

Clinical Endpoints Review:

Devices for Self-management of Type 1 and Insulin-Dependent Type 2 Diabetes



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No financial conflicts to disclose

CER Overview: Glycemic Control

- Two key measures
 - (Hb)A1c: % red blood cells with sugar-coated hemoglobin. Usually averaged over the past 3 months
 - Glycemic variation, i.e., incidence of hyper-/hypoglycemia
- Optimal blood glucose range: 70-180 mg[of sugar]/dL[of blood]
- Hypoglycemia: key issue for older adults
 - Hospital admission rates for hypoglycemia > those for hyperglycemia
 - Dizziness, weakness, trouble speaking, confusion
- Hyperglycemia: can cause ketoacidosis

CER Overview:

Devices for Management of Diabetes

- May be appropriate for patients with Type 1 or insulin-dependent Type 2 diabetes
- Devices included in the CER
 - Continuous glucose monitors (CGMs)
 - Insulin pumps
 - Closed loop systems (CLS),
 - Also called ‘hybrid closed-loop systems’, ‘automated insulin delivery systems’, ‘bionic pancreas’, ‘artificial pancreas’
 - CLS devices incorporate a CGM

CER Methods

- Searched published literature (Embase and PubMed databases), 2018-2023
- Collected research reports on the 3 device types
- Included
 - Systematic reviews of clinical studies
 - Formal consensus statements
 - Prospective clinical trials (RCTs, nonrandomized, single-arm)
- Excluded
 - Case report/case series, cross-sectional, case-control
 - Retrospective
 - Prospective observational studies
- Selection criteria matter if important endpoints/outcomes were missed – Panel Subcommittee considered omissions

Summary of CER Findings: Details

See details in Tables A1, A2 and B
“Executive Summary, Clinical Endpoints Review”
(posted online)

Summary of Findings: Professional Consensus Statements

6
statements:
All Adults

- A1c, hypoglycemia, Level 2 hypoglycemia (6 statements)
- Time in range, Level 2 hyperglycemia (5 statements)

No minimal clinically important definitions (MCIDs) identified

1 statement:
Older Adults
(age ≥ 65 yrs)

- A1c, hypoglycemia, Level 2 hypoglycemia

However, target values have been defined (3 statements)

Summary of Findings: Primary Studies, Surrogate Markers

69 studies:
All Adults

Prioritized (most frequent) outcomes*:

- Time in range
- Level 1 hypoglycemia
- A1c
- Level 1 hyperglycemia

No MCIDs identified in a systematic review of glycemic outcomes

27 studies:
Older Adults
(age ≥ 65 yrs)

Prioritized (most frequent) outcomes:

- Time in range
- Level 1 hypoglycemia
- Level 1 hyperglycemia
- Level 3 hypoglycemia
- A1c

National Institute for Health and Clinical Excellence (UK) and American Diabetes Association: change in A1c of $>0.5\%$ is accepted as clinically significant

*13 additional surrogate markers were infrequently investigated

Summary of Findings: Primary Studies, Patient-Reported Outcomes

69 studies:
All Adults

Quality of life was investigated in 40 of 69 studies, 38 times as an exploratory endpoint.

27 studies:
Older Adults
(age ≥ 65 yrs)

Quality of life was investigated in 13 of 27 studies, always as an exploratory endpoint.

All 4 instruments identified in the CER have been validated; MCIDs have been identified for 3.

Summary of Findings: Primary Studies, Safety (Adverse Events)

69 studies:
All Adults

- Serious adverse events (13 studies)
- Any adverse event (9 studies)

27 studies:
Older Adults
(age ≥ 65 yrs)

- Serious adverse events (13 studies)
- Any adverse event (9 studies)

No MCIDs identified.

Summary of Findings: Primary Studies, Other Observations

- No studies evaluated more than 3 of the 5 endpoints most commonly recommended by professional associations, and few studies evaluated as many as 3.
- Difference in volume of citation

Level 2 hypoglycemia	more common in type 1 than in type 2 diabetes
Time in range	more common for CLS than for pump or CGM
CLS studies	more likely than pump or CGM studies to use level 2 or level 3 hypoglycemia as endpoints
Mean glucose and diabetic ketoacidosis	more likely in CLS studies than for pump or CGM
Time in range	the only endpoint to differ in frequency between studies that enrolled older adults (more frequent) than in studies that did not (less frequent)

Summary of Findings: 4 systematic reviews

- 3 reviews addressed A1C, time in range, and severe hypoglycemia
- 1 review addressed A1C and time in range
- 2 addressed patient-reported outcomes

For Additional Detail

Please refer to the
“Executive Summary, Clinical Endpoints Review”
document posted online.