



CADTH Reference List

Hybrid Closed-Loop Insulin Delivery Systems for People With Type 1 Diabetes

August 2023

Key Messages

- We found 4 health technology assessments, 2 systematic reviews, 39 randomized controlled trials, and 17 nonrandomized studies describing the clinical benefits and harms of commercially available hybrid closed-loop systems versus other insulin delivery methods in people of any age with type 1 diabetes.
- We found 6 economic evaluations describing the cost-effectiveness of commercially available hybrid closed-loop systems versus other insulin delivery methods in people of any age with type 1 diabetes.
- We found 2 evidence-based guidelines regarding the use of commercially available hybrid closed-loop systems in people of any age with type 1 diabetes.

Research Questions

1. What literature describes the potential clinical benefits and harms of commercially available hybrid closed-loop systems versus other insulin delivery methods in people of any age with type 1 diabetes?
2. What literature describes the cost-effectiveness of commercially available hybrid closed-loop systems versus other insulin delivery methods in people of any age with type 1 diabetes?
3. What are the evidence-based guidelines regarding the use of commercially available hybrid closed-loop systems in people of any age with type 1 diabetes?

Methods

Literature Search Methods

An information specialist conducted a literature search on key resources including MEDLINE, the Cochrane Database of Systematic Reviews, the International HTA Database, the websites of Canadian and major international health technology agencies, as well as a focused internet search. The search approach was customized to retrieve a limited set of results, balancing comprehensiveness with relevancy. The search strategy comprised both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. Search concepts were developed based on the elements of the research questions and selection criteria. The main search concepts were hybrid closed loop systems and type 1 diabetes. The search was completed on July 19, 2023, and limited to English-language documents published since March 1, 2020.

Selection Criteria

One reviewer screened literature search results (titles and abstracts) and selected publications according to the inclusion criteria presented in [Table 1](#). Full texts of study publications were not reviewed. Open access full-text versions of evidence-based guidelines were reviewed when available.

Table 1: Selection Criteria

Criteria	Description
Population	Individuals of any age with type 1 diabetes
Intervention	Medtronic MiniMed 670G, Medtronic MiniMed 780G, MiniMed 770G, Tandem Control-IQ, Omnipod Horizon, Omnipod 5, Diabeloop DBLG1, CamAPS FX, iLet Bionic Pancreas, Tidepool Loop, or any other commercially available HCL systems
Comparator(s)	Q1 and Q2: Any commercially available HCL systems or existing insulin delivery methods (e.g., sensor-augmented pumps, closed loops [i.e., an artificial pancreas that requires little to no user input for basal or prandial insulin dosing], open loops [i.e., an insulin pump with or without continuous glucose monitoring that requires substantial user input for basal and prandial insulin dosing], or MDII). Q3: NA
Types of information	Q1: Descriptions of potential clinical benefits (e.g., quality of life, hemoglobin A1C levels, glucose time-in-range metrics) and harms (e.g., episodes of severe hypoglycemia, diabetic ketoacidosis) Q2: Descriptions of cost effectiveness (e.g., incremental cost per clinical benefit, cost per QALY) Q3: Recommendations regarding the use of HCL systems
Study designs	Health technology assessments, systematic reviews, randomized controlled trials, nonrandomized studies, economic evaluations, evidence-based guidelines

HCL = hybrid closed loop; Hemoglobin A1C = glycated hemoglobin; MDII = multiple daily insulin injections; QALY = quality-adjusted life-year

Results

Four health technology assessments,¹⁻⁴ 2 systematic reviews,^{5,6} 39 randomized controlled trials,⁷⁻⁴⁵ and 17 nonrandomized studies⁴⁶⁻⁶² were identified about the clinical benefits and harms of commercially available hybrid closed-loop (HCL) systems versus other insulin delivery methods in people of any age with type 1 diabetes. Six economic evaluations⁶³⁻⁶⁸ were identified about the cost-effectiveness of commercially available HCL systems versus other insulin delivery methods in people of any age with type 1 diabetes. Two evidence-based guidelines^{69,70} regarding the use of commercially available HCL systems in people of any age with type 1 diabetes were identified.

Additional references of potential interest that did not meet the inclusion criteria are provided in [Appendix 1](#). Registered ongoing clinical trials are provided in [Appendix 2](#).

References

Health Technology Assessments

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Systematic Reviews

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Randomized Controlled Trials

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Guidelines and Recommendations

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Refer to Recommendations: 7.4-7.5 (page 2); 7.23-7.24 (page 7)
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Refer to Recommendations 2.9.2 (page 509); 3.2.1-3.2.3 (page 510); 3.4.1 (page 510)

Appendix 1: References of Potential Interest

Previous CADTH Reports

Hybrid Closed-Loop Insulin Delivery Systems for People with Type 1 Diabetes. Ottawa (ON): CADTH; 2021. <https://www.cadth.ca/hybrid-closed-loop-insulin-delivery-systems-people-type-1-diabetes>. Accessed 2023 Jul 27.

Health Technology Assessment

Unclear Methodology

Assessment of insulin pump systems for type 1 diabetes patients English summary. Quebec (QC): INESSS; 2022. https://www.INESSS.qc.ca/fileadmin/doc/INESSS/Rapports/Technologies/INESSS_Insulin_pump_Summary.pdf. Accessed 2023 Jul 27.

Systematic Reviews

Unclear Comparator

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HCL Not Specified

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Unclear Population – Individuals with Type 1 Diabetes Not Specified

Asarani NAM, Reynolds AN, Elbalshy M, et al. Efficacy, safety, and user experience of DIY or open-source artificial pancreas systems: a systematic review. *Acta Diabetol*. 2021; 58(5):539-547. [PubMed](#)

Randomized Controlled Trials

HCL Not Specified

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Appendix 2: Ongoing Clinical Trials

Table 2: Registered Clinical Trials of Hybrid Closed-Loop Systems for People With Type 1 Diabetes

Trial name (registration number); link; country	Population; age	Intervention	Comparator(s)	Study design	Trial phase	Number of expected participants	Expected trial primary completion date
Effect of HCL Insulin Delivery System on Glycemic Control in Patients With T1D (NCT05924932); Study Record Beta ClinicalTrials.gov; Czechia	Patients with type 1 diabetes; ≥ 18 years old	Tandem t:slim X2 with hybrid closed loop system Control IQ, glucose sensor: Dexcom G6	MiniMed 780G with hybrid closed loop system SmartGuard, sensor Guardian 4	Observational NRS	NA	120	December 1 2023
Portable Artificial Pancreas Applied for Youth and Adolescents (PAPAYA 1) (NCT05543850); Study Record Beta ClinicalTrials.gov; Netherlands	Patients with type 1 diabetes; 12 to 18 years old	Bi-hormonal closed-loop control	Open loop control	Crossover RCT	NR	20	April 28 2023
Android Artificial Pancreas System (Android APS) vs. Control-IQ (CODIAC) (NCT05165615); Study Record Beta ClinicalTrials.gov; Czechia	Individuals with type 1 diabetes; ≥ 18 years old	Control-IQ system	AndroidAPS (previous use)	Single arm study	NA	20	June 30, 2022
Comparison With Observational Methods and Performance Assessment From Real-life Experience of Closed-Loop Insulin Delivery Systems (COMPARE-CLIDS) (NCT05932966); Study Record Beta ClinicalTrials.gov; France	Patients with type 1 diabetes; > 16 years old	Tandem Control-IQ system	Smart guard Medtronic 780 system	Observational study	NA	386	December 31, 2023

Trial name (registration number); link; country	Population; age	Intervention	Comparator(s)	Study design	Trial phase	Number of expected participants	Expected trial primary completion date
The Impact of Hybrid Closed-loop Insulin Delivery in Type 1 Diabetes on Glycemic Control and PROMs (INRANGE) (NCT04414280); Study Record Beta ClinicalTrials.gov ; Belgium	Patients with type 1 diabetes; ≥ 8 years older (Medtronic MiniMed 670G and 780G); ≥ 6 years old (Tandem t:slim X2 with Control-IQ)	Medtronic Minimed 670G	Medtronic Minimed 780G; Tandem t:slim X2 with Control-IQ	Observational cohort study	NA	1150	December 31, 2024
Closed Loop From Onset in Type 1 Diabetes (CLOuD) (NCT02871089); Study Record Beta ClinicalTrials.gov ; UK	Individuals with type 1 diabetes; 10 to 16 years old	CamAPS FX	MDI	Multicentre, single-period, parallel design RCT	NR	96	June 2023
Dexcom Hybrid Closed Loop Insulin Pump Study in Type 1 Diabetes (NCT05059860); Study Record Beta ClinicalTrials.gov ; UK	Individuals with type 1 diabetes; ≥ 18 years old	Tandem Control-IQ	Best practice in Scotland	Case- control	NA	30	February 2025
Two Way Crossover Closed Loop MPC vs Control IQ (NCT05799781); Study Record Beta ClinicalTrials.gov ; United States	Individuals with type 1 diabetes; ≥ 18 years old	Fully closed-loop MPC system	T:slim X2 pump with Control IQ	Two way Crossover RCT	NR	30	April 30, 2024
Efficacy of Closed-loop Insulin Therapy in Adults Prone to Hypoglycemia (DCLP2) (NCT04266379); Study Record Beta ClinicalTrials.gov ; France	Individuals with type 1 diabetes with hypoglycemia; ≥ 18 years old	Tandem Control-IQ	SAP therapy	Parallel RCT	NR	72	November 3, 2022

Trial name (registration number); link; country	Population; age	Intervention	Comparator(s)	Study design	Trial phase	Number of expected participants	Expected trial primary completion date
Pregnancy Intervention With a Closed-Loop System (PICLS) Study (PICLS) (NCT03774186); Study Record Beta ClinicalTrials.gov ; United States	Women with type 1 diabetes; 18 to 45	HCL	SAP therapy	Two-centre, open-label, single blind, Parallel RCT	NR	47	March 2022
Artificial Pancreas Technology to Reduce Glycemic Variability and Improve Cardiovascular Health in Type 1 Diabetes (WBH002) (NCT05653518); Study Record Beta ClinicalTrials.gov ; United States	Individuals with type 1 diabetes; 18 to 40 years old	Tandem t:slim X2 with Control-IQ Technology	SAP therapy	Parallel RCT	NR	40	November 30, 2025
Effect of Automated Insulin Delivery on Early-stage Diabetic Complications (AID-Comp) (NCT05477030); Study Record Beta ClinicalTrials.gov ; Italy	Patients with type 1 diabetes; ≥ 18 years old	Medtronic Minimed 780G	SAP therapy with PLGS	Open-label, Parallel RCT	NR	52	January 31, 2023
Automated Insulin Delivery Among Pregnant Women With Type 1 Diabetes (AiDAPT) (NCT04938557); Study Record Beta ClinicalTrials.gov ; UK	Pregnant women with type 1 diabetes; 18 to 45 years old	Automated closed-loop insulin delivery system	Standard insulin delivery system including an insulin pump without closed loop (CSII or MDI)	Multicentre, open-label, two-arm parallel RCT	NR	124	June 30, 2023

Trial name (registration number); link; country	Population; age	Intervention	Comparator(s)	Study design	Trial phase	Number of expected participants	Expected trial primary completion date
Closed-loop Insulin Delivery in Pregnant Women With Type 1 Diabetes (CRISTAL) (NCT04520971); Study Record Beta ClinicalTrials.gov; Belgium, Netherlands	Pregnant women with type 1 diabetes; 18 to 45 years old	Minimed Medtronic 780G	Standard care (continue with current treatment of insulin pump without closed loop or MDI)	Multicentric, open-label parallel RCT	NR	95	May 2023
Multi-centre Trial in Adult and Pediatric Patients With Type 1 Diabetes Using Hybrid Closed Loop System and Control at Home (NCT02748018); Study Record Beta ClinicalTrials.gov; Canada, France, Germany, Italy, New Zealand, Spain, Sweden, UK, United States	Individuals with type 1 diabetes; 2 to 80 years old	HCL (Minimed 670G and 770G insulin pump)	Current treatment (CSII, MDI, or SAP)	Multicentre, parallel RCT	NR	280	July 2023

AP = artificial pancreas; CGM = continuous glucose monitoring; CSII = continuous subcutaneous insulin infusion; HCL = hybrid closed-loop MDI = multiple daily injections MPC = model predictive control; NA = not applicable; NR = not reported; NRS = nonrandomized study; PLGS = predictive low glucose suspend system; RCT = randomized controlled trial; SAP = sensor augmented pump.

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