National Institute for Health and Care Excellence

Diabetes in pregnancy: management from preconception to the postnatal period

[B] Evidence review for managing type 1 diabetes using hybrid closed loop systems

NICE guideline NG3

Evidence underpinning recommendations 1.2.3, 1.9.2, 1.9.3, 1.9.4, 1.15.2, 1.15.4, 1.15.5, 1.15.6, 1.22.1, 1.22.2, 1.24.3, 1.25.2, 1.29.1, 1.30.1, 1.30.2 and research recommendations

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Managing type 1 diabetes using hybrid closed loop systems

1.1 Review question

This evidence review summarises the evidence for:

in people with type 1 diabetes, who are planning to become pregnant, are pregnant, or are in the postpartum period, what is the effectiveness and cost-effectiveness of hybrid closed loop systems to improve maternal and fetal/neonatal outcomes, compared to standard insulin therapy?

Further technical detail can be found in the separate technical appendices for this review.

1.1.1 Summary of the protocol

Table 1: Summary of the protocol (PICOS)

Population	People with type 1 diabetes who are: • planning to become pregnant • pregnant • in the postpartum period (up to 6 months post childbirth)
Intervention	• Hybrid closed loop systems with a licence for use in pregnancy
Comparator	• Real time continuous glucose monitoring with multiple daily insulin injections • Intermittent capillary blood glucose monitoring with continuous subcutaneous insulin infusion • Continuous glucose monitoring with continuous subcutaneous insulin infusion Note: comparison group should be on the same insulin regimen as intervention group.
Outcomes	**Maternal outcomes** 1. % time spent in the pregnancy-specific/postpartum* target glucose range: • Time spent within target glucose range • Time spent above target glucose range • Time spent below target glucose range • Overnight % time spent in range *Pregnancy specific target range: 3.5-7.8 mmol/L. Postpartum target range (same range as for pre-pregnancy): 3·9–10·0 mmol/L

	(Battelino T et al. Diabetes Care 2019;42:1593-1603). 2. Adverse events: • Hypoglycaemia (dichotomous or continuous outcome, depending how it is reported): ○ severe hypoglycaemia (defined as requiring third party assistance) ○ nocturnal hypoglycaemia • Diabetic ketoacidosis (DKA) 3. Quality of Life outcomes - measured using validated tools. For example: • Diabetes Distress Scale • Hypoglycaemia Fear Survey Questionnaire **Fetal/Neonatal outcomes** 4. Neonatal intensive care unit admissions longer than 24 hours 5. Adverse events: ○ Mortality: ▪ pregnancy loss (miscarriage, defined as <24weeks) ▪ stillbirth, ≥24 weeks ▪ neonatal loss, up to 28 days) ○ Neonatal hypoglycaemia ○ Preterm birth ○ Large/ small for gestational age (or however defined in the study, for example, using a customised measure based on gestational age and population norms; dichotomous data preferred).
Study type	Include published full-text papers: • Systematic reviews of RCTs • RCTs

Abbreviations: RCT: Randomised Controlled Trial.

For the full protocol see **appendix A** in the technical appendices document.

1.1.2 Methods and process

This evidence review was developed using the methods and process described in Developing NICE guidelines: the manual. Methods specific to this review question are described in the review protocol and in section 1.1.2.2 below. General methods are described in the **appendix J.**

Declarations of interest were recorded according to NICE's conflicts of interest policy.

1.1.2.1 Search methods

The searches for the effectiveness evidence were run on 22 December 2025. The following databases were searched: Cochrane Database of Systematic Reviews (CDSR) (Wiley); Cochrane Central Register of Controlled Trials (CENTRAL) (Wiley); Embase (Ovid); MEDLINE ALL (Ovid); and Epistemonikos. Limits were applied to remove editorials, conference abstracts, empty registry entries and references not published in the English language.

The searches for the cost effectiveness evidence (economic evaluations) were run on 9 January 2026. The following databases were searched: Embase (Ovid); MEDLINE ALL (Ovid); and INAHTA. Limits were applied to remove animal studies, editorials, conference abstracts, empty registry entries and references not published in the English language. The validated NICE cost utility filter was used on MEDLINE and Embase

A NICE senior information specialist (SIS) conducted the searches. The MEDLINE strategy was quality assured by another NICE SIS. All translated search strategies were peer reviewed to ensure their accuracy. Both procedures were adapted from the 2015 PRESS Guideline Statement.

Further details and full search strategies for each database are provided in **Appendix B**.

1.1.2.2 Methods specific to this review

The review followed the methods described in the review protocol, with several additional procedures applied specifically for this evidence review.

In line with the protocol, we extracted, analysed and stratified the outcomes based on the intervention i.e., pregnancy-specific HCL compared to standard care and non-pregnancy specific HCL compared to standard care. Pregnancy-specific HCL systems were defined as HCL systems that:

- are licenced for use in pregnancy,
- allow the target or optimum blood glucose level to be set below 5 mmol/L,

- enable both the lower and upper limits of the target range to be set in line with the international consensus range - see Clinical Targets for Continuous Glucose Monitoring Data Interpretation: Recommendations From the International Consensus on Time in Range - PubMed, and

- have evidence of a clinically relevant improvement in glycaemic outcomes. Clinically relevant improvement is defined as an increase of at least 5% in time spent within the pregnancy glucose target range (3.5 to 7.8 mmol/L) compared with standard care using continuous glucose monitoring and standard insulin delivery by multiple daily injections or insulin pump therapy.

Any other HCL devices, licenced for use in pregnancy, were defined as non-pregnancy-specific HCL systems in this review. Outcomes were also stratified by the stages of pregnancy i.e. preconception, during pregnancy, and postnatal periods. We also sought data to enable further stratification by clinically relevant time points (for example, before and after 24 weeks' gestation, and 0–3 months and 4–6 months postpartum). Where data were not available for later or more granular time points i.e. before and after 24 weeks' gestation, and 0-3 months and 4-6 months postpartum, analyses were conducted using the broader preconception, pregnancy, and postnatal periods only, and outcomes were not stratified further.

When studies reported outcomes at multiple time points (for example, by trimester), and no overall combined estimate was provided, the time-specific data were assessed for variability. If the results showed minimal differences between time points, the review team extracted either the dataset with the largest number of participants or the dataset judged to be the most representative. When a study provided both time-specific estimates and an overall pooled result, the overall estimate was extracted in accordance with NICE's preference for the least selective and most comprehensive summary.

Minimally important differences (MIDs) were pre-specified to support judgements about whether observed differences were likely to be clinically meaningful.

For the percentage of time spent in the target glucose range (TIR), a MID of 5% change in time in range was applied. This threshold had previously been used in the development of NICE guideline NG3, based on the findings of Batelino et al (2019).

For the quality-of-life outcome, the diabetes distress scale, a MID of 0.25 units was used. This threshold is based on the findings of Banks et al (2023).

For all dichotomous outcomes, the line of no effect as a MID and statistical significance was used to assess the effectiveness of intervention. The judgement relied on whether the 95% confidence interval crossed the value indicating no difference between the intervention and comparator. The line of no effect is 1 for relative measures such as risk ratio (RR), odds ratio (OR) and Peto OR, and 0 for absolute measures such as risk difference (RD).

1.1.3 Effectiveness evidence

1.1.3.1 Included studies

Study selection

A systematic search was carried out to identify potentially relevant studies as detailed in **appendix J** in the technical appendices document. See **appendix B** in the technical appendices document for the literature search strategy. The study selection process is presented as a PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) flow diagram in **appendix C** in the technical appendices document.

Two studies, the AiDAPT and CRISTAL trial, (reported in 4 papers, Lee 2023, Lee 2025, Benhalima 2024 and Beunen 2024) were included. The AiDAPT trial evaluated the impact of pregnancy-specific HCL system compared to standard care, while CRISTAL trial looked at non-pregnancy-specific HCL system compared to standard care. Lee 2025 and Beunen 2024 are pre-specified extension studies of AiDAPT and CRISTAL trial. Only the AiDAPT trial reported evidence on breastfeeding status during the postpartum phase which was

summarised narratively. For a summary of the studies included see Table 2, and for full references see the list of included studies 1.1.11.1).

1.1.3.2 Excluded studies

Details of studies excluded at full text, along with the primary reason for exclusion, are given in **appendix I** in the technical appendices document.

1.1.4 Summary of studies included in the effectiveness evidence

Table 3 Summary of studies included in the effectiveness evidence

Study details	Population	Intervention	Comparator	Outcomes
Benhalima, 2024 Location: Europe (Belgium and Netherlands) Funding source: non-industry; devices provided by industry	N = 95 • n = 46 hybrid closed loop group • n = 49 standard care group **Week of gestation**, at randomisation (median; IQR): • Hybrid closed loop group - 10.3 (8.9 to 11.9) • Standard care group - 10.1 (8.5 to 11.6) **Insulin delivery mode at baseline** (n; %): Multiple daily injections: • Hybrid closed loop group: 2/46; % = 4.3	Automated hybrid closed-loop insulin delivery (MiniMed 780G), consisting of 780G insulin pump and Accu-Chek Guide Link meter with Guardian Link 3 transmitter and Guardian 3 sensor or newer Guardian 4 transmitter and Guardian 4 sensor.	Standard care. Participants continued multiple daily injections or insulin pump therapy, or an HCL therapy used as open-loop system, with insulin doses adjusted to meet standard glucose targets	**Note: Trial was only powered to detect the difference for % time spent in the range, % time spent overnight and % time spent below the range.** **Maternal outcomes:** • % time spent in the pregnancy-specific target glucose range • Time spent above pregnancy-specific target glucose range • Time spent below pregnancy-specific target glucose range • Overnight % time spent in pregnancy-specific target glucose range • Adverse events ○ Hypoglycaemia (severe)

Study details	Population	Intervention	Comparator	Outcomes
	• Standard care group: 2/49; % = 4.1 Automated insulin delivery: • Hybrid closed loop group: 44/46; % = 95.7 • Standard care group: 47/49; % = 95.9			○ Diabetic ketoacidosis **Fetal/Neonatal outcomes** • Neonatal intensive care unit admissions longer than 24 hours • Adverse events ○ Mortality (pregnancy loss, neonatal loss) ○ Stillbirth ○ Neonatal loss ○ Neonatal hypoglycaemia ○ Preterm birth Gestational age (large, small) **Device-related adverse events**
Beunen, 2024 Location: Europe (Belgium and Netherlands)	**Intrapartum (day of delivery)** N = 72 • n = 27 hybrid closed loop group	Automated hybrid closed-loop insulin delivery (MiniMed 780G), consisting of 780G insulin pump and Accu-Chek Guide Link meter with Guardian Link 3 transmitter and	Standard care. Participants continued multiple daily injections or insulin pump therapy, or an HCL therapy used as open-loop system,	**Note: Trial was not powered to detect the effect of non-pregnancy-specific HCL for any outcomes.** **Maternal outcomes:**

Study details	Population	Intervention	Comparator	Outcomes
Funding source: non-industry; devices provided by industry	• n = 45 standard care group **Postnatal (to discharge; median day 4)** N = 71 • n = 37 hybrid closed loop group • n = 34 standard care group	Guardian 3 sensor or newer Guardian 4 transmitter and Guardian 4 sensor	with insulin doses adjusted to meet standard glucose targets	• % time spent in the non-pregnancy specific target glucose range • Time spent above non-pregnancy specific target glucose range • Time spent below non-pregnancy specific target glucose range • Overnight % time spent in pregnancy-specific target glucose range
Lee, 2023 Location: United Kingdom Funding source: non-industry; devices provided by industry	N = 124 • n = 61 hybrid closed loop group • n = 63 standard care group **Week of gestation**, at enrolment (median; IQR): • Hybrid closed loop group - 10.3 (8 to 11.7)	Automated hybrid closed-loop insulin delivery (CamAPS FX (CamDiab, Cambridge, UK)), an app running on an unlocked Android smartphone (Samsung Galaxy S8–12).	Standard care. Participants continued multiple daily injections or insulin pump therapy, with insulin doses adjusted to meet standard glucose targets	**Note: Trial was only powered to detect the difference for % time spent in the range, % time spent overnight and % time spent above the range.** **Maternal outcomes:** • % time spent in the pregnancy-specific target glucose range

Study details	Population	Intervention	Comparator	Outcomes
	• Standard care group - 10.3 (8 to 11.7) **Insulin delivery mode at baseline** (n; %): Multiple daily injections: • Hybrid closed loop group: 27; % = 44 • Standard care group: 37; % = 59 Automated insulin delivery: • Hybrid closed loop group: 2; % = 3 • Standard care group: 1; % = 2			• Time spent above pregnancy-specific target glucose range • Overnight % time spent in pregnancy-specific target glucose range • Adverse events o Hypoglycaemia (severe) o Diabetic ketoacidosis • Quality of Life outcomes (measured using Diabetes Distress Scale) **Fetal/Neonatal outcomes** • Neonatal intensive care unit admissions longer than 24 hours • Adverse events o Mortality (pregnancy loss, neonatal loss) o Neonatal hypoglycaemia o Preterm birth

Study details	Population	Intervention	Comparator	Outcomes
				○ Gestational age (large, small) **Device-related adverse events**
Lee, 2025 Location: United Kingdom Funding source: non-industry; devices provided by industry	N = 57 • n = 28 hybrid closed loop group • n = 29 standard care group **Age** (mean; SD): • Hybrid closed loop group: 32 (4) • Standard care group: 30 (4) **Insulin delivery mode at baseline** (n; %): Pump: • Hybrid closed loop group: 15; % = 54 • Standard care group: 11; % = 38	Hybrid closed loop system comprising the CamAPS FX app on an Android smartphone, a Dana Diabecare RS insulin pump, and a Dexcom G6 CGM, all linked via Bluetooth	Standard care. Participants continued their usual insulin therapy, either multiple daily injections or pump therapy	**Note: Unclear if trial was powered to detect the effect of pregnancy-specific HCL for any outcomes.** **Maternal outcomes:** • % time spent in the non-pregnancy specific target glucose range ○ Sub-grouped by baby feeding practices • Time spent above non-pregnancy specific target glucose range ○ Sub-grouped by baby feeding practices • Time spent below non-pregnancy specific target glucose range

Study details	Population	Intervention	Comparator	Outcomes
	Multiple dose injections: • Hybrid closed loop group: 12; % = 43 • Standard care group: 17; % = 59 Automated insulin delivery: • Hybrid closed loop group: 1; % = 4 • Standard care group: 1; % = 3			• Adverse events o Hypoglycaemia (severe) o Diabetic ketoacidosis **Device-related adverse events**

Abbreviations: AHCL: advanced hybrid closed loop; BMI: Body Mass Index; CGM: continuous glucose monitor; HbA1c: Haemoglobin A1c; IQR: Interquartile Range; NR: not reported; SAPT: Sensor Augmented Pump Therapy; SD: Standard Deviation.

See **appendix D** in the technical appendices document for full evidence tables.

1.1.5 Summary of effectiveness evidence

1.1.5.1 Planning of pregnancy period

No evidence was found for the planning of pregnancy period.

1.1.5.2 During pregnancy period

Evidence suggests that pregnancy-specific HCL systems provide greater glycaemic benefit than standard care by increasing both overall and overnight time spent in the pregnancy target glucose range and reducing time spent above the target range. In contrast, evidence for non–pregnancy-specific HCL systems indicates that these systems, when compared to standard care, may lead to little to no difference in overall or above target time in range, have no effect on time spent below the target glucose range, and primarily offer benefit through increased overnight time in range..

The trials for both interventions were not powered to detect a difference between HCL systems and standard care for maternal and neonatal adverse events.

The evidence suggests that pregnancy-specific HCL systems may result in little to no difference in quality of life (diabetes distress) and preterm births compared to standard care. Moreover, non-pregnancy-specific HCL systems showed similar effect for babies born small for gestational age compared to standard care, but the evidence is very uncertain for both interventions.

The evidence is very uncertain about the effect of pregnancy-specific and non-pregnancy-specific HCL compared to standard care for:

- Maternal severe hypoglycaemias
- Diabetic ketoacidosis
- Neonatal intensive care unit admissions longer than 24 hours
- Pregnancy loss (miscarriage, defined as <24weeks)

- Neonatal loss, up to 28 days
- Stillbirth
- Neonatal hypoglycaemia
- Large for gestational age

1.1.5.3 Intrapartum period (defined as day of delivery)

No evidence was found for the intrapartum period for pregnancy-specific HCL compared to standard care.

Evidence for the intrapartum period for non-pregnancy-specific HCL compared with standard care comes from the pre-specified extension phase of the CRISTAL trial. In this extension, participants continued in the same intervention groups to which they had originally been assigned during pregnancy, but entry into the intrapartum phase required participants to decide whether they wished to continue with their allocated treatment. Those who opted to switch treatment were excluded from the final extension-phase analysis. Importantly, the study suggests that no re-randomisation occurred during this period. As a result, the intrapartum comparison reflects continuation of the original trial groups rather than a newly randomised group. Furthermore, the authors note that the CRISTAL trial was underpowered to detect the difference between non-pregnancy-specific HCL and standard care for glycaemic management during the intrapartum period.

Evidence suggests that non-pregnancy-specific HCL may result in little to no difference in improving overall, overnight, above and below % time spent in target glucose range compared to standard care, but the evidence is very uncertain.

1.1.5.4 During postnatal period:

Evidence for the postnatal period came from the prespecified extension studies of both the AiDAPT and CRISTAL trials. The AiDAPT extension compared pregnancy specific HCL with standard care, while the CRISTAL extension evaluated nonpregnancy specific HCL versus standard care. In both studies, participants remained in their originally randomised groups, although continuation into the postnatal phase required participants to opt in rather than undergo new randomisation. For the AiDAPT extension, the six participants that discontinued HCL did so for reasons unrelated to adverse events or poor glucose management. Baseline characteristics remained balanced between groups and intention-to-treat analysis was conducted to include all randomised participants. In contrast, the CRISTAL extension did not report baseline characteristics for either arm during the postnatal period and the choice of switching treatment was not related to any adverse events. During the CRISTAL extension phase, 62.8% participants continued using HCL and 34.9% switched or discontinued and were not included in the final analysis. Additionally, the CRISTAL trial was underpowered to detect the difference between non-pregnancy-specific HCL and standard care for all outcomes, and it is unclear whether the AiDAPT trial was sufficiently powered to detect the difference between pregnancy-specific HCL and standard care during postnatal period.

The evidence showed that pregnancy-specific HCL led to increased overall % time spent in target range and reduced % time spent above the target range compared to standard care. In contrast, non-pregnancy-specific HCL had little to no effect in improving glycaemic outcomes such as overall, overnight, above and below % time spent in target glucose range compared to standard care, but the evidence was very uncertain.

The evidence was very uncertain about the effect of pregnancy-specific and non-pregnancy-specific HCL compared to standard care for maternal severe hypoglycaemic or diabetic ketoacidosis events.

Evidence for sub-groups:

Evidence on % time spent in the postpartum glucose target range, sub-grouped by feeding practice, was only informed by the AiDAPT trial. Therefore, planned subgroup analysis to assess between study heterogeneity could not be undertaken, and findings were summarised narratively.

At 24 weeks after birth, 36% (10/28) of participants using psHCL systems and 42% (11/26) in the standard care group exclusively breastfed, while 57% (16/28) in the psHCL group and 50% (13/26) in the standard care group exclusively formula fed.

At 3–6 months postpartum, among participants who were exclusively breastfeeding, mean time in the postpartum glucose target range was higher in the psHCL group than in the standard care group (69% ± 11% vs 60% ± 16%). Among those exclusively formula feeding, compared to those exclusively breastfeeding, mean time in range was similar in the psHCL group (69% ± 8%) but lower and more variable in the standard care group (44% ± 20%).

Moreover, at 3–6 months postpartum, mean time spent above the postpartum glucose target range was lower in the psHCL arm than in the standard care arm across both feeding subgroups. Among participants who were exclusively breastfeeding, mean time above range was 28 ± 11% with psHCL compared with 35± 17% with standard care. In the exclusive formula-feeding group, mean time above range was 29± 9% with psHCL and was substantially higher and more variable with standard care at 53± 21%.

Overall, across both feeding groups, higher time in range and lower time above range were observed in participants using psHCL compared with standard care, with the largest difference seen among those exclusively formula feeding.

Evidence for secondary outcome:

Evidence for device related adverse events associated with HCL systems was sought across all included studies. Evidence suggested that device related

adverse events associated with pregnancy-specific and non-pregnancy-specific HCL systems were uncommon and mostly related to infusion set issues, sensor failures, or connectivity problems. Reported device-related adverse events varied considerably across studies; therefore, findings were summarised narratively and certainty around the evidence was not assessed. Reported events ranged from symptomatic hyperglycaemia and moderate ketosis to episodes of severe hypoglycaemia, often triggered by user error, infusion set blockage, sensor warmup failures, or loss of communication between system components. Similar CGM related issues also occurred in the standard care groups, indicating that most events reflect known challenges with sensor and pump technologies rather than risks unique to closed loop systems.

See **appendix F** in the technical appendices document for a GRADE summary table containing full details for all outcomes.

1.1.6 Economic evidence

1.1.6.1 Included studies

A search was performed to identify published economic evaluations of relevance to this review question. See the literature search strategy in **appendix B** in the technical appendices document.

One economic study was identified which was applicable to this review question. (see economic study selection flow chart in **appendix G** in the technical appendices document).

One Belgian study compared advanced hybrid closed loop vs standard care in a pregnant population with type 1 diabetes and with a gestational age of <12 weeks (Azahaf 2025). Characteristics of the included economic study are summarised in **Error! Reference source not found.**. Full details of these studies are provided in the economic evidence study extraction tables in **appendix H** in the technical appendices document.

1.1.6.2 Excluded studies

No economic studies were reviewed at full text and excluded from this review.

Table 4: Summary of characteristics of included study

Study details	Study design and type of analysis	Population	Interventions and comparators	Perspective	Primary outcome	Time horizon
Azahaf 2025 Belgium	**Study design:** Decision analytic model **Source of effectiveness data:** CRISTAL trial, Benhalima 2024 (study is included in review of effectiveness evidence) N= 95 **Type of analysis:** Cost-effectiveness, cost-consequence	Pregnant population with type 1 diabetes and with a gestational age of <12 weeks.	Standard Care (insulin injections, standalone insulin pump or sensor augmented pump therapy) The MiniMed™ 780G AHCL therapy system - (this meets the definition of non-pregnancy specific)	Belgian healthcare payer	Time in range Time below range	28 weeks

Abbreviations: AHCL: advanced hybrid closed loop (this meets the definition of non-pregnancy specific)

1.1.7 Summary of economic evidence

See Table 5 for a summary of the economic evidence and **appendix H** in the technical appendices document for the economic evidence study extraction tables.

Table 5: Economic evidence summary table

Study	Applicability and limitations	Incremental cost[1]	Incremental effects	Cost effectiveness[1]	Uncertainty[1]	Economic evidence statement
Azahaf 2025 (Belgium)	Partially applicable[2] Potentially serious limitations[3]	-£200 Cost year: 2024	**Time in range:** AHCL 24 more minutes in range (95% CI: 8 minutes, 30 minutes) **Time below range:** AHCL 19 minutes less below range (95% CI: -32 minutes, -7 minutes)	AHCL dominant	Probability of AHCL being dominant: 73% Probability of AHCL being dominant for different scenarios with respect to intervention attributable hospitalisation costs and source of model outcome data: Scenario 1: 59% Scenario 2: 80% Scenario 3: 79%	Compared to standard care , AHCL was dominant, with lower cost and a higher level as benefit as measured by time in range and time below range

Abbreviations: AHCL=advanced hybrid closed loop (non-pregnancy specific); CI=confidence interval RCT=randomised controlled trial;

1. Other currencies were converted to pound sterling using IMF Purchasing Power Parities: *https://eppi.ioe.ac.uk/costconversion/default.aspx*.

2. A non-NHS setting and standard care control were all on pumps which may not be representative of UK populations. Analysis does not use QALYs despite the CRISTAL trial including health related quality of life outcomes. Outcome were intermediate measures of treatment benefit

3. Departures from pre-specified protocol and limited effectiveness to short term outcomes. PSA was undertaken but some concerns about arbitrary rules used for parameterisation (e.g. Standard errors are assumed to be 20% for all parameters and across all scenarios).

1.1.8 Economic model

No original economic modelling was completed for this review question as the primary purpose of this update was to align NG3 (2015) with NICE's technology appraisal guidance on hybrid closed loop systems (TA943, 2023) which made reference to NHS England's implementation plan for this.

1.1.9 Committee discussion and interpretation of the evidence

1.1.9.1 What are the key issues and priorities relating to this question?

The committee were mindful of NICE's technology appraisal guidance on hybrid closed loop systems (TA943, 2023), which recommends HCL as an option for managing blood glucose levels in type 1 diabetes for women, trans men and non-binary people who are planning a pregnancy. They noted that TA943 only recommends HCL systems if they are procured at a cost-effective price agreed by the companies and NHS England, and implemented following NHS England's implementation plan. Of note, given TA943 does not specify whether HCL systems should be pregnancy specific, or not, for those planning for pregnancy or during pregnancy, the committee felt they could add value by considering the relevant evidence.

The committee agreed that Type 1 diabetes in pregnancy carries serious maternal and neonatal risks, with outcomes strongly determined by glycaemic levels during the preconception period and early pregnancy. Members highlighted that poor glycaemia is linked to severe maternal and neonatal complications. This makes the optimisation of glucose management when planning for pregnancy and during pregnancy a major clinical priority. Although there was no evidence assessing the effectiveness of pregnancy-specific hybrid closed loop systems (psHCL) during preconception and early pregnancy, the committee stressed that improving glucose levels early in pregnancy significantly reduces risk. Therefore early intervention and equitable access to effective technologies, such as psHCL, are essential.

There is only one major trial for psHCL (AiDAPT) and one trial for non-pregnancy specific hybrid closed loop systems (non-psHCL) (CRISTAL) informing recommendations. The committee acknowledged that evidence for psHCL showed, during pregnancy, improved glycaemic control compared with standard care, increased overall and overnight time in the pregnancy target glucose range and reduced time above range. Evidence for non-psHCL only showed benefit in improving overnight time in range during pregnancy. They

also noted that psHCL systems may result in little to no difference in improving quality of life or preterm births. Non-psHCL showed similar effect for babies born small for gestational age compared to standard care, but the evidence was very uncertain for both interventions. Moreover, evidence was very uncertain for both interventions for severe maternal hypoglycaemia, diabetic ketoacidosis, NICU admission >24 hours, pregnancy loss, neonatal loss, stillbirths, neonatal hypoglycaemia, and large for gestational age .

After considering the evidence base, the committee agreed that psHCL showed an evidence of benefit during the pregnancy and postnatal period when compared to standard care. During pregnancy, psHCL demonstrated a greater effect than non-psHCL systems when compared to standard care, particularly for outcomes the trials were powered to assess, namely improvements in time in range (TiR).

The committee acknowledged that the association between maternal glucose levels during pregnancy and pregnancy outcomes is well established. Therefore, the committee were confident that the improvements in glycaemic control observed in the AiDAPT and CRISTAL trials would translate into clinically relevant health benefits for pregnant people and for their babies.

Furthermore, members drew from their expertise and highlighted that even people with good baseline glycaemic management can attain further improvement with a psHCL. In addition to the clinical evidence, lay member's lived experience was also noted, in that although they began pregnancy with good glycaemic management on a non-psHCL, they experienced further meaningful improvement after switching to a psHCL. This personal account reinforced the committee's view of the added value of psHCL. Overall, the committee agreed that the desirable glycaemic effects demonstrated by psHCL are meaningful and likely important for reducing maternal and neonatal risk during the pregnancy and potnatal period. Evidence from the AiDAPT and CRISTAL trials showed improvements in maternal glucose outcomes, particularly time in range, which were the outcomes the trials were powered to assess. Although evidence for adverse maternal and neonatal

outcomes was identified, the committee noted that the trials were not powered to detect difference between the intervention and standard care for these outcomes and that the evidence was therefore uncertain. The committee did not rely on this evidence alone when forming recommendations. Due to the lack of evidence regarding adverse maternal and neonatal outcomes the committee made a research recommendation.

The committee felt strongly that this additional benefit of psHCL over non-psHCL should be regularly conveyed to people at each clinical appointment. Whilst acknowledging the role of shared decision making, they also suggested that people who are currently on non-psHCL should be encouraged to switch to a psHCL if planning a pregnancy or if they are pregnant.

The committee noted that both the AiDAPT and CRISTAL trials were not powered for many safety outcomes or neonatal endpoints and there was limited evidence found to demonstrate harm. They queried the differences reported in neonatal outcomes particularly noting the higher preterm birth rates in intervention arms. However, NICU admissions were lower in the AiDAPT trial intervention (psHCL) arm despite higher rates of preterm births. Due to the lack of evidence regarding outcomes in neonates the committee made a research recommendation.

The committee discussed and agreed a set of priority outcomes, highlighting the rationale for each. Time in Range (TiR) was identified as the key outcome, with members noting that it is accepted clinically as a strong predictor of neonatal outcomes and the principal glycaemic target during pregnancy. The committee agreed that a TiR of 70% or above should be reflected as an important benchmark. The pregnancy specific target glucose range of 3.5-7.8 mmol/L during pregnancy was acknowledged as the international consensus range - see Clinical Targets for Continuous Glucose Monitoring Data Interpretation: Recommendations From the International Consensus on Time in Range - PubMed

Hypoglycaemia avoidance was also prioritised. However, the committee noted conflicting thresholds, highlighting that while hypoglycaemia is commonly

defined as glucose levels below 4 mmol/L, the proposed lower limit of the pregnancy target range extends down to 3.5 mmol/L. It was noted that when considering whether to treat hypoglycaemia, attention needs to be given to the trend in addition to the absolute value. The risk of hypoglycaemia is dependent on the individual when they are within the 3.5 – 4mmol/L range. The committee wanted the recommendations to provide clarity and ensure patient safety, they noted how important individualised care plans are for people in these circumstances.

The committee were particularly keen to ensure that all people eligible to use psHCL systems are competent to use them effectively and able to gain benefit from the technology. Therefore, the committee discussed what a structured education programme should be, highlighting the need for it to be evidence based, individually tailored and audited. They discussed what qualified as adequate education, how competence should be defined, and how patient engagement should be assessed.

The committee discussed the importance of glycaemic control before conception and in early pregnancy, recognising this period as critical for improving maternal and neonatal outcomes in women with type 1 diabetes. Members noted that evidence to inform optimal pre-conception glycaemic targets was not reviewed as part of this guideline update. Several challenges in the pre-conception period were identified. While some members felt that pregnancy-level glucose targets should be applied before conception to reduce early pregnancy risk, others raised concerns that this could increase the risk of hypoglycaemia and diabetes burnout, particularly for people who may take longer to conceive.

The committee noted that evidence on pre-conception glycaemic targets was not reviewed as part of this guideline update. This issue had been considered previously in NG3 (2015), which concluded that recommending pregnancy-level targets before conception could increase the risk of prolonged hypoglycaemia and discourage engagement with pre-pregnancy care in the absence of direct evidence. As evidence had not been considered

regarding these glucose ranges in preconception, the committee concluded that pregnancy specific glucose targets should not be imposed during the preconception phase. For this update, the committee considered whether evidence for use of psHCL systems during pregnancy could inform decision-making for the preconception period. The committee agreed that, although this represents indirect evidence, extrapolation was reasonable given the shared mechanisms for improving glycaemic control and the importance of achieving good glycaemic control as early as possible. Members noted that being established on a psHCL system when trying to conceive means that, if pregnancy occurs, the baby is likely to benefit from improved maternal glucose control during the crucial early weeks of pregnancy. The committee acknowledged the associated uncertainty but considered this approach clinically appropriate.

The committee also discussed intrapartum care with respect to glucose management, noting that existing JBDS guidance is widely used but remains consensus-based, contributing to variation in practice. Members agreed that individualised care plans for intrapartum and immediate postpartum glucose management should be completed by 36 weeks' gestation at the latest, while noting that initiating these discussions at the first pregnancy booking appointment may represent best practice and could help optimise outcomes. The use of an HCL during birth and the glucose target ranges immediately after birth should be considered in these individual care plans. The committee emphasised that people in labour may require additional medications such as steroids or magnesium sulphate, which may necessitate adjustments to HCL settings use.

The potential risks and benefits of discontinuing psHCL systems during labour and switching to intravenous dextrose or a variable-rate intravenous insulin infusion (VRIII) were also considered. The committee concluded that it is generally safer to continue HCL use during birth provided that the person, or their carer, is able to fully monitor glucose readings and make appropriate adjustments. The availability of an 'ease-off' function on HCL systems was

noted, and consideration of its use should be in line with manufacturer guidance.

Postnatally, the committee agreed that immediate adjustment of HCL settings is essential to ensure safe glucose targets during the early postpartum period. For people with well-managed glucose during pregnancy, settings may be returned to pre-pregnancy parameters. The committee also highlighted the importance of a carbohydrate-containing postnatal snack to reduce the risk of hypoglycaemia, which typically does not require additional insulin.

Finally, the committee discussed postnatal implementation of HCL. The committee debated whether to recommend continuation of HCL systems for at least six months or longer postnatally. While evidence on breastfeeding status was limited, the Committee recognised the benefits of good glycaemic management during the postnatal period, including when breastfeeding, and in the preconception period for future pregnancies. They discussed funding and equitable and fair access to HCL technologies in line with NHS England's implementation plan. Therefore, the committee agreed to recommend that women, trans men and non-binary people with type 1 diabetes are offered the option to remain on a pregnancy-specific HCL system for at least six months after birth.

Overall, the committee reaffirmed that the outcomes of greatest importance driving their decision-making were time in range, avoidance of hypoglycaemia, intrapartum safety (including DKA prevention), and ensuring equitable access to technology - especially given the substantial variation in HCL availability and pump services across regions.

1.1.9.2 Certainty of evidence and the balance of effects

The committee agreed that the overall certainty of the evidence is low. The recommendation is largely based on a single RCT (AiDAPT), which was powered for maternal glucose outcomes but was not powered for adverse maternal or neonatal outcomes. Evidence of benefit was shown for improved overall and overnight time in glucose target range in the psHCL arm

compared to standard care and reduced time spent above the target range. The committee noted that absence of evidence of harm in the psHCL arm cannot be interpreted as evidence of safety given that the study was not powered to detect evidence of harm.

Overall, the committee agreed that the desirable effects are likely to outweigh any potential undesirable effects, despite the low certainty of evidence. The balance favours the intervention, provided it is delivered within a carefully supported and supervised pathway that includes individualised education and safety planning. They stressed that careful implementation and robust clinical oversight, especially during intrapartum care if switching from pump/HCL therapy, are essential to mitigate risks such as DKA. Of particular note, was the necessity of having an alternative basal insulin available prior to pumps being removed.

On balance, the committee concluded that the benefits of psHCL, particularly improved TiR, likely outweigh the remaining uncertainties and potential risks, and that psHCL represents a favourable intervention when appropriate clinical support structures are in place.

1.1.9.3 Resources and cost-effectiveness

The guideline committee were aware of NICE Technology Appraisal 943 (TA943) (Overview | Hybrid closed loop systems for managing blood glucose levels in type 1 diabetes | Guidance | NICE) which recommended HCL's as an option for managing blood glucose levels in type 1 diabetes (T1D) for people who are pregnant or are planning to become pregnant. The committee was also aware that NHS England already had a 5-year implementation strategy (NHS England » Hybrid closed loop technologies: 5-year implementation strategy) and funding to ensure that eligible patients received equitable access to HCL systems. In this context, the committee considered the cost-effectiveness of HCL systems in their deliberations over what strength of recommendation was appropriate for this clinical guideline update for pregnant people and those planning a pregnancy. They also made an

assessment as to whether it would be cost-effective to extend the period of HCL eligibility to the post-natal period.

Given the existence of TA943, no original economic analysis was undertaken to support this guideline committee. However, a systematic review was undertaken which retrieved one published economic evaluation (Azahaf 2025) which the committee utilised in their decision making. This analysis utilised clinical results derived from the CRISTAL trial, one of the few published RCT's on the use of HCL's in pregnancy.

The committee noted that Azahaf 2025 reported that the Advanced HCL's might be cost saving relative to standard care, which comprised insulin injections, standalone insulin pump or sensor augmented pump therapy. Uncertainty with respect to the magnitude and direction of the cost saving was noted. Nevertheless, the committee considered it likely that the reduced hospitalisation costs from better blood glucose management would offset at least some of the additional costs associated with using an HCL system.

Azahaf 2025 was appraised as being partially applicable to the NHS and with potentially serious limitations. Costing was undertaken from the perspective of the Belgian health care payer and there is some uncertainty to what extent the mix of management represented by standard care would accurately reflect the UK context. One of the limitations of this study was that it had departed from the pre-specified study protocol and not considered longer term outcomes. However, the committee reflected that the shorter duration of pregnancy made it more difficult to undertake trials in this population than in the wider T1D population. Another limitation of the analysis was that an assessment of effectiveness was limited to time in range and time below range. These are intermediate measures of effectiveness and ideally there would have been data on 'harder' pregnancy outcomes and an assessment of QALY gain in order that the value of money of the recommendations could have been benchmarked against other NHS services. However, the committee reasoned that the relationship between blood glucose management and improved

maternal and neonatal outcomes was well established, and that any positive effect on blood glucose levels would translate into better pregnancy results. Therefore, they considered that the more limited scope and horizon of the analysis might have led to the cost-effectiveness being under-estimated. In particular they concluded it reasonable that the benefits that were observed in blood glucose management supported the reduction in hospitalisation costs that were also observed. They also believed that reduced hospitalisation was likely to reflect improved pregnancy outcomes.

Moreover, the committee believed that a pregnancy specific HCL system would lead to greater benefits for little additional cost when compared to the non-pregnancy specific HCL system used in the CRISTAL trial. This view was based on the outcomes of the AiDAPT trial which showed clearer evidence of benefit with a pregnancy specific HCL compared to standard care than that shown in the CRISTAL trial with a non pregnancy specific HCL compared to standard care. Therefore, they considered that recommending a pregnancy specific HCL was likely to be cost-effective for the NHS.

The committee were strongly of the opinion, based on their knowledge, and experience, that the best maternal and neonatal outcomes would be achieved if good glycaemic management was established prior to conception. Therefore, they considered that it would be cost-effective to recommend pregnancy specific HCL systems for those planning a pregnancy.

1.1.9.4 Equity

The committee agreed that HCL systems have the potential to either reduce or widen health inequities, depending on how they are implemented. Without careful planning, there is a substantial risk that disadvantaged groups may be excluded from the benefits of psHCL systems because of barriers related to low literacy and numeracy, people who do not speak English, sensory impairment, digital literacy, social deprivation, or access to structured education and specialist services i.e., MDT. Members highlighted that some

people may struggle with carbohydrate counting or may not speak English yet can still achieve significant improvements in time in range (TiR), especially through the automated basal component of HCL systems. Also, limited training access may reduce a person's ability to troubleshoot device issues promptly, which could affect safety and overall benefit. They emphasised the importance of an "enablist" approach to avoid widening disparities. Strict MDT requirements could unintentionally block access for people whose local services rely heavily on diabetes specialist nurses or dietitians rather than full MDT structures.

The committee recognised that some groups of people face the effects of cumulative disadvantage, such as lower health literacy, or less access to diabetes technology before pregnancy. Such groups are liable to enter pregnancy with poorer baseline glucose levels and may only present once pregnant. Such differences, as well as differences in pre-pregnancy access and ability to efficiently utilise HCL systems, may reduce the absolute benefit seen in these groups, in terms of glucose management. Gaining access to HCL systems only once pregnant, will be particularly impactful on neonatal outcomes. It is known that improvements in the mother's TiR during early pregnancy has a proportionally larger impact on neonatal outcomes than at later stages of the pregnancy. The committee were mindful that recommendations should seek to support disadvantaged groups to fully benefit from HCL systems, and to address inequalities rather than exacerbate them.

Inequalities were highlighted for people who can't become pregnant. There may also be preconception access issues for those who must travel long distances to centres capable of supporting HCL use. Members agreed wording should support equitable access for all who can become pregnant.

To reduce inequities, the committee emphasised several implementation priorities. First, training, education and support should be clearly defined but flexible, ensuring that people receive information on all aspects of HCL use in

their preferred format, including accessible formats for people with visual impairment, consistent with NHS Accessible Information.

Second, recommendations should avoid overly restrictive MDT wording, allowing services with limited staffing to still support access through available clinicians with appropriate expertise.

Third, support should focus on safety and troubleshooting rather than demanding perfect carb-counting skills, so that more people including those with low numeracy can use HCL safely and benefit from it.

Finally, services should take proactive steps to ensure that people perceived to be at risk of disadvantage, receive timely education, early access before pregnancy where possible, and continuity of support across primary and secondary care.

1.1.9.5 Feasibility

The committee agreed that psHCL systems are feasible to implement across NHS services in line with the NHSE Implementation Plan. However, members stressed that successful implementation depends heavily on local infrastructure, MDT capacity, staff expertise, and the ability of services to provide consistent onboarding and troubleshooting support throughout pregnancy.

Urgent issues were also identified relating to variation in practice across trusts. The committee noted that across England, there is inconsistent access to pump services, differing interpretations of the NICE technology appraisal guidance, and significant variation in clinicians' familiarity with psHCL use during pregnancy.

A key feasibility challenge discussed by the committee was the significant variation in MDT skill levels, with regards to HCL systems, across trusts. While some sites benefit from established multidisciplinary teams with substantial pump and HCL experience, others lack full MDT provision and instead rely on individual clinicians - often diabetes specialist nurses or

dietitians. The committee agreed that the guideline should not be overly prescriptive about MDT composition because service models vary across regions, but members strongly agreed that every MDT should include a dietitian to ensure safe and effective support for HCL users.

Service fragmentation was identified as another barrier. The committee highlighted the need for more joined up working across primary care, maternity services, and diabetes specialist teams, noting that inconsistent communication between sectors can compromise safe and timely adjustment of HCL settings during pregnancy. Better integration was viewed as essential for feasibility, especially as pump related issues may require input from different parts of the system. The committee further noted that implementation feasibility is influenced by workforce capacity. In many services, diabetes specialist nurses, dietitians, and other specialists already operate at full capacity, limiting their ability to support the rapid onboarding required for HCL system use during pregnancy. Therefore, the committee made a recommendation that psHCL should be accessible and tailored for the person and their carers according to their needs and preferences. which should be in line with NICE's guideline on patient experience in adult NHS services. This is also in line with NHS England's implementation plan, which aims to ensure equitable access to HCL and to reduce health inequalities.

The committee also acknowledged the importance of ensuring that people starting on HCL systems have meaningfully engaged with the training needed for competent and safe use. While some manufacturers provide checklists or competency tools, members agreed that the key priority is supporting users to understand how to operate the system safely, rather than relying on rigid or prescriptive measures of completion. They emphasised that training should enable people to use HCL confidently and should not act as a barrier to access, recognising that meaningful engagement may look different for different individuals.

The committee also discussed practical issues relating to device licensing and use of HCL systems in theatre environments. Members noted that some

pump manufacturers advise removal of the device in surgical settings - such as when diathermy or general anaesthesia is used. They acknowledged that in these situations, continuing HCL during intrapartum care may not be safe or feasible, as manufacturer guidance must be followed. They emphasised that if a pump needs to be removed in line with these instructions, services must ensure an appropriate alternative source of basal insulin is provided to reduce the risk of DKA. The committee recognised that feasibility during surgical interventions will therefore depend on the specific manufacturer guidance for each device and noted that variation in local hospital policies on pump removal and intrapartum management contributes to inconsistent and potentially unsafe practice. They agreed that clearer, locally developed safety protocols would help support safe and feasible implementation without contravening device requirements. As soon as clinicians feel it is safe to do so, they should discuss reconnecting the HCL with the person.

The committee also recognised broader structural barriers such as current regional variability in pump service availability, which may require people to travel long distances to access training or specialist support. This was seen as a major feasibility constraint, particularly for those with limited financial, social, or logistical capacity to travel. However, the committee were aware that the NHSE Implementation Plan should address this.

Overall, the committee agreed that HCL systems are feasible to implement, as they are already used across NHS services according to the NHS England's implementation plan.. However, implementation may be limited by barriers such as variation in MDT capacity, differences in staff expertise with HCL, and inequalities related to numeracy, language, or access to structured training. Addressing these barriers through flexible training, inclusive guidance, and clear implementation support will be essential for equitable and effective delivery of the intervention.

1.1.9.6 Strength of the recommendations

The committee agreed to offer psHCL systems for people with type 1 diabetes who are planning pregnancy, during pregnancyand the postnatal period,

despite the overall low certainty of the evidence. The evidence base was informed primarily by a small single study (AiDAPT trial), with evidence available for use during pregnancy and the postnatal period, and an absence of direct evidence for the pre-conception and intrapartum periods. The committee made these recommendations because the desirable effects of HCL - particularly improvements in TiR and early pregnancy glucose management, were considered clinically important and directly relevant to maternal and neonatal outcomes in the UK healthcare context. Considering the evidence presented and the clinical expertise, the committee also acknowledged that psHCL systems appear more beneficial than non-psHCL systems, with more meaningful improvements demonstrated for the outcomes the AiDAPT trial was powered to assess. These combined factors supported the committee's decision to recommend psHCL for people with type 1 diabetes during preconception period, pregnancy and postpartum period.

Lay members from the committee gave their experiences of using HCL systems and clinical experience alongside the evidence found suggests meaningful glycaemic benefits. Therefore, members supported an offer recommendation alongside competence requirements and MDT oversight.

The committee also noted that implementation challenges - such as training needs, MDT variation, and risks of widening inequalities could be mitigated through supportive, flexible, and inclusive recommendations.

The strength of the recommendation therefore reflects the high clinical importance of achieving optimal glycaemic management for planning pregnancy, during pregnancy and the immediate postnatal period, the substantial potential benefits observed in the outcomes the trial was powered for, and the committee's confidence that the intervention can be delivered safely and effectively within existing NHS structures in line with the NHSE Implementation Plan, even in the context of limited and low-certainty evidence.

1.1.10 Recommendations supported by this evidence review

This evidence review supports recommendations 1.2.3, 1.9.2, 1.9.3, 1.9.4, 1.15.2, 1.15.4, 1.15.5, 1.15.6, 1.22.1, 1.22.2, 1.24.3, 1.25.2, 1.29.1, 1.30.1, 1.30.2 and the two research recommendations on the effectiveness of hybrid closed loop system in reducing neonatal and maternal adverse events. The evidence for all recommendations is based on the current evidence review, except for recommendation 1.24.3, which is informed by the current review and the 2008 and 2015 reviews.

1.1.11 References

1.1.11.1 Effectiveness evidence

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1.1.11.2 Economic evidence

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type 1 diabetes in pregnancy: an economic evaluation of the CRISTAL trial. EClinical Medicine 81: 103106

1.1.11.3 Miscellaneous

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