NICE National Institute for Health and Care Excellence

NICE guidance

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

Technology appraisal guidance
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Your responsibility

The recommendations in this guidance represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, health professionals are expected to take this guidance fully into account, alongside the individual needs, preferences and values of their patients. The application of the recommendations in this guidance is at the discretion of health professionals and their individual patients and do not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the Yellow Card Scheme.

Commissioners and/or providers have a responsibility to provide the funding required to enable the guidance to be applied when individual health professionals and their patients wish to use it, in accordance with the NHS Constitution. They should do so in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

Contents

This guidance replaces DG21.

1 Recommendations

Access to hybrid closed loop systems will be through a 5-year phased roll out in line with NHS England's implementation plan. For enquiries about cost-effective pricing, contact Leigh.Carr@supplychain.nhs.uk.

1.1 Hybrid closed loop (HCL) systems are recommended as an option for managing blood glucose levels in type 1 diabetes for adults who have an HbA1c of 58 mmol/mol (7.5%) or more, or have disabling hypoglycaemia, despite best possible management with at least 1 of the following:

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

HCL systems are only recommended if they are procured at a cost-effective price agreed by the companies and NHS England, and implemented following NHS England's implementation plan.

1.2 HCL systems are recommended as an option for managing blood glucose levels in type 1 diabetes for children and young people. HCL systems are only recommended if they are procured at a cost-effective price agreed by the companies and NHS England, and implemented following NHS England's implementation plan.

1.3 HCL systems are recommended as an option for managing blood glucose levels in type 1 diabetes for women, trans men and non-binary people who are pregnant or planning to become pregnant. HCL systems are only recommended if they are procured at a cost-effective price agreed by the companies and NHS England, and implemented following NHS England's implementation plan.

1.4 Only use HCL systems with the support of a trained multidisciplinary team experienced in CSII and continuous glucose monitoring in type 1 diabetes.

1.5 Only use HCL systems if the person or their carer:

- is able to use them, and
- is offered approved face-to-face or digital structured education programmes, or
- is competent in insulin dosing and adjustments.

1.6 These recommendations are not intended to affect use of HCL systems that was started in the NHS before this guidance was published. People using HCL 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.

What this means in practice

HCL systems must be funded in the NHS in England for the condition and populations in the recommendations, if they are considered the most suitable option for managing blood glucose levels. HCL systems must be funded in England within 5 years of final publication of this guidance.

There is enough evidence to show that HCL systems provide benefits and value for money, so they can be used routinely across the NHS in these populations.

The choice of components or system is based on a person's preference and whether the system has the appropriate licence for use. Whether HCL systems are licensed for use in pregnancy or in children or young people may differ.

NICE has produced tools and resources to support the implementation of this guidance.

Why the committee made these recommendations

Standard care for type 1 diabetes involves regularly measuring blood glucose levels by self-monitoring (blood testing) or by using a continuous glucose monitor (real-time or intermittently scanned). Blood glucose levels are managed with multiple daily insulin injections or by using a pump to inject insulin under the skin (CSII). The aim of treatment is to decrease blood glucose levels and keep them within a healthy range.

Continuously managing blood glucose levels is a substantial mental burden for people with type 1 diabetes and their families or carers. HCL systems deliver insulin automatically using a calculation based on continuous glucose measurements. The systems do not need as much input from the person, but manual insulin dosing is still needed sometimes, for example, around mealtimes. So, they may reduce the mental burden and improve people's quality of life.

Clinical trial and real-world evidence shows that HCL systems are more effective than standard care at maintaining blood glucose levels within a healthy range.

There is uncertainty in the economic model, so the systems need to be procured at a cost-effective price agreed by the companies who manufacture HCL systems and NHS England. This will mean the HCL systems are likely to be cost effective for adults who have an HbA1c level of 58 mmol/mol (7.5%) or more, or have disabling hypoglycaemia (when hypoglycaemia occurs frequently or without warning, so the person is constantly anxious about having hypoglycaemic episodes). So, HCL systems are recommended for these people. HCL systems are likely to be more cost effective for children and young people than adults, so they are also recommended for children and young people irrespective of their HbA1c level. And because blood glucose levels are harder to manage in pregnancy, they are also recommended for women, trans men and non-binary people with type 1 diabetes who are pregnant or planning to become pregnant.

2 Information about hybrid closed loop systems

Clinical need and practice

Type 1 diabetes

2.1 It is estimated that approximately 400,000 people in the UK are living with type 1 diabetes, including around 29,000 children. In type 1 diabetes, a person's blood glucose level becomes too high (hyperglycaemia) because there is no, or very little, production of insulin by the pancreas. Blood glucose levels can only be regulated by giving insulin to prevent hyperglycaemia. If type 1 diabetes is not well controlled, people are at increased risk of long-term complications of hyperglycaemia, including microvascular damage such as retinopathy and blindness, nephropathy and neuropathy. They are also at increased risk of macrovascular complications such as ischaemic heart disease, stroke and peripheral vascular disease.

2.2 The goal of treating type 1 diabetes is to keep blood glucose within a healthy range by providing the body with supplemental insulin. If the level of circulating insulin becomes too high, blood glucose levels can become too low leading to hypoglycaemia (also known as a hypo).

2.3 Managing type 1 diabetes usually involves:

- regularly measuring blood glucose levels
- multiple daily insulin injections or continuous subcutaneous insulin infusion (CSII)
- lifestyle adjustments
- periodic assessment of blood glucose control.

Blood glucose monitoring can be done by self-monitoring (capillary blood

testing), or by real-time continuous (rtCGM) or intermittently scanned continuous glucose monitors (isCGM). Long term monitoring of blood glucose control can be done by measuring HbA1c level, which reflects the average plasma glucose over the last 8 to 12 weeks. Time in range is a measure of blood glucose control that shows the percentage of time a person spends within a target glucose range (3.9 to 10 mmol/litre). Time below range (less than 3.9 mmol/litre) is associated with increased risk of severe hypoglycaemia. Time above range (more than 10 mmol/litre) indicates increased risk of complications and diabetic ketoacidosis.

2.4 NICE's recommendations on blood and plasma glucose in type 1 and type 2 diabetes in children and young people, type 1 diabetes in adults and diabetes in pregnancy recommend that people with type 1 diabetes should aim for a target HbA1c level of 48 mmol/mol (6.5%) or lower, or an individualised target set in pregnancy, to minimise the risk of long-term complications from diabetes. In practice, an individualised HbA1c target, taking into account the risk of hypoglycaemia, may be agreed with people with diabetes and carers.

The interventions

2.5 Hybrid closed loop (HCL) systems use a mathematical algorithm to deliver insulin automatically in response to continuously monitored interstitial fluid glucose levels. They use a combination of real-time glucose monitoring from a continuous glucose monitor (CGM) device and a control algorithm to direct insulin delivery through CSII. Different HCL systems are available, and some are built by combining interoperable components from different companies. Because of the large number of combinations of components available to the NHS, this appraisal considers HCL systems as a class of technologies rather than individual components or systems. Expert advice received by NICE during scoping suggested that in practice, minimal differences in outcomes would be expected between systems if used as intended. The choice of components or system is based on a person's preference and whether the system has the appropriate licence for use. Whether HCL systems are licensed for use in pregnancy or in children or young people may differ. Any future systems comprised of components from different manufacturers must show interoperability and be equivalent to current systems in terms of patient benefits.

2.6 At the time of scoping the following systems and interoperable components were available:

- SmartGuard control algorithm (Medtronic) with Guardian 4 CGM sensor (Medtronic) and MiniMed 780G insulin pump (Medtronic). These components are not available for use with components from other companies.
- Control IQ control algorithm (Tandem Diabetes Care/Air Liquide) with Dexcom G6 CGM sensor (Dexcom) and t:slim X2 insulin pump (Tandem Diabetes Care/Air Liquide).
- CamAPS FX control algorithm (CamDiab) with Dexcom G6 CGM sensor (Dexcom) and either:
  - DANA i insulin pump (Advanced Therapeutics UK Ltd) or
  - mylife YpsoPump (Ypsomed).

  This is not an exhaustive list, and other systems and interoperable components are available.

The comparators

2.7 There are 2 comparators:

- CSII plus rtCGM (non-integrated)
- CSII plus isCGM (non-integrated).

Price

2.8 A range of HCL systems is available from different companies. Individual components of different systems are sometimes combined. The external assessment group received NHS supply chain costs for the various systems at April 2023 prices. A clinical expert provided market share estimates for the different systems. The appraisal model base case used a weighted average of the 4-year cost from various companies. This resulted in a 4-year total cost of

£22,735 and an average annual cost of £5,684.

2.9 To give an incremental cost-effectiveness ratio of £20,000 per quality-adjusted life year gained, the companies will need to agree discounts with NHS England, on behalf of the relevant health bodies, for HCL systems to be procured by the NHS. The size of the discounts will be commercial in confidence.

3 Committee discussion

The diagnostics advisory committee considered evidence from a number of sources. See the committee papers for full details of the evidence. After consultation, the external assessment group (EAG) updated the network meta-analysis and the economic model.

Clinical need

People with type 1 diabetes, families and carers

3.1 Patient experts explained that the mental load of living with diabetes is significant. This is because people with diabetes (and their parents or carers) look at a lot of data and have to make a lot of calculations and decisions about their insulin dose every day. This can be exhausting, can affect people's mood, and frequently leads to burn out. People with diabetes and their families can also be woken by continuous glucose monitor (CGM) alarms, causing sleep disruption. The patient experts explained that managing glucose levels is a lot of work and can affect home life, education, training or work. Although a CGM and continuous subcutaneous insulin infusion (CSII) can help maintain blood glucose control, if they are not integrated then this still involves substantial user input, which can be a mental burden. A parent of a child with diabetes said that the mental burden significantly affected their quality of life. They highlighted that children are less able to recognise the symptoms of hypoglycaemia and hyperglycaemia, and this is a constant worry for parents when they are apart from their children. They also explained that disrupted sleep was a significant problem, with parents waking multiple times a night to monitor their child's blood sugar and administer glucose or insulin. The committee concluded that managing type 1 diabetes is a substantial mental burden on people with diabetes and their families. It further concluded that automated technologies such as hybrid closed loop (HCL) systems can reduce some of the burden, and improve quality of life for people, their families and carers.

Inequalities

Access to technology and care

3.2 Access to technology and appropriate care was highlighted by patient experts as a major concern, and they explained that the process was often slow, frustrating and demoralising. Patient and clinical experts said access to technology is a postcode lottery. They also noted that there are inequality issues related to family background and socioeconomic status. Clinical experts said that the automation offered by HCL systems could help reduce some of the inequalities for people who find it difficult to maintain healthy blood glucose levels. These inequalities can include a language barrier, a lower level of education or a learning disability. A clinical expert said that NHS England (NHSE) has set out priorities for access, to help reduce these healthcare inequalities. A clinical expert also highlighted that the effective use of technologies was an important consideration. They said that improvements in the availability of and access to patient training were needed. They noted that many centres do not have enough trained staff in their clinical teams to provide patient training. The committee concluded that improvements were needed to make sure there was no postcode lottery in access to HCL systems and care. It further concluded that people should be supported to use the systems.

Clinical effectiveness

Evidence and generalisability

3.3 The EAG used 3 different sources to assess the clinical effectiveness of HCL systems. These were randomised controlled trials (RCTs), NHSE study data from adults (the NHSE adult pilot study), and NHSE study data from children and young people (the NHSE children and young adult pilot study). A clinical expert said that they had some concerns about patient recruitment in the RCTs. They noted that people in RCTs usually have more motivation and a better ability to self-manage their diabetes than some other people with diabetes in the NHS. The RCTs were small in terms of patient numbers and were heterogeneous. Most RCTs included children and young adults. The EAG said that the NHSE pilot

studies had limitations, because they were non-randomised, with a before-and-after study design and no control group. But the clinical experts explained that a strength of the pilot studies was that they included a broader range of people than are usually recruited to RCTs. One clinical expert explained that the NHSE adult pilot study selected centres from around the country, but these were skewed towards adults in lower socioeconomic areas. Some clinical experts and committee members said that the populations in the NHSE pilot studies were a better reflection of populations in NHS practice. This was because they included people who may find it difficult to meet glucose targets and who may experience more severe physical and psychological effects of type 1 diabetes. The committee concluded that both the RCTs and the NHSE adult pilot study were not fully generalisable to the type 1 diabetes population in the NHS.

Adult baseline characteristics

3.4 The baseline HbA1c levels differed between the RCTs and the NHSE adult pilot study. The people in the RCTs had lower HbA1c levels at baseline (56 mmol/mol to 67 mmol/mol [7.3% to 8.3%]) than in the NHSE adult pilot study (around 79 mmol/mol [9.4%]). A clinical expert explained that National Diabetes Audit data shows that over 65% of people with type 1 diabetes have an HbA1c of over 58 mmol/mol (7.5%). Clinical experts explained that people with higher HbA1c levels at baseline would be expected to have a greater reduction after treatment. Before consultation, the EAG's original network meta-analysis of the RCT data showed that HCL systems were associated with a decrease in HbA1c of 3.1 mmol/mol (-0.29 percentage points) compared with CSII plus CGM. But the NHSE adult pilot study reported a decrease in HbA1c of 16.2 mmol/mol (-1.5 percentage points). Some clinical experts said that they preferred the NHSE adult pilot baseline and HbA1c effect, because this was a better representation of real-world NHS practice. The committee concluded that for many people with type 1 diabetes in the NHS, the baseline HbA1c would likely be higher than that reported in the RCTs, so HCL systems may reduce HbA1c more than that estimated from the original RCT network meta-analysis. But the extent of the difference was highly uncertain. The committee further concluded that differences in baseline HbA1c levels between the RCTs and NHSE pilot studies led to substantial differences in the reported HbA1c change.

Effectiveness of rtCGM compared with isCGM

3.5 Most of the RCTs compared HCL systems with CSII plus real-time CGM (rtCGM). No RCTs compared HCL systems with CSII plus intermittently scanned CGM (isCGM). People in the NHSE adult pilot study had previously been on CSII plus isCGM before moving on to an HCL system. In the NHS most people use isCGM, so after consultation, the EAG did another network meta-analysis, which included a comparison between isCGM and rtCGM. The analysis included the RCTs from the network meta-analysis used before consultation, plus studies from NICE's guideline on type 1 diabetes in adults, which compared rtCGM with isCGM. The EAG said that the studies were heterogeneous, and those comparing rtCGM with isCGM included people having multiple daily injections with or without CSII. But it assumed that the net effect for rtCGM compared with isCGM would be the same as the net effect for CSII plus rtCGM compared with CSII plus isCGM. The weighted average HbA1c baseline from the studies in the analysis was around 62 mmol/mol (7.8%). The results showed that HCL systems were associated with a decrease in HbA1c of 3 mmol/mol (-0.28 percentage points) compared with CSII plus rtCGM. They also showed that CSII plus rtCGM was associated with a decrease in HbA1c of 4 mmol/mol (-0.36 percentage points) compared with CSII plus isCGM. The committee concluded that although these results are uncertain, they indicate an approximate difference in effect in HbA1c changes between HCL systems and CSII plus isCGM, and a difference in effect between rtCGM and isCGM.

Regression analyses of baseline HbA1c compared with change in HbA1c

3.6 The EAG did some exploratory regression analyses comparing baseline HbA1c with HbA1c change. This is because people with a higher baseline HbA1c are expected to have a greater reduction in HbA1c after using an HCL system than people with a lower baseline HbA1c. Two analyses were done: 1 for HCL systems compared with CSII plus rtCGM and 1 for CSII plus rtCGM compared with CSII plus isCGM. The effects from each of these were then coupled together to estimate the effect of HCL systems on HbA1c from baseline compared with CSII plus isCGM. The estimated HbA1c change at a baseline of 58 mmol/mol (7.5%) HbA1C between:

- HCL and CSII plus rtCGM was 2 mmol/mol (-0.23 percentage points)
- CSII plus rtCGM and CSII plus isCGM was 4 mmol/mol (-0.36 percentage points).

This gave a total HbA1c change of 6 mmol/mol (-0.59 percentage points). The EAG said that the regression analyses were highly uncertain because only 5 studies were included in the regression that provided the slope parameter. The studies were heterogeneous in terms of their design, duration, and age range of participants. The committee said that although the regression analyses were uncertain, they indicated a greater HbA1c effect size as the baseline HbA1c increases, which reflected what clinical experts expect to see in practice. It concluded that the regression analyses should be included in the economic modelling.

Population subgroups

Children and young people

3.7 Before consultation, the EAG's subgroup analyses showed that in the RCT children and young adults (under 18 years) subgroup, the change in HbA1c for HCL systems was greater (-0.31 percentage points, 95% confidence interval [CI] -0.43 to -0.20) than the adult subgroup (-0.24 percentage points, 95% CI -0.32 to -0.15). The NHSE children and young people pilot had a lower baseline HbA1c than the adult pilot study of around 62 mmol/mol (7.9%). The decrease in HbA1c after using HCL systems was lower than the adult pilot, at 7 mmol/mol (-0.7 percentage points) after using HCL systems for 6 months. Data was not presented on age groups specified in NICE's scope for HCL systems in type 1 diabetes (that is, 5 years and under, 6 to 11 years and 12 to 19 years). A clinical expert explained that in the NHSE children and young people pilot, child age subgroups were not reported because of the low numbers of children in certain age groups that were using devices.

Pregnancy

3.8 In the initial EAG report, there was only 1 small study on HCL systems' effectiveness in pregnancy. The EAG said that it was difficult to draw firm conclusions in this population. But the committee thought that there could be greater benefits of HCL systems in pregnancy, because blood glucose control is harder to maintain and there is a risk to both the mother and unborn baby. A clinical expert said that HbA1c is a less effective clinical measure of diabetes control in pregnancy. The committee noted that it would be difficult to do studies of HCL systems in pregnancy because the duration of pregnancy is relatively short. This would complicate study design and data collection. During consultation, new evidence was submitted to NICE on the results of the Automated insulin Delivery Amongst Pregnant women with Type 1 diabetes (AiDAPT) trial. This was an open-label, multicentre, randomised, 2-arm parallel group trial comparing HCL systems with standard insulin delivery (CSII or multiple daily injections) plus CGM. The primary outcome of the AiDAPT trial was the percentage of time in the pregnancy-specific glucose target range (3.5 to 7.8 mmol/litre). The results showed a statistically significant increase in time in the pregnancy-specific target range in the HCL systems group compared with the group having standard insulin delivery. The committee concluded that although there was limited evidence, the effectiveness of HCL systems in pregnancy would likely be greater than in the general adult population.

Economic model and cost effectiveness

Baseline characteristics and HbA1c effects

3.9 Before consultation, the EAG's base-case model key baseline characteristics used data from the 2019 to 2020 National Diabetes Audit subgroup for people on CSII. The baseline HbA1c from this data was 64 mmol/mol (8.0%) and the EAG applied the estimated HbA1c decrease from the RCT network meta-analysis of 3.1 mmol/mol (-0.29 percentage points). In separate scenario analyses the EAG used the NHSE adult pilot study baseline characteristics, with an HbA1c baseline of 79 mmol/mol (9.4%), and applied the HbA1c decrease from:

- the RCT network meta-analysis (3.1 mmol/mol [-0.29 percentage points]) or

- the NHSE pilot (16.2 mmol/mol [-1.5 percentage points]).

  When the NHSE adult pilot baseline characteristics and HbA1c effect were used, the resulting incremental cost-effectiveness ratio (ICER) was substantially lower than the original base case (£12,398 compared with £178,925 per quality-adjusted life year [QALY] gained). In the updated analysis the EAG updated the technology costs and included the difference in effectiveness between CSII plus rtCGM and CSII plus isCGM. This resulted in a base-case ICER of £101,753. The EAG did scenario analyses including a regression analysis (see section 3.6), which linked different baseline HbA1c values to changes in HbA1c. This resulted in ICERs ranging:

- from £158,444 for a baseline HbA1c of 57 mmol/mol (7.4%) with a 6 mmol/mol (-0.56 percentage point) reduction

- to £50,243 for a baseline HbA1c of 75 mmol/mol (9.0%) with an 11 mmol/mol (-0.97 percentage point) reduction.

  The committee said that all these analyses were useful to help understand how the ICER would change with different changes in HbA1c. It further noted that the change in HbA1c reported in the NHSE adult study pilot was a good representation of what could be achieved for people with higher HbA1c levels. In the EAG's original analysis, a baseline HbA1c of 79 mmol/mol (9.4%) and a reduction of 16.2 mmol/mol (-1.5 percentage points) showed HCL systems to be cost effective. But the committee said that using this data in the model would be equivalent to restricting HCL system access to people with much higher-than-average HbA1c levels. It noted that the RCTs showed that people with lower HbA1c levels could also benefit. So, the committee preferred a baseline HbA1c of 58 mmol/mol (7.5%) because this is a common clinical target for people who have a higher HbA1c. The studies used in the preferred regression analysis also had a mean baseline HbA1c of 7.5%. The committee recalled the uncertainty in the regression analyses and concluded that it was unclear what the true HbA1c effect estimate would be. Without any directly observed data, a decrease of 7 mmol/mol (-0.59 percentage points) from a baseline of 58 mmol/mol (7.5%) was a reasonable estimate. It further concluded that the change in HbA1c substantially affected the ICER and whether HCL systems could be considered cost effective.

Comparators

3.10 The population in the economic model was people on a single technology (CSII, rtCGM or isCGM). In the model they could then move to a non-integrated system or to an HCL system. The comparators used for the economic modelling were CSII plus rtCGM (non-integrated) and CSII plus isCGM (non-integrated). NICE's guideline on type 1 diabetes in adults recommends that people should be offered either rtCGM or isCGM, based on their individual preferences. A clinical expert explained that around 80% of people now have a CGM device. In the economic model base case, the EAG grouped the comparator technologies together as CGM plus CSII and assumed 90% of people were on isCGM and 10% were on rtCGM. In the exploratory analysis in children and young people, the EAG assumed 75% were on isCGM and 25% were on rtCGM. Clinical experts explained that in the clinical-effectiveness evidence, when it was reported, all comparators in the RCTs used rtCGM. They also said that rtCGM and isCGM are not the same in terms of cost or clinical effectiveness. The model was updated after consultation, and included HbA1c effect estimates for HCL systems compared with CSII plus rtCGM, and CSII plus rtCGM compared with CSII plus isCGM as part of a pooled comparator (see section 3.5).

Hypoglycaemic events

3.11 In the updated economic model, non-severe hypoglycaemic events and severe hypoglycaemic events were only included in scenario analyses. The EAG said that these annual event rates were highly uncertain. When non-severe and severe hypoglycaemic events were included, the ICERs were reduced from the base-case ICER of £101,753 per QALY gained to a range of between £71,491 and £97,310 per QALY gained. The position within the range depended on what source the EAG used for the hypoglycaemic event disutility values and how the events were costed. In 1 of the scenario analyses that included non-severe and severe hypoglycaemic events, the EAG costed non-severe hypoglycaemic events at £5 per event. This resulted in an ICER of £82,797 per QALY gained. The committee concluded that its preferred base case included non-severe and severe hypoglycaemic events, with non-severe events costed at £5 per event.

Uncaptured benefits: carer disutility

3.12 In the updated economic model, the EAG did an exploratory analysis for adults which doubled the quality-of-life effects associated with non-severe and severe hypoglycaemic events. This was done to account for the effects on carers and/or families. This reduced the ICER from the base case of £101,753 per QALY gained to £71,491 per QALY gained. In the EAG's updated exploratory modelling for children and young people, a scenario analysis included an estimate of carer disutility. In this analysis the quality-of-life effects associated with non-severe hypoglycaemic events and severe hypoglycaemic events were tripled for 10 years and then doubled for the remaining years. This was to account for the effect on quality of life for a child with type 1 diabetes, as well as the effect on 2 parents caring for the child. This reduced the ICER from the base case of £79,664 per QALY gained to £52,784 per QALY gained. The committee noted that these analyses were exploratory, because there was no good data to show the effect that HCL systems have on the quality of life of a person caring for someone with type 1 diabetes. It concluded that impact on carer quality of life could not be captured accurately in the modelling.

Uncaptured benefits: mental burden

3.13 Clinical experts expressed concerns that the reduced mental burden (see section 3.1) that HCL systems provide may not be captured adequately in the model. The committee considered a paper by Polonsky et al. (2022) which evaluated psychosocial outcomes for adults with type 1 diabetes using an automated insulin delivery system. The EAG explained that although this study reported improvements in various psychosocial outcomes such as diabetes distress, these could not be mapped onto EQ-5D for use in the economic model. The committee understood that there was no other quantitative evidence that could be used to estimate the value of these potential quality-of-life benefits. The committee agreed that there were potential quality-of-life benefits of HCL systems not captured in the model, including the effect on learning and education, ability to work, mental burden and fear of hypoglycaemic events. The committee concluded that because of these uncaptured benefits, the health economic model was likely to undervalue the effect of HCL systems on quality of life.

Time horizon and long-term effects

3.14 In the base-case economic model, the time horizon was 60 years and the effect on HbA1c was assumed to last for the duration of the model. The time horizon and HbA1c effect duration were key drivers of the model results. Scenarios that reduced the time horizon or duration of the HbA1c effect all resulted in higher ICERs. Some clinical experts said that they would expect the improvements in HbA1c to be maintained. The committee concluded that although there were uncertainties in the modelling of long-term effects and that this may have overestimated the cost effectiveness, it agreed with the time horizon of 60 years and the lasting HbA1c effect.

Complication rates and costs

3.15 Before consultation, the EAG's economic analysis used costs related to stroke from NICE's guideline on type 1 diabetes in adults, which were £4,728 in the first year, £175 in subsequent years, and £1,332 for death from stroke within 30 days. After consultation the EAG updated its analysis, and took costs related to stroke from an analysis of the UK Prospective Diabetes Study (UKPDS; a randomised, multicentre trial of glycaemic therapies in 5,102 people with newly diagnosed type 2 diabetes) based on costs for a 40-year-old woman (non-fatal stroke £6,011, history of stroke £673 and fatal stroke £3,727). Although these costs are higher than those from NICE's guideline on type 1 diabetes in adults, the committee noted that they had a negligible effect on the ICER. The EAG said that the incidence of kidney and eye complications may be overestimated in the model, and there was uncertainty around the modelling of these long-term effects. The EAG provided a scenario analysis that reduced these costs proportionately to their overestimation, resulting in a small increase in the ICER. A clinical expert said that the complications data from the Diabetes Control and Complications Trial and the Epidemiology of Diabetes Interventions and Complications follow-up study that is used in the model may not be representative of the UK population. The population in these studies is mainly White, while the UK population is more ethnically diverse, with some ethnicities having higher susceptibilities to certain diseases. The committee noted that there was a lack of real-world data on complication rates and costs in the UK population, but concluded that its preferred base case was to include the

analysis that reduced these costs proportionately to their overestimation.

Cost effectiveness for children and young people

3.16 After consultation, the EAG updated its exploratory modelling in children and young people. It used the revised network meta-analysis to apply the net effect for CSII plus rtCGM compared with CSII plus isCGM in addition to the net effect for HCL systems compared with CSII plus rtCGM (see section 3.5). This showed that HCL systems appear to be more cost effective in children and young people than in adults. The assumption that 75% of children are on CSII plus isCGM and 25% are on CSII plus rtCGM, resulted in an updated base-case ICER of £79,664 per QALY gained. When the analysis included adjusted complication costs (see section 3.15) the ICER increased to £93,778 per QALY gained. In scenarios that included non-severe and severe hypoglycaemic events, the ICERs were reduced to between £65,108 per QALY gained and £75,595 per QALY gained, depending on the source used to value the disutility associated with hypoglycaemic events. The EAG said that there was some uncertainty in the results of the exploratory modelling in children. This was because of uncertainty around the modelled long-term survival and how much clinical data from children was used in the model. Clinical experts explained that children and young people could have added benefits from HCL systems. For example, HCL systems can help:

- younger children who may not recognise symptoms of hypoglycaemia and may also have unpredictable eating patterns, frequent unscheduled activity, and changing insulin requirements associated with growth
- older children with glucose control during the physiological changes that happen at puberty.

So, HCL systems could provide children and young people, and their families, with more freedom and reduce the mental burden on parents and carers (see section 3.1). Considering these points, the committee thought that HCL systems could benefit all children and young people with type 1 diabetes irrespective of their HbA1c level. The committee concluded that although there was some uncertainty, HCL systems are likely to be more cost effective for children and young people than for adults.

Cost effectiveness in pregnancy

3.17 There was a lack of evidence about the cost effectiveness of HCL systems in managing blood glucose in pregnancy for people with type 1 diabetes. But the committee recalled that the effectiveness of HCL systems in pregnancy would likely be greater than in the general adult population (see section 3.8). So, HCL systems would likely be cost effective for women, trans men and non-binary people who are pregnant or planning to become pregnant.

Costs in the economic model

3.18 The committee considered an analysis including confidential prices submitted to NHS supply chain by the companies. It noted that using these prices resulted in lower ICERs but not to within the range that NICE would consider a cost-effective use of NHS resources. The committee also considered a threshold analysis on average 4-year costs to help them understand the effect of costs of HCL systems on the ICER (see section 2.8). It noted that relatively small reductions in costs resulted in large reductions in the ICER. The committee concluded that the cost of the HCL systems was a key driver of the cost-effectiveness results.

Preferred base case and ICER

3.19 The committee considered the EAG's updated economic analyses and decided on its preferred base case costs and assumptions. These were:

- 58 mmol/mol (7.5%) HbA1c at baseline (see section 3.9)
- including the regression analyses (see section 3.6)
- different effect sizes for HCL systems compared with CSII plus isCGM and CSII plus rtCGM
  - -0.59 percentage points HbA1c reduction for HCL compared with CSII plus isCGM (see section 3.6), and
  - -0.23 percentage points HbA1c reduction for HCL compared with CSII plus rtCGM (see section 3.6)

- adjusted complications cost to account for possible overestimation in the economic model (see section 3.15)
- non-severe and severe hypoglycaemic events included for both quality-of-life utility estimates and costs (see section 3.11)
- non-severe hypoglycaemic events costed at £5 per event
- no carer quality of life effect from non-severe and severe hypoglycaemic events (see section 3.12)
- 60-year time horizon and maintenance of HbA1c effects (see section 3.14)
- updated stroke costs (see section 3.15).

  The EAG also revised the costs used in the model based on feedback from NHS supply chain. This resulted in an updated 4-year total cost for HCL systems of £21,659. Using the committee's preferred assumptions and updated costs results in an ICER of £104,003 per QALY gained.

Acceptable ICER

3.20 NICE's guide to the methods of technology appraisal 2013 notes that above a most plausible ICER of £20,000 per QALY gained, judgements about the acceptability of a technology as an effective use of NHS resources will take into account the degree of certainty around the ICER. The committee will be more cautious about recommending a technology if it is less certain about the ICERs presented. The committee noted that the following aspects of the model affect the ICER:

- uncaptured benefits in the economic model related to reduced mental burden, and parent and carer anxiety
- rates of hypoglycaemic events and the disutility and cost of these
- rates of eye and kidney complications
- what baseline HbA1c level is used in the model

- what the HbA1c effect size is after using HCL systems (which depends on the baseline level)
- duration of the HbA1c effect
- modelling of longer-term effects when using the base-case time horizon of 60 years
- effectiveness of isCGM with CSII compared with HCL systems.

Many of the scenarios tested by the EAG resulted in ICERs much higher than NICE would consider to be a cost-effective use of NHS resources. There is uncertainty around the assumptions that should be used in the base case, so there is a risk of decision error. So, it agreed that an acceptable ICER would be around £20,000 per QALY gained.

Other factors

Innovation

3.21 The committee considered whether HCL systems are innovative. It noted that these systems enhance existing devices by using an algorithm to integrate rtCGM data with CSII. The committee concluded that although HCL systems provide an alternative treatment option for people with type 1 diabetes, it thought that an ICER of £20,000 per QALY gained was acceptable.

Conclusions

Recommendations

3.22 The committee said that the clinical-effectiveness evidence showed that HCL systems are likely to improve blood glucose control in type 1 diabetes. This effect appears to be greater for people with higher baseline HbA1c levels, although the extent of the true effect is uncertain. The committee noted that HCL systems are

also effective for people with lower baseline HbA1c levels of around 58 mmol/mol (7.5%). The committee also said that HCL systems are likely to be more cost effective for children than for adults. It also noted that HCL systems are likely to be cost effective for women, trans men and non-binary people who are pregnant or planning to become pregnant. It noted the many uncaptured benefits in terms of reduced mental burden, reduced parent and carer anxiety, and improved quality of life. These would be expected to decrease the ICER, although it was uncertain by how much. So, there is uncertainty in the cost-effectiveness analyses, with wide ranging ICERs depending on the scenarios tested. The committee concluded that at the current average price, HCL systems are unlikely to be cost effective, but it recognised the potential benefits to people. It concluded that despite the uncertainty, if the companies and NHSE agree a cost-effective price for the systems on behalf of the relevant health bodies (see section 2.9), HCL systems should be recommended for:

- adults with type 1 diabetes who have an HbA1c of 58 mmol/mol (7.5%) or more, or have disabling hypoglycaemia, despite best possible management with at least 1 of the following:
  - CSII
  - rtCGM
  - isCGM
- children and young people
- women, trans men and non-binary people who are pregnant or planning to become pregnant.

Type 3c diabetes and cystic fibrosis diabetes

3.23 The committee considered other types of diabetes that could benefit from HCL systems:

- type 3c diabetes in which the pancreas is damaged and stops producing enough insulin for the body, and
- cystic fibrosis diabetes in which a build-up of mucus causes inflammation

and scarring of the pancreas, which then cannot produce enough insulin for the body.

The committee noted that no evidence was found on the use of HCL systems for these conditions. It considered that the clinical benefits in people with these conditions were likely to be similar to the clinical benefits for people with type 1 diabetes. It concluded that HCL systems could be useful in this group but this was outside NICE's scope for HCL systems in type 1 diabetes.

4 Implementation

4.1 Section 7 of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013 requires integrated care boards, NHS England and, with respect to their public health functions, local authorities to comply with the recommendations in this appraisal within 3 months of its date of publication. The normal period of compliance has been extended to 5 years for this technology because NHS England submitted a funding variation request, which was accepted by NICE after a period of public consultation. NHS England's justification for the funding variation request is:

- **Need for specialist support:** People with diabetes, their families and their carers need training and specialist support to use insulin pumps, glucose monitors and hybrid closed loop (HCL) systems effectively.
- **Variation in access:** Provision of diabetes technologies varies significantly across the country. Expertise in and capacity to provide insulin pump services are often concentrated in larger diabetes teaching centres, with fewer resources at smaller diabetes centres and district general hospitals.
- **Clinical capacity:** There is a lack of adequately trained staff, so investment and time is needed to recruit and train staff to support effective use of HCL systems and reduce variation in access across the country.
- **Health inequalities:** Without a planned introduction of HCL systems and continued investment in staffing capacity and training in HCL systems there is a risk of exacerbating health inequalities related to age, socioeconomic status, ethnicity, language barriers, and access to smartphones and the internet, all of which could affect uptake of HCL systems.
- **Patient benefit:** The phased rollout is not expected to adversely affect outcomes for people eligible for HCL systems. The National Diabetes Audit has shown that many people with type 1 diabetes have improved glycaemic control using continuous glucose monitors and insulin pumps. Effective implementation of HCL systems will represent a further advance in achieving optimal glycaemic control.

- **Variation in procurement:** Procurement of diabetes technologies varies considerably. To resolve this variation and ensure trusts can access nationally mandated cost-effective prices, NHS England will need to develop a new commercial framework through a formal procurement process. This is expected to take time and resource to develop and test with suppliers.

  This extension is made under Section 7(5) of the Regulations.

4.2 Based on the commercial framework and the recommendations in this guidance, NHS England has developed a 5-year implementation plan with advice and guidance to NHS providers on the phased uptake approach. The strategy will centre on improving health outcomes and reducing health inequalities. The phased rollout will initially start with:

- children
- young people
- women, trans men and non-binary people who are pregnant or planning to become pregnant and
- adults who already use pumps who want to transition to an HCL system (over time, this will be extended to people who want to start using a pump for the first time).

  Key elements of the strategy will include workforce, patient education, commercial, stakeholder engagement and data.

4.3 The Welsh ministers have issued directions to the NHS in Wales on implementing NICE technology appraisal guidance. When a NICE technology appraisal recommends the use of a drug or treatment, or other technology, the NHS in Wales must usually provide funding and resources for it within 2 months of the first publication of the final appraisal document. For HCL systems, the period of compliance in Wales is extended to 5 years. This is for the reasons in section 4.1 and is in line with NHS England's funding variation request. The NHS Wales Executive will develop a 5-year implementation plan for this technology with guidance and support to health boards on the phased approach.

4.4 When NICE recommends a treatment 'as an option', the NHS must make sure it is available within the 5-year period set out in the paragraphs above. This means that, if a person has type 1 diabetes and the doctor responsible for their care thinks that an HCL system is the right treatment, it should be available for use, in line with NICE's recommendations, the funding variation request and NHS England's implementation plan.

4.5 The funding variation assumes that NHS England and NHS Wales are able to maintain cost-effective prices as per NICE's recommendations. NHS England, or NHS providers, will only purchase HCL systems in line with these recommendations. As new technology emerges, NHS England or NHS providers reserve the right to do further commercial activity to ensure HCL systems continue to deliver value for the NHS.

5 Committee members and NICE project team

Committee members

This topic was considered by the diagnostics advisory committee, which is a standing advisory committee of NICE.

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

The minutes of each diagnostics advisory committee meeting, which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

Chair

Brian Shine
Chair, diagnostics advisory committee

NICE project team

Each technology appraisal is assigned to a team consisting of 1 or more health technology analysts (who act as technical leads for the appraisal), a technical adviser and a project manager.

Tosin Oladapo and Simon Webster
Technical leads

Frances Nixon
Technical adviser

Alexandra Sexton, Donna Barnes and Toni Gasse

Project managers

Update information

January 2026: 'What this means in practice box' added.

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