured interview, the answers related to distress, QoL and satisfaction were more homogeneous compared to questionnaires: participants reported a positive experience and manifested a positive attitude toward the CL technology, intended as easy to use and apt to improve glycemic targets.[70]

9 | DISCUSSION

This systematic review showed that HCL systems led to improved or unchanged PROs, such as diabetes-related burden, FOH, QoL and treatment satisfaction, whereas the quality of sleep substantially improved, in youths with T1D and their parents. This review also highlights conflicting results for PROs, using different questionnaires to assess the same outcome.

The efficacy and safety of HCL systems have been assessed in several studies, where glycemic measures such as HbA1c and CGM metrics were the primary outcome measures. In contrast, so far, the evidence related to the impact of HCL systems on PROs in youths with T1D and their parents is less strong and ~~findings from~~ different studies have been often been reported discordant findings.[4,5,11] However, PROS are utmost importance for the successful implementation of any new technologies and they can support the selection of candidates for HCL systems with true expectations and to intercept barriers or difficulties that may arise later.[4,11]

Our systematic review showed that, in most pediatric participants and their parents, diabetes-related distress and burden did not improve when compared to SAP with or without PLGS, probably because most of the studies were not powered to detect subtle differences in this outcome,[68] and specific questionnaires highlighting the differences between SAP and HCL.

With regards to FOH, this was unchanged compared to SAP in most studies on HCL and these results likely reflect, once again, the small sample size[73] or the fact that FOH scores at study entry were already relatively low, likely because youths with a medical history of severe hypoglycemia were not included in the studies for safety reasons.[58] Of interest, FOH improved in studies on second-generation HCL, and this could be related to the additional feature of the second-generation HCL compared to first-generation HCL, which could provide further reassurance. However, differences in study design and populations could have also contributed to differences in outcomes between the two systems.

Improved QoL and satisfaction in HCL users, as reported in some studies, was associated with positive feedback about technology, reported as easy to use and associated with lower burden and less and even more reliable alarms.[67] Different questionnaires to test HCL systems acceptance were used in the analysed studies, and they were mainly based on the technology acceptance model (TAM model), and this could explain some of the

discrepancies in results across studies and highlights the need of implementing a single validated questionnaire to allow accurate comparisons of studies results.

Sleep was perceived and reported as improved by youths and their parents, due to a reduction in worries about nocturnal hypoglycaemia and fewer night-time awakenings to check glucose levels. However, these results were not confirmed by a study based on actigraphy, where the lack of a positive effect on sleep was attributed to the short follow-up and the need for more time to learn and get used to new technologies.[57]

Some limitations of the studies included in this systematic review need to be acknowledged. Firstly, the sample size of most studies was small (just over 15 participants), primarily including Caucasian people, and the study populations were relatively selective and not representative of the whole population of youths with T1D and their parents, due to some inclusion criteria such as HbA1c close to the target, or focus on specific subgroups, such as adolescents with suboptimal glycaemic outcomes.[62] In addition, trials might have included subgroups of particularly motivated youths as well as excluded youths with a previous history of frequent hypoglycaemic episodes for safety reasons; these factors could already have influenced the baseline status of psychological outcomes. Secondly, insulin regimes prior to HCL systems implementation differed across studies, including either MDI without CGM, or CSII, or SAP with PLGS. In addition, among the 13 studies with moderate to high level of evidence, none compared the HCL system to the best currently available contemporary therapy (SAP+PLGS for first-generation HCL and first-generation HCL for second-generation HCL), but only to SAP. Another limitation was that psychological measures were included as secondary outcomes in all but two studies. In addition, although we excluded studies using not previously validated questionnaires,[48,52] often several different versions of validated questionnaires were administered to subsets of study participants (i.e. children, adolescents and parents), limiting the potential to identify statistically or clinically meaningful differences between study groups.[67] Finally, although we analysed studies with at least 3-month HCL duration hypothesizing this as being the minimum time for participants to adapt to HCL use and have a reliable interpretation of the outcomes, we cannot exclude that, in some individuals, psychosocial measures could require a longer time to improve.

10 | CONCLUSIONS

Data on PROs in the paediatric population using HCL systems are still limited, but many studies on this topic are ongoing. Whereas, understandably soon after the introduction of these new technologies, efficacy in terms of TIR, HbA1c and safety were the main outcomes included in clinical studies, over time the importance of PROs assessment has progressively emerged. This systematic review highlights inconsistencies among studies in terms of PROs related to differences in study design, and population as well as the questionnaires used. Therefore, there is a strong need for future larger studies using consistent validated methods, with PROS as the primary outcome, including an adequate sample size, representative of the whole population of youths with T1D, in terms of ethnicity and sociodemographic background. Validated questionnaires, particularly on HCL satisfaction, and the use of actigraphy to assess sleep quality should be considered to address existing gaps in the literature.

Given that HCL systems are not fully automated, it is important that paediatric diabetes teams appropriately educate youths with diabetes and their families, and set realistic expectations from the system, and provide support to overcome barriers for optimal management of the system.

AUTHOR CONTRIBUTIONS

Roberto Franceschi and Enza Mozzillo made a substantial contribution to the design of this literature review, in the acquisition of data, their interpretation and analysis as well as in the writing of the manuscript. Enza Mozzillo and Roberto Franceschi selected the articles for this literary review. Letizia Leonardi, Martina Girardi, Francesco Maria Rosanio and Francesca Di Candia contributed to the analysis of studies included in the review. M. Loredana Marcovecchio performed a critical revision of the manuscript and performed a thorough proofreading of the manuscript. All the authors have approved the version to publish.

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CONFLICT OF INTEREST STATEMENT

The authors have no conflict of interest to declare.

DATA AVAILABILITY STATEMENT

All databases generated for this study are included in the article.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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