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Hybrid closed loop systems for managing blood glucose levels in type 1 diabetes

Comments on the assessment consultation document

Diagnostics advisory committee

24 May 2023

NICE National Institute for Health and Care Excellence

Provisional recommendations (1)

1.1 Hybrid closed loop systems are recommended as an option for managing blood glucose levels in type 1 diabetes for people who are having difficulty managing their condition and have an average HbA1c of around 64 mmol/mol (8.0%) or more, despite optimal management with at least 1 of the following:

- continuous subcutaneous insulin infusion
- real-time continuous glucose monitoring
- intermittently scanned continuous glucose monitoring.

Hybrid closed loops systems are only recommended if the companies and NHS England agree a cost-effective price for the systems on behalf of the relevant health bodies

1.2 Hybrid closed loop systems are recommended as an option for managing blood glucose levels in type 1 diabetes for people who are pregnant or planning a pregnancy. Hybrid closed loops systems are only recommended if the companies and NHS England agree a cost-effective price for the systems on behalf of the relevant health bodies

Provisional recommendations (2)

1.3 Only use hybrid closed loop systems with the support of a trained multidisciplinary team experienced in continuous subcutaneous insulin infusion and continuous glucose monitoring in type 1 diabetes.

1.4 Only use hybrid closed loop systems if the person or their carer:

- understands and is able to use them
- is also attending a type 1 diabetes structured education programme.

1.5 These recommendations are not intended to affect use of hybrid closed loop systems that was started in the NHS before this guidance was published. People using hybrid closed loop systems outside these recommendations may continue until they and their NHS clinician consider it appropriate to stop. For children and young people, this decision should be made jointly by them, their clinician and their parents or carers.

Public consultation summary (1)

Over 300 stakeholders submitted comments, including:

- Patients and carers
- Diabetes Technology Network UK
- Families With Diabetes National Network
- National Children and Young People's Diabetes Network
- Healthcare professionals

Consultees and commentators:

- Diabetes UK
- Insulet International Ltd
- Juvenile diabetes research foundation (JDRF)
- NHS England

Companies:

- Advanced Therapeutics (UK)
- CamDiab
- Dexcom International
- Medtronic
- Tandem Diabetes Care Inc.
- Ypsomed Limited

Clinical experts

Public consultation summary (2)

- Around 850 comments were received
- 24 topic themes:
  - Access and equality
  - Compatibility with TA151
  - Comparator
  - Complications
  - Cost effectiveness and model
  - Costs
  - Children and young people
  - Editorial
  - Evidence
  - General
  - Hypoglycaemia
  - Implementation
  - Innovation
  - Mental burden
  - Multiple themes
  - Other measurement criteria
  - Other subgroups
  - Pregnancy
  - Quality of life
  - Recommendations
  - Structured education
  - Supportive
  - Technology
  - Threshold

Comments presented have been edited for length and clarity. Numbers of comments in each theme are approximate

EAG addendum

The EAG did extra analyses following consultation comments:

- Updated technology and complication costs
- Updated analysis on NSHEs and SHEs
- Indirect comparison of isCGM versus rtCGM
- Regression analyses on net effect on HbA1c by baseline HbA1c
- Updated cost-effectiveness results (adults and children)

EAG addendum: technology costs

- The previous EAG report incorrectly applied the costs of the Freestyle Libre 3 to CSII+isCGM. The addendum applies costs of the Freestyle Libre 2, and takes into account costs of Dexcom One.
- The EAG has estimated costs for CSII+isCGM by using the CSII+rtCGM costs and substituting the NHS drug tariff isCGM sensor and rtCGM transmitter costs.
- The costs for HCL and CSII+rtCGM have been provided by NHS supply chain. These do not include any volume discounts or any proposed future discounts.
- The previous EAG costings slightly inflated the costs of HCL systems to take into account some sensors not lasting their full lifespan. All the companies have since indicated that users can phone for a free replacement sensor should this occur. The addendum removes this element.
- It is assumed that only 10% of Dexcom 6 users require a receiver.
- Market share estimates have been provided by Professor Partha Kar

EAG addendum: technology costs

HCL system costs	Year 1	Years 2-4	4 Year	Share
Ypsomed/Dexcom G6/CamAPS	£8,171	£5,706	£25,289	10%
Advanced Therapeutics/Dexcom G6/CamAPS	£7,650	£4,975	£22,575	10%
Air Liquide/Dexcom G6/CamAPS	£7,785	£4,980	£22,724	18%
Medtronic (780G/Guardian 4)	£8,051	£4,768	£22,355	63%

CSII+rtCGM system costs	Year 1	Years 2-4	4 Year	Share
CSII+rtCGM: Freestyle Libre 3				3%
Ypsomed	[redacted]	[redacted]	[redacted]	33%
Medtronic				33%
Insulet				33%
CSII+rtCGM: Dexcom G6				97%
Ypsomed	[redacted]	[redacted]	[redacted]	33%
Medtronic				33%
Insulet				33%

CSII+isCGM system costs	Year 1	Years 2-4	4 Year	Share
CSII+isCGM: Freestyle Libre 2				80%
Ypsomed	[redacted]	[redacted]	[redacted]	33%
Medtronic				33%
Insulet				33%
CSII+rtCGM: Dexcom One				20%
Ypsomed	[redacted]	[redacted]	[redacted]	33%
Medtronic				33%
Insulet				33%

EAG addendum: technology costs

Base case costs – weighted average	Year 1	Years 2-4	4 Year	Annual
HCL	£7,976	£4,920	£22,735	£5,684
CSII+rtCGM	£6,675	£4,891	£21,348	£5,337
CSII+isCGM	£4,951	£3,168	£14,454	£3,614
CSII+CGM pooled (90% CSII+isCGM)	£5,124	£3,340	£15,144	£3,786

Scenario – lowest cost system	Year 1	Years 2-4	4 Year	Annual
HCL	£8,051	£4,768	£22,355	£5,589
CSII+rtCGM	£7,205	£4,319	£20,163	£5,041
CSII+isCGM	£5,482	£2,596	£13,270	£3,317
CSII+CGM pooled (90% CSII+isCGM)	£5,654	£2,768	£13,959	£3,490

	Description	Net QALY	Net Cost	ICER
BASE	Base case – weighted average technology costs	0.332	£33,802	£101,753
BASE	Base case – least costly system costs	0.332	£37,246	£112,118

Question: How reasonable is the market share data?
Question: Which technology costs are the most appropriate – is use of market share data appropriate or would the cheapest system be mainly used?

EAG addendum: complication costs

- **The EAC applies the cost for stroke in the year of the event at £4,728 and £175 in subsequent years. To provide comparison, average per patient costs of £15,000 - £30,000 (Youman et al. 2002), and separately £13,452 in year one to £17,963 after five years (Xu et al. 2018) … reported in the published literature.**

The EAG revised its base case costs of stroke estimates to the UKPDS 84 health care costs for a 40 year old female, providing scenarios of (A) the UKPDS 84 health care costs for a 60 year old female, (B) adding 30% of the social care costs of £5,125 for the first year and £2,726 in subsequent years and (C) applying the original EAG report costs to illustrate the effect of this change.

Gender	Male (40 years)	Male (60 years)	Female (40 years)	Female (60 years)
Non-fatal stroke	£5,610	£7,989	£6,011	£8,360
History of stroke	£625	£1,030	£673	£1,115
Fatal stroke	£3,517	£4,044	£3,727	£4,198

	Description	Net QALY	Net Cost	ICER
BASE	Base case (40 year old female)	0.332	£33,802	£101,753
SA03A	Stroke costs 60 year old	0.332	£33,784	£101,697
SA03B	Stroke costs with social care costs	0.332	£33,778	£101,681
SA03C	Stroke costs previous EAG base case	0.332	£33,817	£101,799

Question: Which assumption around stroke costs is the most appropriate?

EAG addendum: complication costs

There is concern that the IQVIA core diabetes model overestimates complication events, including end stage renal disease (371%), retinopathy (152%), neuropathy (131%) and cardiovascular disease (174%) compared with those observed in the DCCT/EDIC study (McEwan et al. 2014). The EAG presents a scenario analysis that reduces these costs proportionately to their overestimation.

	Description	Net QALY	Net Cost	ICER
BASE	Base case	0.332	£33,802	£101,753
SA06	Adjusted complication costs	0.332	£35,617	£107,215

Question: Which complication costs are the most appropriate?

Quality of life: 21 comments

- The closed loop system has completely changed my life. It has allowed me to carry on working in my job as an NHS nurse, a job I have 20 years experience in but was struggling to manage. It has reduced my time in hospital as inpatient and outpatient, allowed me to continue to contribute to society as professional care giver and as a tax payer rather than being a recipient of benefits and care.
- The control IQ technology has taken away so much of the fear and effect of night time hypos/hypers.
- I do not believe the quality adjusted life year figure used in the analyses takes full consideration of the benefits gained from better sleep with no CGM alarms for both patient and partner, improved quality of family life without having to deal with both severe and non-severe hypos, reduced worry about diabetes complications, reduction/exclusion of hypoglycaemic episodes interrupting daily life.
- With Omnipod 5, adults experienced a significant reduction in diabetes distress ($p<0.0001$) on the Type 1 Diabetes Distress Scale (T1DDS) (Polonsky 2022). This type of evidence indicates that the impact on mental burden of diabetes is an important factor without which the cost effectiveness of HCL cannot reliably be estimated.

Cost effectiveness and model (1): 25 comments

- **It is concerning to use the same base case from the EAG report for evaluating the cost-effectiveness of HCL systems in patients with type 1 DM … despite the … exclusion of SHE and NSHE events from the base case.**
- **The EAC has assumed NSHE have no cost to the NHS. Brod et al (2011) and Orozco-Beltran et al. (2014) report that 8% - 25% of NSHE are associated with additional HCP appointments in people with T1D … this could represent a substantial cost to the NHS.**

Exploratory annual rates of severe hypoglycaemic events (SHEs) and non-severe hypoglycaemic events (NSHEs)

	NSHEs		SHEs
	NMA and NG17	NMA alone	NMA alone
HCL	20.80	20.80	0.26
CSII+rtCGM	25.43	25.43	0.26
CSII+isCGM	24.03	1.60	0.39

The EAG exploration of hypoglycaemic events uses Gordon et al. to value NSHEs and Nauck et al. to value SHEs. Scenarios using only Gordon et al. and the historically more commonly applied Currie et al. are presented. A scenario that doubles the disutilities associated with hypoglycaemic events (to account for carer disutility) is presented.

In common with other NICE assessments, inc. NG17, the EAG previously assumed that NSHEs result in no costs to the NHS or PSS. The EAG now presents a scenario that costs NSHEs at £5 per event.

EAG addendum: NSHEs and SHEs

	Description	Net QALY	Net Cost	ICER
BASE	Base case (no NSHEs or SHEs included)	0.332	£33,802	£101,753
SA07A	NSHEs HCL 20.8 annual	0.337	£33,802	£100,307
SA07B	NSHEs HCL 57.2 annual	0.338	£33,802	£100,004
SA07C	NSHEs HCL 13.0 annual	0.336	£33,802	£100,538
SA07D	NSHEs HCL 90.0 annual	0.338	£33,802	£99,967
SA08	SA07A plus SHEs	0.399	£33,358	£83,520
SA13	SA08 with NSHEs from NMA	0.349	£33,358	£95,615

Question: Should NSHEs and SHEs be included in the model? If so, at what annual rate?

SA08	NSHEs: Gordon; SHEs: Nauck	0.399	£33,358	£83,520
SA09A	SA08 using Currie values	0.384	£33,358	£86,907
SA09B	SA08 using Gordon values	0.343	£33,358	£97,310
SA12	SA08 with double HE disutility	0.467	£33,358	£71,491

Question: If included, how should NSHEs and SHEs be valued?

SA08	NSHEs: no cost; SHEs: £1.83 (no medical attention)/£542 (medical attention; 37.9%)	0.399	£33,358	£83,520
SA10A	SA08 with £36/£628 SHE cost	0.399	£33,242	£83,230
SA10B	SA08 with £381 SHE cost	0.399	£32,982	£82,580
SA11	SA08 with NSHE cost £5	0.399	£33,069	£82,797

Question: If included, how should NSHEs and SHEs be costed?

Cost effectiveness and model (2): 25 comments

- **The present health economic calculations using RCTs data are flawed… The… efficacy assessment utilised exclusively RCTs which applied [rtCGM] in the comparator group but costed [isCGM] in the comparator for the health economic calculations. This is incorrect unless it can be demonstrated that a therapy with [isCGM] and [rtCGM] provide the same outcomes… The health economic calculations should have used [rt]CGM in the comparator and not [is]CGM.**

EAG addendum analysis: isCGM vs rtCGM

- 15 studies in updated NMA (see addendum table 7)
- Studies were heterogeneous and rtCGM compared with isCGM involved people on MDI and/or pump therapy
- For the overall weighted mean HbA1c baseline of around 7.8%, the NMA estimated a net effect for HCL over CSII+rtCGM of -0.28%
- The NMA net HbA1c effect for rtCGM compared with isCGM was -0.36%

Reference CSII+CGM	HbA1c %	Time in range (% between 3.9-10 mmol/l)	Time above range (% above 10 mmol/l)	Time below range (% below 3.9 mmol/l)	Time below range (% below < 3.0 mmol/l)
HCL	-0.26 (-0.41, -0.10)	8.38 (6.26, 10.50)	-7.83 (-11.18, -4.49)	-0.47 (-3.15, 2.21)	-0.03 (-0.20, 0.14)
rt-CGM	0.02 (-0.15, 0.19)	-0.22 (-2.75, 2.30)	-0.57 (-4.39, 3.24)	0.36 (-2.61, 3.34)	-0.03 (-0.26, 0.19)
is-CGM	0.38 (0.15, 0.62)	-6.27 (-10.24, -2.31)	5.12 (-0.70, 10.95)	-3.91 (-8.02, 0.20)	0.29 (-0.05, 0.64)

EAG addendum: HbA1c regression analysis (1)

- 9 studies were considered for inclusion in the unweighted regression analysis: 7 RCTs and 2 single arm studies
- 1 RCT (Steno 780G study) abstract was submitted by Medtronic. The EAG were unable to weight the Steno trial because of missing data, and therefore the weighted regressions do not include this study
- 7 RCTs were considered for inclusion in the weighted regressions: 5 compared HCL with CSII+rtCGM (Benhamou, Boughton, Tauschmann, Ware A, Ware B), and 2 compared HCL with CSII+CGM (Thabit (adults), Thabit (children)).
- The regression selected for the economic analysis used Benhamou assuming a baseline of 7.69%, weighted studies by their standard errors and omitted the Thabit studies (see pages 4 to 16 of addendum).
- The regression estimated a net effect size of around -0.34% at a baseline of 7.8% for HCL vs. CSII+rtCGM. The EAG applied the slope parameter of the regression to the central NMA estimate (-0.28% at a mean baseline of 7.8%).
- This resulted in the following estimated net effect sizes for HCL vs CSII+rtCGM by baseline HbA1c:

Exploration of HbA1c net effect by baseline HbA1c: HCL vs CSII+rtCGM

Baseline HbA1c (%)	7.4	7.6	7.8	8.0	8.2	8.4	8.6	8.8	9.0
Net HbA1c (%)	-0.21	-0.24	**-0.28**	-0.32	-0.35	-0.39	-0.42	-0.46	-0.49

EAG addendum: HbA1c regression analysis (2)

When the net effects of HCL vs CSII+rtCGM from the previous table are coupled with the net effect of CSII+rtCGM vs CSII+isCGM of -0.36% from the NMA this results in the following net effects by baseline HbA1c (single regression [SA01]):

Using single regression: modelled effect sizes by baseline HbA1c (SA01)

Baseline HbA1c (%)	7.4	7.6	7.8	8.0	8.2	8.4	8.6	8.8	9.0
CSII+isCGM (%)	0.00	0.00	**0.00**	0.00	0.00	0.00	0.00	0.00	0.00
CSII+rtCGM (%)	-0.36	-0.36	**-0.36**	-0.36	-0.36	-0.36	-0.36	-0.36	-0.36
HCL (%)	-0.57	-0.60	**-0.64**	-0.68	-0.71	-0.75	-0.78	-0.82	-0.85

The above analyses do not apply any adjustment for the effect of baseline HbA1c on the net effect of rtCGM compared with isCGM. The EAG views this regression as highly uncertain and unreliable. Also… much of the comparison was between MDI+rtCGM and MDI+isCGM rather than between CSII+rtCGM and CSII+isCGM.

EAG addendum: HbA1c regression analysis (3)

- The regression estimated a net effect size of around -0.30% at a baseline of 7.5% for CSII+rtCGM vs CSII+isCGM. The EAG applied the slope parameter of the regression to the central NMA estimate (-0.36% at a mean baseline of 7.5%).
- This resulted in the following estimated net effect sizes for CSII+rtCGM vs CSII+isCGM by baseline HbA1c:

Baseline HbA1c (%)	7.4	7.6	7.8	8.0	8.2	8.4	8.6	8.8	9.0
Net HbA1c (%)	-0.35	-0.37	-0.38	-0.40	-0.42	-0.43	-0.45	-0.46	-0.48

- When the net effects of CSII+rtCGM vs CSII+isCGM are coupled with the net effects for HCL vs CSII+rtCGM this results in the following net effects for by baseline HbA1c (using both regressions [SA02]):

Baseline HbA1c (%)	7.4	7.6	7.8	8.0	8.2	8.4	8.6	8.8	9.0
CSII+isCGM (%)	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
CSII+rtCGM (%)	-0.35	-0.37	-0.38	-0.40	-0.42	-0.43	-0.45	-0.46	-0.48
HCL (%)	-0.56	-0.61	-0.66	-0.71	-0.77	-0.82	-0.87	-0.92	-0.97

Questions: Should a regression be applied?
Should the single HCL-rtCGM regression of net change by baseline HbA1c be applied?
Should both HCL-rtCGM and rtCGM-isCGM regressions of net change by baseline HbA1c be applied?

EAG addendum: HbA1c regression results (1)

The EAG pooled the modelled results for CSII+isCGM and CSII+rtCGM with their total costs and total QALYs being weighted 90% and 10% respectively.

Pooled analysis: HCL vs CSII+CGM: weighted average costing using HCL-rtCGM regression

	Description	Net QALY	Net Cost	ICER
BASE	Base case	0.332	£33,802	£101,753
SA01A	HCL-rtCGM regression, baseline HbA1c 7.4%	0.228	£36,109	£158,444
SA01B	HCL-rtCGM regression, baseline HbA1c 7.6%	0.273	£35,410	£129,896
SA01C	HCL-rtCGM regression, baseline HbA1c 7.8%	0.292	£34,249	£117,410
SA01D	HCL-rtCGM regression, baseline HbA1c 8%	0.331	£33,500	£101,146
SA01E	HCL-rtCGM regression, baseline HbA1c 8.2%	0.386	£32,522	£84,231
SA01F	HCL-rtCGM regression, baseline HbA1c 8.4%	0.398	£31,496	£79,037
SA01G	HCL-rtCGM regression, baseline HbA1c 8.6%	0.415	£30,049	£72,478
SA01H	HCL-rtCGM regression, baseline HbA1c 8.8%	0.467	£28,591	£61,222
SA01I	HCL-rtCGM regression, baseline HbA1c 9%	0.541	£27,207	£50,243

EAG addendum: HbA1c regression results (2)

Pooled analysis: HCL vs CSII+CGM: weighted average costing using HCL-rtCGM and rtCGM-isCGM regressions

	Description	Net QALY	Net Cost	ICER
SA02A	HCL-rtCGM and rtCGM-isCGM regressions, baseline HbA1c 7.4%	0.247	£36,335	£146,869
SA02B	HCL-rtCGM and rtCGM-isCGM regressions, baseline HbA1c 7.6%	0.280	£35,392	£126,265
SA02C	HCL-rtCGM and rtCGM-isCGM regressions, baseline HbA1c 7.8%	0.309	£34,095	£110,341
SA02D	HCL-rtCGM and rtCGM-isCGM regressions, baseline HbA1c 8%	0.334	£33,287	£99,544
SA02E	HCL-rtCGM and rtCGM-isCGM regressions, baseline HbA1c 8.2%	0.394	£32,331	£82,058
SA02F	HCL-rtCGM and rtCGM-isCGM regressions, baseline HbA1c 8.4%	0.426	£30,852	£72,371
SA02G	HCL-rtCGM and rtCGM-isCGM regressions, baseline HbA1c 8.6%	0.460	£29,827	£64,883
SA02H	HCL-rtCGM and rtCGM-isCGM regressions, baseline HbA1c 8.8%	0.519	£28,603	£55,112
SA02I	HCL-rtCGM and rtCGM-isCGM regressions, baseline HbA1c 9%	0.590	£26,696	£45,277

Threshold: 128 comments

- **Access should be available to all Type 1 patients**
- **…my good control is achieved by an almost obsessive level of monitoring my glucose levels, and depriving myself of most carbs …it is so demotivating to know that by living so strictly I am depriving myself of the technology that could enable me to live more freely.**
- **…the closed loop system could improve my quality of life greatly so it seems very unfair that I am being denied access to this because my blood sugar is too well controlled.**
- **There is a real risk that patients do themselves harm by allowing their condition to deteriorate in order to qualify for the freedom afforded by hybrid closed loop systems.**

Mental burden: 58 comments

- **This is a condition that requires CONSTANT monitoring, awareness and cautiousness (of what we eat, insulin dose, activities we do etc). It isn't just a mental load, it's mentally exhausting and debilitating.**
- **...I suffer with lack of sleep due to CGM alarm waking me due to hypos through the night, and through the day, and I am constantly recalculating insulin doses trying to solve hypos, and it has caused very low mood, exhaustion, and anxiety...**
- **The stress of T1D and managing glucose levels is playing a part in increasing depression leading to more suicide attempts.**
- **Mental health should also play a part in how people are assessed for eligibility.**

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Hypoglycaemia: 20 comments

- Can consideration be given to people who have difficulty managing their diabetes due to disabling hypos that impact on their quality of life/ability to work etc. This group are often achieving a HbA1c below these targets due to the number of hypos they are experiencing
- NICE guidance TA151 makes clear that insulin pump therapy is recommended as a treatment option for adults and children 12 years and older with T1D who experience disabling hypoglycaemia.

Other measurement criteria (time in range): 16 comments

- **HbA1c can be a misleading metric... there is now evidence to suggest TIR is a more important and revealing metric... Two patients may have identical HbA1c results, but very different TIR. The... patient with lower TIR is at higher risk of complications.**
- **Time in Range (TIR) and Coefficient of Variation (%CoV) data... provide a more complete picture of diabetic control.**

Other subgroups: 36 comments

- Peri-menopausal and menopausal women
- Those with learning difficulties, impaired cognitive function due to age, mental health [conditions] or brain injury
- Those with several chronic health conditions on multiple treatments trying to cope with them all
- People with complications of diabetes
- During chemotherapy
- During puberty
- Those with extreme needle phobia
- Type 3c diabetes; cystic fibrosis related diabetes; those with a T2 diagnosis who are actually LADA/MODY
- Those already on pumps with CGM; those who are currently self-funding closed loop.

Compatibility with TA151: 6 comments

- **This is not compatible with current NICE recommendations for pump therapy (TA151), which is only possible in children aged under 12 years, and in those aged 12 years and over with an HbA1c over 69mmol/mol [8.5%].**
- **One fundamental issue is how this aligns with existing TA guidance specifically TA151 for Insulin Pumps… A specific aspect, that requires consideration, is the impact of the guidance on children under the age of 12 years. We would be grateful if HCL therapy could be considered as a treatment option for all children under the age of 12 years, regardless of their average HbA1c.**

Children and young people: 102 comments

- **There are significant additional challenges associated with managing T1D in younger children… recognising and expressing the symptoms of hypoglycaemia, unpredictability of eating patterns, frequent unscheduled activity, and changing insulin requirements associated with growth. HCL therapy provides additional clinical benefits, compared with standard insulin pump and CGM options, in overcoming these difficulties."**
- **HCL therapy is already viewed as standard practice in many centres, particularly for very young children, and there is a risk that this guidance will result in a backwards step in paediatric diabetes management… it will build in the requirement for a high HbA1c with the associated long-term effects on metabolic memory and risk of diabetes complications before this technology can be considered.**

3.11 The EAG's exploratory modelling in children and young people showed that HCL systems appear to be more cost effective than in adults… The committee concluded that although there was some uncertainty, HCL systems are likely to be more cost effective for children than adults

Previous EAG exploratory paediatric modelling: HbA1c (s.e.) changes

	NMA	NMA paed.
HCL	-0.28% (0.033%)	-0.31% (0.059%)
CSII+rtCGM	0.00%	0.00%

EAG addendum: Children and young people

Given the revised NMA… the EAG applied the NMA net effect for CSII+rtCGM over CSII+isCGM of -0.36% and the NMA net effect for HCL vs CSII+rtCGM of -0.31%. But it should be noted that all rtCGM vs isCGM studies were in an adult population.

CSII+isCGM	-0.00%
CSII+rtCGM	-0.36%
HCL	-0.67%

CSII+rtCGM may be used more in the paediatric population than in the adult population… Therefore, the EAG did exploratory analyses based upon a market share of 75% CSII+isCGM and 25% CSII+rtCGM.

	Description	Net QALY	Net Cost	ICER
BASE	Base case	0.378	£30,133	£79,664
SA01	0.045% annual worsening	0.442	£28,799	£65,119
SA02	Pittsburg CVD risk equations	0.331	£30,016	£90,614
SA03	Adjusted complication costs	0.378	£35,471	£93,778
SA04A	NSHEs HCL 20.8 annual	0.386	£30,133	£78,152
SA04B	NSHEs HCL 57.2 annual	0.387	£30,133	£77,773
SA04C	NSHEs HCL 13.0 annual	0.384	£30,133	£78,406
SA04D	NSHEs HCL 90.0 annual	0.388	£30,133	£77,690
SA05	SA04A plus SHEs	0.455	£29,637	£65,108
SA06A	SA05 using Currie values	0.448	£29,637	£66,082
SA06B	SA05 using Gordon values	0.392	£29,637	£75,595
SA07	SA05 HE QoL x3 10 years, x2 after	0.561	£29,637	£52,784

Pregnancy: 30 comments

- **I have been through 2 pregnancies with Type 1 diabetes and it is extremely difficult. I would wholeheartedly agree that this solution would benefit pregnant people.**
- **What is recommended after pregnancy? Continue or discontinue hybrid closed loop?**
- **How would we define “planning a pregnancy”?**
- **None of the current closed loop systems are licensed in pregnancy, the target glucose cannot be changed (factory setting) and therefore doesn’t fit with our current pregnancy guidelines**

1.2 Hybrid closed loop systems are recommended as an option for managing blood glucose levels in type 1 diabetes for people who are pregnant or planning a pregnancy.

Pregnancy: new evidence

- **I would like to draw the committees attention to the following… large randomised controlled trial currently on-going in the UK: NCT04938557 (Automated Insulin Delivery Amongst Pregnant Women With Type 1 Diabetes [AiDAPT])**

An open-label, multi-centre, randomized, two-arm parallel group trial comparing automated closed-loop and standard insulin delivery.

124 pregnant women between 18 and 45 years of age with Type 1 Diabetes of at least 12 months' duration on standard insulin delivery (CSII or MDI) will be recruited through outpatient antenatal diabetes clinics. Women fulfilling the eligibility criteria will be randomized to automated insulin delivery (AiD) or to continue standard patient-directed insulin delivery (CSII or MDI) without AiD.

Estimated completion date June 2023.

An abstract was provided to the EAG but it did not report data in a way that could be synthesised

Recommendations: 17 comments

- **...it is quite possible to have a reasonable HbA1c whilst having highly uncontrolled Type 1 diabetes (high - low swings, excessive hypoglycaemic episodes) it seems inappropriate to recommend the technology only if both factors are met. Please consider changing this to "or".**
- **..."optimal management" seems conflicting and unnecessary here. If someone is having difficulty managing their condition, or has an HbA1c above ... 6.5% let alone above ... 8.0%, then their management cannot be "optimal".**
- **..."having difficulty" is too easy [to] misinterpret. This should be a measure of the burden of diabetes, for example, how often the patient checks their glucose during the day, how often do they check their glucose during the night, how many corrections (insulin or glucose) do they make every day, do they restrict their diet solely to achieve their HbA1c value.**

1.1 Hybrid closed loop systems are recommended as an option for managing blood glucose levels in type 1 diabetes for people who are having difficulty managing their condition and have an average HbA1c of around 64 mmol/mol (8.0%) or more, despite optimal management with at least 1 of the following:

- continuous subcutaneous insulin infusion
- real-time continuous glucose monitoring
- intermittently scanned continuous glucose monitoring.

Structured education: 43 comments

- **We need to ensure we aren't disadvantaging those who are unable to attend a programme. (e.g., those unable to get time off due to work/carer roles and very often low socioeconomic conditions or proficiency in digital courses or unable to speak English)**
- **Improvements to the availability of, and access to, patient training are needed.**
- **I would suggest changing the wording to "offering approved structured education programmes (face to face or digital) or ensuring person with diabetes demonstrates equivalent competencies in functional insulin dosing".**
- **There is separate HCL specific education on how to bolus pre meals, how to identify infusion site failures and deal with illness … change to " attendance at HCL specific education"**

1.4 Only use hybrid closed loop systems if the person or their carer:

- understands and is able to use them
- is also attending a type 1 diabetes structured education programme.

Innovation: 3 comments

- **The principle of a closed loop system has been considered for decades to be the 'holy grail' of diabetes treatment short of a cure. To declare such a treatment option as 'not sufficiently innovative' is astonishing.**
- **This recent systematic review (Syeed et al 2022) includes eight criteria to determine innovation attributes. The algorithm used to integrate rtGCM data with CSII would fall within these criteria which would justify consideration of a higher ICER, namely, 'novelty, step-change, an improvement over existing technologies, substantial benefits, an improvement over existing technologies, convenience and/or adherence, added value, acceptable cost, and uncounted benefits'.**
- **The changes that HCL make to HbA1c coupled with QoL improvements are truly innovative from a patient/caregiver perspective**

3.15 … The committee concluded that although HCL systems provide an alternative treatment option for people with type 1 diabetes, the level of innovation is not sufficient to justify consideration of a higher ICER (over £20,000 per QALY gained).

Technology: 36 comments

- **Based on the evidence below, it cannot be assumed that insulin pumps are equivalent in terms of accuracy when delivering lower doses of insulin*.**
- **Clearly state in the guidance which commercially available systems are licensed for use in pregnancy and young**
- **We recommend that the wording is amended to make explicit reference to the need to adhere to a process of shared decision making between patients and clinicians in deciding which components and system is right for them.**

NICE DCD sections 2.5 and 2.6

* Ziegler et al. 2021; Ziegler at al. 2020; Girardot et al. 2020; Laubner et al. 2019

Costs: 21 comments

- **The final TA needs an accompanying resource template, broken down for each ICS.**
- **It is very unclear… what price point will need to be reached for this guideline to be agreed and published. This needs to be much clearer… as we anticipate that new systems will enter the market - ICB's / other decision makers will need clarity on whether each new system will be included in prescribable options.**
- **The EAG produced a threshold analysis to calculate the price that gives an ICER of £20,000… this has not been shared within the consultation so we do not have the opportunity to comment on this analysis. As this… is likely to inform pricing discussions with NHS England, we ask that it is shared with consultees along with the preferred assumption for the ICER of the Committee.**

1.1 …Hybrid closed loops systems are only recommended if the companies and NHS England agree a cost-effective price for the systems on behalf of the relevant health bodies.

Access and equality: 39 comments

- **Often T1Ds will travel considerable distances to attend clinic with the trained staff and the access to the technology they need. The postcode lottery also affects which HCL system the patient will be able to access.**
- **We had to apply 3 times for pump funding for our daughter - despite full support from the hospital team, the CCG kept refusing. In the end I had to involve my MP. Not everyone has the mental resilience or the economic status (access to laptop etc.) to be able to do this and it is unfair that you should have to.**
- **It is vital that the uptake of HCL should reflect the diversity of the T1 community. It would be a tragedy if the same inequalities in the uptake of CGM are seen with HCL, as the most deprived socioeconomic strata are likely to derive the most benefit.**
- **Some who have sight loss find using the various technologies difficult, as the technologies themselves often have no accessibility features. These systems seem to be no different.**

Implementation: 40 comments

- …should include a recommendation to NHSE and the other bodies in devolved nations, to consider funding resources for these devices. Many ICS already operate with funding challenges. Even if considered cost-effective, may systems may consider that such devices are not affordable without funding to support implementation. Without new funding stream, this may impact other service provision and/or other service users.
- We wondered if some advice about an initial step-wise approach to prioritisation of eligible patients would be useful.
- There is a need to increase capacity and capability of the healthcare professionals who will be implementing and supporting the use of the HCL systems.

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Additional consultation comments

Comments were also received and themed as:

- **Comparator (3 comments)**
- **Complications (4 comments)**
- **Editorial changes (19 comments)**
- **Evidence (6 comments, where relevant these have been discussed throughout)**
- **General (19 comments)**
- **Multiple themes (73 comments that covered more than 1 theme covered in this presentation)**
- **Supportive of the draft guidance (20 comments)**

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Thank you