Cost-effectiveness of advanced hybrid closed loop therapy compared to standard insulin therapy for type 1 diabetes in pregnancy: an economic evaluation of the CRISTAL trial

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Summary

Background A multicentre, randomised controlled trial (the CRISTAL trial), demonstrated the safety and efficacy of MiniMed™ 780G advanced hybrid closed loop (AHCL) therapy during pregnancy, showing improved glycaemic control overnight, less hypoglycaemia, and improved treatment satisfaction compared to standard insulin therapy (SoC, mainly open-loop insulin pump therapy). This study aimed to assess the cost-effectiveness of AHCL, which has a higher initial cost, compared to SoC in pregnant women with type 1 diabetes (T1D).

Methods A decision tree model was developed to estimate the cost-effectiveness of AHCL compared to SoC in pregnant women with T1D, covering pregnancy to birth and postpartum hospital discharge (a time horizon of 28 weeks). Total costs per strategy (in 2024 euros, €) were calculated from a healthcare payer perspective. The base-case analysis derived prevalence of pregnancy complications and hospitalisations directly related to diabetes management from the CRISTAL trial. Uncertainty was analysed by exploring multiple scenarios and sensitivity analyses.

Findings In the base-case analysis, the cost of using AHCL during pregnancy was estimated at €13,988.75 (95% CI: €12,240 to €16,062) compared to €14,221.33 (95% CI: €12,380 to €16,420) for SoC, indicating cost-savings of €232.57 per individual, alongside the demonstrated clinical benefits of AHCL. The primary cost driver was the AHCL device cost. This cost was offset by savings from shorter and less frequent hospital admissions (mainly due to severe hypoglycaemia and dysregulated diabetes) in the AHCL group compared to SoC. In our probabilistic sensitivity analysis, AHCL was dominant in 73% of the simulated cost-effectiveness pairs.

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Interpretation AHCL might be cost-saving compared to SoC for pregnant women with T1D. However, more robust data are needed to assess the potential impact of AHCL therapy on pregnancy and long-term health outcomes.

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Keywords: Cost-effectiveness; Healthcare costs; Economic evaluation; Type 1 diabetes; Pregnancy; Advanced hybrid closed loop therapy; Randomised controlled trial

Research in context

Evidence before this study

We searched PubMed for studies in English up to the second of July 2024, on cost-utility and cost-effectiveness analyses comparing advanced hybrid closed loop therapy (AHCL) and standard insulin therapy in pregnant women with type 1 diabetes (T1D). We used search terms including but not limited to "type 1 diabetes", "pregnancy", "closed-loop therapy", "closed-loop insulin delivery", "automated insulin delivery", "advanced hybrid closed loop therapy", in combination with the terms "cost-effectiveness", "cost-utility", "cost-benefit", "cost-minimisation", "economic evaluation", and "healthcare costs". Recent studies have demonstrated benefit of AHCL use in pregnancies complicated by T1D. The AiDAPT trial evaluated an approved AHCL system for use in pregnancy (CamAPS® FX), and demonstrated a 10% increase in pregnancy-specific time in range compared to standard insulin therapy in a pregnant population with T1D. Recently, the CRISTAL trial, evaluating an AHCL (MiniMed™ 780G) not approved for use in pregnancy, has also demonstrated benefits of AHCL compared to SoC, with improved pregnancy-specific time in range overnight, less hypoglycaemia and improved treatment satisfaction. However, despite its demonstrated clinical effectiveness, there is a lack of data on the economic impact of AHCL compared to SoC in pregnant individuals with T1D. We could not find any economic evaluation studies on AHCL use in pregnancies complicated by T1D.

Added value of this study

This is the first cost-effectiveness study comparing costs and effects of AHCL therapy with SoC in pregnancies complicated by T1D, based on the CRISTAL trial, which was a large randomised controlled trial comparing AHCL (MiniMed™ 780G) with SoC in pregnant people with T1D. Women in the SoC group used mainly open-loop insulin pump therapy, more specifically the MiniMed™ 640G or MiniMed™ 780G in manual insulin delivery mode. For a conservative cost comparison, the lower-cost MiniMed™ 640G was assumed for the entire SoC group. Although there was remaining uncertainty, we find that AHCL therapy results in estimated net cost savings of €232.57 per individual compared to SoC. The higher cost of the MiniMed™ 780G was completely offset by the lower probability and cost of diabetes-related complications during pregnancy requiring hospital admission in the AHCL group, as indicated by the conservative base-case analysis. In more inclusive scenarios, cost savings were higher, further suggesting an economic advantage of AHCL therapy, in addition to the clinical benefits demonstrated in the CRISTAL trial.

Implications of all the available evidence

Besides providing some clinical benefits, [such as improved glycaemic control overnight (an additional 24 min per night), less hypoglycaemia (19 min less per day and 7 min less per night) and improved treatment satisfaction], AHCL therapy with MiniMed™ 780G might also be cost-saving compared to SoC for pregnant women with T1D, mainly based on reduction in hospitalisations for severe hypoglycaemia and dysregulated diabetes in the CRISTAL trial.

Introduction

Type 1 diabetes (T1D) poses considerable challenges for pregnant women aiming for tight glycaemic control to mitigate adverse pregnancy outcomes. Suboptimal glycaemic control around the time of conception is associated with congenital anomalies and miscarriage, whereas hyperglycaemia throughout pregnancy is linked to other pregnancy complications such as pre-eclampsia, caesarean sections (C-sections), large-for-gestational age (LGA) infants, and neonatal intensive care unit (NICU) admissions.[1] A retrospective study in Belgium showed that approximately 45% of pregnant women with T1D delivered a LGA infant and 67% received a C-section, and these rates did not improve over time.[2]

In recent years, significant advancements have been made in diabetes care, offering promising treatment options for managing T1D, such as advanced hybrid closed loop (AHCL) therapy.[3–5] While the use of these AHCL systems is increasing, a barrier to adoption can be the higher cost of the devices. However, although AHCL technology is more expensive, studies outside

pregnancy have shown its potential cost-effectiveness over a patient lifetime compared to standard insulin therapy (SoC).[6,7]

In pregnancy, AHCL systems have shown to be safe and effective options to manage T1D.[1,8] The CRISTAL trial showed that use of MiniMed™ 780G (Medtronic, Northridge, CA, USA) in the AHCL group did not significantly improve overall time in the pregnancy-specific target range but achieved statistically significant improvements in glycaemic control overnight (an additional 24 min per night), reductions in hypoglycaemia (19 min less per day and 7 min less per night), and increased treatment satisfaction in pregnant women with T1D compared to SoC.[1] Given these clinical benefits, assessing the cost implications of AHCL therapy in pregnancy is crucial for policy-makers to make informed decisions about its potential implementation.

By using data derived from the CRISTAL trial, this study aimed to conduct the first cost-effectiveness estimation of AHCL therapy compared to SoC in pregnant women with T1D from the Belgian healthcare payer perspective.

Methods

Description of the CRISTAL trial

The CRISTAL trial, a double-arm, parallel-group, open-label, binational, multicentre randomised controlled trial (RCT), compared the MiniMed™ 780G AHCL system (intervention group) to SoC (control group with insulin injections, standalone insulin pump or sensor-augmented pump therapy) in pregnancies complicated by T1D.[9] This trial is registered with ClinicalTrials.gov (NCT04520971). A total of 95 pregnant women were randomly assigned (1:1) to AHCL therapy (n = 46) or SoC (n = 49), of whom 43 and 46 completed the trial, respectively. The eligibility criteria and a full description of the study procedures and results of the CRISTAL trial have been published previously.[1,9]

In summary, the CRISTAL trial demonstrated the efficacy of the MiniMed™ 780G AHCL system compared to SoC, showing at least equivalent outcomes for the primary outcome [mean proportion of time spent in the pregnancy-specific target glucose range 3.5–7.8 mmol/L or 63–140 mg/dL (TIRp)] and statistically significant improvements in the key secondary outcomes [overnight TIRp, proportion of time spent below the pregnancy-specific target glucose range (TBRp), and overnight TBRp]. In addition, the AHCL group showed statistically significant improvements in treatment satisfaction, as measured by the Diabetes Treatment Satisfaction Questionnaire (DTSQ) status and change satisfaction points, compared to SoC. Although the trial was not powered to assess pregnancy outcomes, trends were observed in the AHCL group, including reduced excessive gestational weight gain (EGWG) and a lower frequency of NICU admissions for neonatal hypoglycaemia. Additionally, the C-section rate was 49% in the AHCL group compared to 64% in the SoC group, albeit without a statistically significant difference.[1] Health-related quality of life (HRQoL) data, collected throughout pregnancy using the SF-36 survey, showed no meaningful differences between the groups.[1]

Ethics

This study was conducted in accordance with the Declaration of Helsinki and applicable regulatory requirements. The study was approved by the medical ethics review committees of participating centres, and Belgian and Dutch national competent authorities (Belgian registration number: B3222020000272; Dutch registration number NL78535.000.21). Participants provided written informed consent before any study-related activity.

Decision tree model

To estimate the cost-effectiveness of implementing AHCL therapy compared to SoC in pregnant women with T1D, a decision tree model was constructed using TreeAge Pro 2021 software (Williamstown, MA, USA). Since the primary outcome of the CRISTAL trial was not statistically significant, and the study was not powered to assess differences in pregnancy outcomes, a comprehensive long-term economic analysis (including indirect costs), as initially described in the protocol, was not performed.[9] Instead, this analysis considers only direct healthcare costs associated with short-term pregnancy outcomes over a time horizon of 28 weeks, corresponding to the duration of AHCL use (in the intervention group) throughout pregnancy. This was defined based on randomisation at a median of 10.1 weeks' gestation in the CRISTAL trial and an assumed full-term pregnancy duration of 38 weeks.[1] Fig. 1 provides a schematic representation of the decision tree model's structure. The branches were designed to reflect the pregnancy outcomes observed in the CRISTAL trial that directly influence healthcare costs. The AHCL (in the upper main branch) and SoC (in the lower main branch) groups follow the same structure and sequence of outcomes. Individual maternal and neonatal complications were bundled in decision nodes based on the treatment they received (with versus without hospitalisation). Treatment with hospitalisation during pregnancy included maternal hospital admission due to dysregulated diabetes, hyperglycaemia, severe hypoglycaemia, and/or diabetic ketoacidosis (DKA). Treatment without hospitalisation during pregnancy refers to outpatient care for gestational hypertension, preeclampsia, and EGWG. Both groups, those with complicated pregnancies and those with non-complicated pregnancies, subsequently follow the same path, involving the mode of delivery. Stillbirths and the possibility of a brachial-plexus injury (BPI, often related to the vaginal birth of

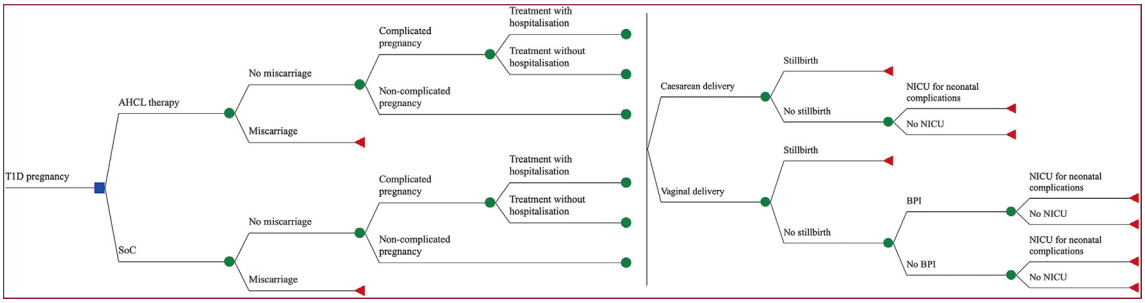

Fig. 1: **Decision tree model.**
The blue square represents the decision point between the two strategies. Green circles are probability nodes, representing uncertain events with branches showing possible outcomes. All probabilities of outcomes emanating from the same node sum to 1. The red triangles are terminal points representing the final outcomes. The vertical line in the decision tree model indicates that the subsequent subtrees follow the same structure and are therefore not shown in detail. The decision tree, read from left to right, first accounts for the possibility of miscarriage. For pregnancies continuing beyond 20 weeks, patients with complicated pregnancies face two potential scenarios: treatment with hospitalisation or treatment without hospitalisation. Delivery can be vaginal or through a C-section, with possibilities for stillbirth and BPI from vaginal deliveries. BPI is used in the decision tree model as a representative outcome of shoulder dystocia, without separately modelling shoulder dystocia, as both outcomes have a relatively small probability of occurring (approximately 1%).[10] N(I)CU admissions include preterm birth, hypoglycaemia, hyperbilirubinemia, and neonatal respiratory distress, as per NICE guidelines.[11] Abbreviations: T1D type 1 diabetes; AHCL advanced hybrid closed loop; BPI brachial plexus injury; N(I)CU neonatal (intensive) care unit.

a LGA infant) were modelled because of their substantial impact as consequences of suboptimal glycaemic control during pregnancy. The model ends with the type of neonatal care received. Neonates not requiring NICU admission were presumed to stay with the mother without additional treatment requirements.

Data and probability parameters

The CRISTAL trial provided the first data directly comparing AHCL therapy using the MiniMed™ 780G to SoC during pregnancy. Although the trial was primarily powered to measure TIRp and lacked sufficient power to reliably estimate prevalence rates for pregnancy outcomes, it remains the only relevant study on T1D pregnancies managed with the MiniMed™ 780G. To minimise the potential impact of the trial's limited power, only prevalence rates for outcomes during pregnancy were derived from the CRISTAL trial.[1] While the CRISTAL trial also captured data on pregnancy complications, supplementary data from a UK national cohort study and the CONCEPTT RCT were used for mode of delivery, birth injuries, NICU admissions, and perinatal mortality.[12,13] Existing literature provides data on the management of T1D in pregnancy with SoC. Due to the lack of adequately powered studies specifically examining pregnancy outcomes associated with AHCL use, the same SoC prevalence rates were applied to both the AHCL and SoC groups to maintain consistency. An overview of the probability parameters is provided in Table 1.

Costs

An overview of the cost parameters and components, expressed in euros (€) for the year 2024, is provided in Table 2. Total costs reflect the estimated cost on the Belgian market borne by the healthcare payer. This includes all direct costs associated with diabetes management, encompassing device use, healthcare services, and medications, from the onset of pregnancy until postpartum discharge of both the mother and neonate. Diabetes management device costs comprise three components: the insulin pump, and continuous glucose monitoring (CGM) consisting of the Guardian 3 or 4 sensor and transmitter. To avoid inflating costs, the use of the Guardian 3 CGM was assumed for all participants in both the AHCL and SoC groups. Although more participants in the SoC group used the Guardian 4 CGM, the Guardian 3 CGM is less costly yet equally effective in both AHCL and SoC strategies. The MiniMed™ 780G insulin pump in auto mode was used by the AHCL group. The majority of the SoC group used either the MiniMed™ 780G in manual mode (47.83%) or the MiniMed™ 640G (39.13%). To ensure that the cost comparisons are conservative, it was assumed that the entire SoC group used the lower-cost MiniMed™ 640G exclusively, given the functional similarity of insulin delivery between the MiniMed™ 780G in manual mode and the MiniMed™ 640G.

Since re-hospitalisations are not modelled, the average hospital duration is calculated as a total per patient rather than per admission, as this maintains consistency with the probability parameters, which are also calculated on a patient level. The hospital stay of neonates not admitted to the NICU is included in the delivery cost. All cost parameters include physician costs, either explicitly or implicitly through hospitalisation costs. Costs were not discounted as the time horizon of the analysis was less

than one year. Detailed calculations of the cost components are provided in the Supplementary Table S1 (Appendix p.3).[18–20]

Base case analysis

The base-case analysis is designed to offer the most conservative estimate by only including hospitalisations directly related to diabetes management –specifically for dysregulated diabetes, hyperglycaemia, severe hypoglycaemia, and DKA–, as observed in the CRISTAL trial.[1] This scenario aims to provide a lower-bound estimate by using trial data only to calculate the costs most directly related to diabetes management during pregnancy, based on the parameters detailed in Tables 1 and 2.

Uncertainty analysis

To account for the sensitivity of the results to changes in parameter estimates, univariate sensitivity analyses were employed. This involved constructing an interval for all input parameters by subtracting and adding 20% from each estimate. The parameter estimates were then varied individually within their respective 20% intervals to assess the impact on the results and identify the most influential parameters.

Furthermore, to explore the conditions under which the initial higher cost of the MiniMed™ 780G used in the AHCL group could be offset, a deterministic multivariate sensitivity analysis was conducted. In this analysis, both the cost of the MiniMed™ 780G and the number of hospitalisation days in the SoC group were varied from the base-case estimates in Table 2. Moreover, three scenarios were explored by varying the data source and the types of hospitalisations included in the base-case.

Scenario 1 was built on the base-case by including additional hospitalisations generally associated with diabetes, that were excluded from the base-case due to ambiguous links to diabetes management as potential secondary diagnoses. These hospitalisations include cases of DKA induced by pregnancy-related nausea and vomiting, gastroenteritis with DKA, and a COVID-19 infection with hyperglycaemia and DKA. The aim of modelling these ambiguous cases is to assess how their inclusion might influence the overall cost-effectiveness results, ensuring that the analysis covers all relevant potential outcomes.

In scenario 2, only hospitalisations strictly related to diabetes management were included, similar to the base-case. However, by relying solely on trial data for all modelled outcomes, this scenario reflects the direct evidence provided by the trial, offering a comparison that does not rely on external literature rates for pregnancy outcomes.

Finally, scenario 3 also used CRISTAL trial data but included additional hospitalisations with ambiguous links to diabetes management. This scenario provides a more inclusive view, similar to scenario 1, but fully grounded in trial data. Supplementary Tables S2 and S3 (Appendix pp.4–6) provide an overview of the probability and cost components used in each scenario. Details on the hospitalisations in each scenario are reported in Supplementary Table S4 (Appendix p.7).

To address the uncertainty inherent in the probability, cost, and effect parameters, a probabilistic sensitivity analysis was conducted. This analysis involved defining a distribution for all uncertain input parameters and using Monte Carlo simulations to generate 10,000 cost-effectiveness pairs representing potential combinations of incremental costs and effects. The distributions of the input parameters were defined by assuming a 20% standard deviation from the base-case values reported in Tables 1 and 2. Two separate effectiveness measures, TIRp (overnight) and TBRp (including both day and overnight improvements), expressed in minutes, were selected to simulate cost-effectiveness pairs, as both demonstrated statistically significant improvements in the trial.[1] A normal distribution was employed for both TIRp (overnight) and TBRp. The primary outcome of the CRISTAL trial, overall TIRp, was not used as the effectiveness outcome as the difference between AHCL and SoC was not statistically significant.[1] The incremental cost-effectiveness ratio (ICER) comparing the incremental costs with the incremental clinical effects, is used to evaluate whether the additional health gains from AHCL

Probability parameters	Base-case value (95% CI)	Distribution	Source
Miscarriage			
AHCL therapy	0.08 (0.05, 0.11)	Beta	Literature[12]
SoC	0.08 (0.05, 0.11)	Beta	Literature[12]
Complicated pregnancy			
AHCL therapy	0.49 (0.30, 0.68)	Beta	CRISTAL[1]
SoC	0.67 (0.42, 0.88)	Beta	CRISTAL[1]
Treatment with hospitalisation			
AHCL therapy	0.05 (0.08, 0.19)	Beta	CRISTAL[1]
SoC	0.13 (0.03, 0.07)	Beta	CRISTAL[1]
Caesarean delivery			
AHCL therapy	0.63 (0.37, 0.85)	Beta	Literature[13]
SoC	0.63 (0.37, 0.85)	Beta	Literature[13]
Stillbirth			
AHCL therapy	0.01 (0.006, 0.14)	Beta	Literature[13]
SoC	0.01 (0.006, 0.14)	Beta	Literature[13]
BPI	0.01 (0.004, 0.14)	Beta	Literature[13]
N(I)CU admission			
AHCL therapy	0.43 (0.27, 0.60)	Beta	Literature[12]
SoC	0.43 (0.27, 0.60)	Beta	Literature[12]

The base-case analysis uses literature data for perinatal outcomes with parameters applied consistently to both randomisation groups. Standard errors are assumed to be 20% for all parameters and across all scenarios. A beta distribution was used for probabilities, as it is suited for variables bounded between 0 and 1. The 95% confidence intervals represent the range within which the true parameter values are expected to lie based on the Monte Carlo simulations. Abbreviations: AHCL advanced hybrid closed loop; SoC standard insulin therapy; BPI brachial plexus injury; N(I)CU neonatal (intensive) care unit; CI confidence interval.

Table 1: **Probability parameters and distributions used in the base-case analysis for the AHCL and SoC groups.**

Cost component	Base-case value €	Distribution	95% CI	Source
AHCL technology				
MiniMed™ 780G	5096.24	NA[a]	NA[a]	Commercial source: MyDiabetesCare website[14]
Guardian 3 sensor	58.67[b]	NA[a]	NA[a]	University Hospital Leuven (2023)
Guardian 3 transmitter	351.19	NA[a]	NA[a]	University Hospital Leuven (2023)
SoC technology				
MiniMed™ 640G	4542.10	NA[a]	NA[a]	Commercial source: MyDiabetesCare website[14]
Guardian 3 sensor	58.67[b]	NA[a]	NA[a]	University Hospital Leuven (2023)
Guardian 3 transmitter	351.19	NA[a]	NA[a]	University Hospital Leuven (2023)
Miscarriage	1082.76[c]	Gamma	(700.52, 1545.15)	Literature[15]
Treatment with hospitalisation (AHCL)				
Total average cost per patient	2828.34			
Average cost per day	942.78	Gamma	(602.52, 1352.18)	Belgian NIHDI data (2021) and literature[16]
Average days per patient	3	Gamma	(2, 4)	CRISTAL[1]
Treatment with hospitalisation (SoC)				
Total average cost per patient	10,841.97			
Average cost per day	942.78	Gamma	(602.52, 1352.18)	Belgian NIHDI data (2021) and literature[16]
Average days per patient	11.5	Gamma	(7, 16)	CRISTAL[1]
Treatment without hospitalisation				
AHCL therapy	217.17	Gamma	(140.44, 310.05)	Composite parameter, see Appendix Table S1
SoC	144.18	Gamma	(93.27, 205.25)	Composite parameter, see Appendix Table S1
Delivery				
Caesarean	5437.95[d]	Gamma	(3509.83, 7734.95)	Belgian NIHDI data (2021) and CRISTAL[1]
Vaginal	3412.66[d]	Gamma	(2204.49, 4877.98)	Belgian NIHDI data (2021) and CRISTAL[1]
Stillbirth				
Stillbirth through vaginal delivery	4308.84[e]	Gamma	(2772.29, 6110.59)	Belgian NIHDI data (2021)
Stillbirth through caesarean delivery	6294.39[e]	Gamma	(4080.53, 9011.45)	Belgian NIHDI data (2021)
BPI	1462.39[f]	Gamma	(938.71, 2087.78)	Composite parameter, see Appendix Table S1
N(I)CU admission (AHCL)				
Average cost per day	990.98	Gamma	(638.90, 1401.34)	Belgian NIHDI data (2021)
Duration of an admission	6	Gamma	(4, 8)	Literature[17] and CRISTAL[1]
N(I)CU admission (SoC)				
Average cost per day	990.98	Gamma	(638.90, 1401.34)	Belgian NIHDI data (2021)
Duration of an admission	6	Gamma	(4, 8)	Literature[17] and CRISTAL[1]

Standard errors are assumed to be 20% for all cost components and across all scenarios. Distributions are defined for every cost component included in the Monte Carlo simulations. [a]Distribution not applicable as the purchase cost is given and not subject to variation. [b]The Guardian 3 sensor was assumed for all participants in both AHCL and SoC groups. Sensor replacement was assumed every 7 days during 28 weeks. [c]Miscarriage cost includes pregnancy termination associated with a 24–48-hour hospitalisation. [d]Delivery cost includes an average hospital stay of 5 days for C-sections and 3 days for vaginal deliveries. These durations align with Belgian NIHDI data. [e]Stillbirth cost includes a complicated caesarean/vaginal delivery and a follow-up consultation with a gynaecologist. [f]BPI cost includes a complicated delivery, diagnostic costs and kinesiotherapy. Where applicable, costs were adjusted to 2024 values using the Belgian Consumer Price Index (CPI). Abbreviations: NIHDI National Institute for Health and Disability Insurance; AHCL advanced hybrid closed loop; SoC standard insulin therapy; N(I)CU neonatal (intensive) care unit; BPI brachial plexus injury; NA not applicable; € euros; 95% CI 95 percent confidence interval.

Table 2: **Costs components and distributions used in the base-case analysis for the AHCL and SoC groups.**

therapy can be achieved at an acceptable cost. However, when AHCL is the dominant strategy (improved outcomes at lower costs), an ICER is less informative and typically not reported.[21] Cost-effectiveness pairs and planes were generated using RStudio (Version 2024.09.0+375).

Role of the funding source

UZ Leuven was the sponsor of the investigator-initiated CRISTAL trial. Trial funding was provided by the Diabetes Liga Research Fund (grant number 2020-J1191940-218926), and Medtronic (Northridge, CA, USA) provided devices and an unrestricted grant for academic research. Representatives from the Diabetes Liga (representing people living with diabetes and healthcare professionals in diabetes care) and Medtronic received a copy of the manuscript before submission. The funders had no role in trial design, data collection, data analysis, data interpretation, writing of the manuscript, or the decision to submit the manuscript for publication.

Results

The results of the base-case cost-effectiveness analysis and the Monte Carlo simulations performed on the

decision tree model are displayed in Figs. 2 and 3 and Table 3. The total healthcare cost per patient was estimated at €13,988.75 with AHCL therapy and €14,221.33 with SoC, resulting in a cost difference of approximately €232.57 (95% CI: €–1,066 to €297), favouring AHCL therapy. The mean incremental effects are an increase of 24 min in overnight TIRp (95% CI: 8.32 to 39.06) and a reduction of 19 min in TBRp (95% CI: −31.54 to −7.06).[1] Fig. 3 illustrates the uncertainty in these results using two separate cost-effectiveness planes, one for each key secondary outcome: TIRp overnight and TBRp. The cost-effectiveness planes classify outcomes based on whether AHCL is more or less effective, and more or less costly, compared to SoC.

Based on 10,000 simulations, AHCL was, on average, more effective and less costly (i.e., dominant) compared with SoC. Overall, 73% of the cost-effectiveness pairs indicate that AHCL was more effective and less costly, while 27% of pairs suggest AHCL was more effective (higher TIRp overnight, lower TBRp) but also more costly. Consequently, the estimated ICERs indicated dominance, with values of €–10.43 per incremental minute improved TIRp overnight and €–11.96 per incremental minute reduced TBRp.

The univariate sensitivity analysis is presented in the tornado diagram in Fig. 4, showing that the estimated cost difference of €232.57 is most sensitive to changes in the cost of the MiniMed™ 780G device, and the probability and associated cost of complicated pregnancies requiring hospitalisation in the SoC group. These results are further explained by calculated data from the base-case analysis in Table 1, where 1 out of 20 participants with complicated pregnancies required hospitalisation in the AHCL group, resulting in a conditional probability of 0.05. In the SoC group, 4 out of 30 participants with complicated pregnancies required hospitalisation, resulting in a conditional probability of 0.13. Additionally, hospitalisations in the AHCL group were shorter, leading to lower healthcare costs for complicated pregnancies. Specifically, as reported in Table 2, the AHCL group had an average length of hospital stay of three days per patient at a daily cost of €942.78, resulting in a total cost of €2,828.34 per hospitalised patient. In contrast, the SoC group had an average length of stay of 11.5 days per patient with a daily cost of €943.78, resulting in a total cost of €10,841.97 per hospitalised patient.

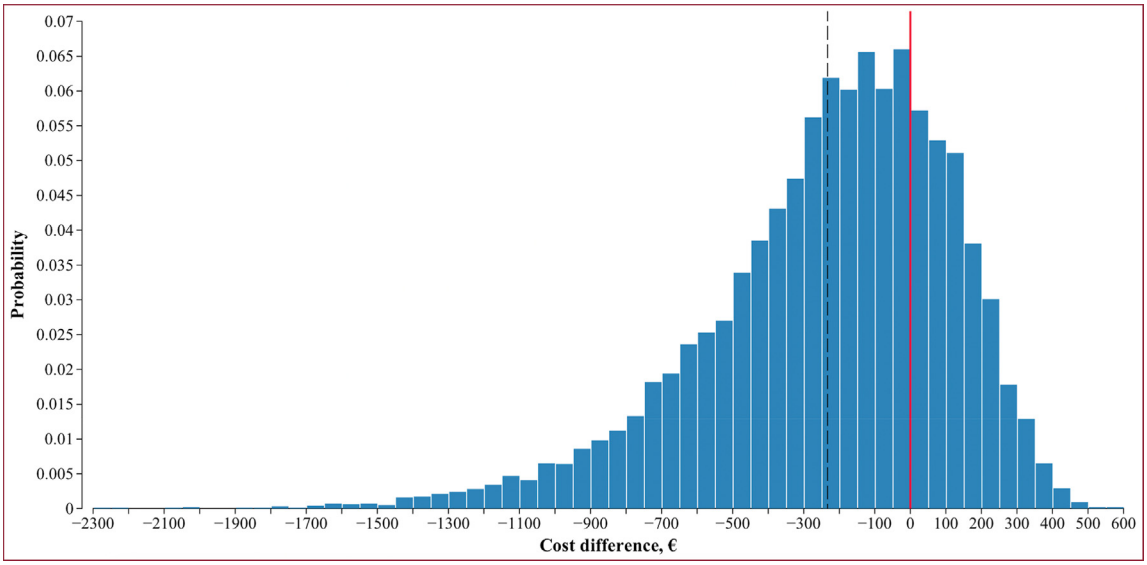

Fig. 2: **Probability distribution of the incremental cost in the base-case analysis, based on 10,000 Monte Carlo simulations (AHCL therapy vs. SoC).**

The results of the Monte Carlo simulations reflect the impact of sampled parameter uncertainties on the model results. The means represent averages from 10,000 simulations, each incorporating an assumed standard deviation of 20% for uncertain parameters (as reported in Tables 1 and 2). The histogram displays the distribution of the cost difference (€) between the AHCL therapy group and the SoC group across 10,000 simulations. The x-axis represents the difference in costs between AHCL therapy and SoC, ranging from approximately –2,300 to 600 euros. The y-axis represents the probability density of the cost differences, with higher bars indicating more frequent outcomes. The dashed line, positioned at –233€, represents the estimated incremental cost difference. The red solid line, positioned at 0 €, marks the point where the cost difference between AHCL and SoC is zero. The area to the left of the red line represents 73% of the simulated outcomes. In these cases, the additional cost of the MiniMed™ 780G device is offset by healthcare cost savings, indicating that AHCL is cost-saving. The area to the right of the red line represents 27% of the simulated outcomes. In these cases, SoC becomes cost-saving compared to AHCL. The distribution is left-skewed, with most of the values left of the red vertical line indicating that in most simulations, AHCL therapy results in cost savings (negative cost differences). Abbreviations: AHCL advanced hybrid closed loop; SoC standard insulin therapy; € euros.

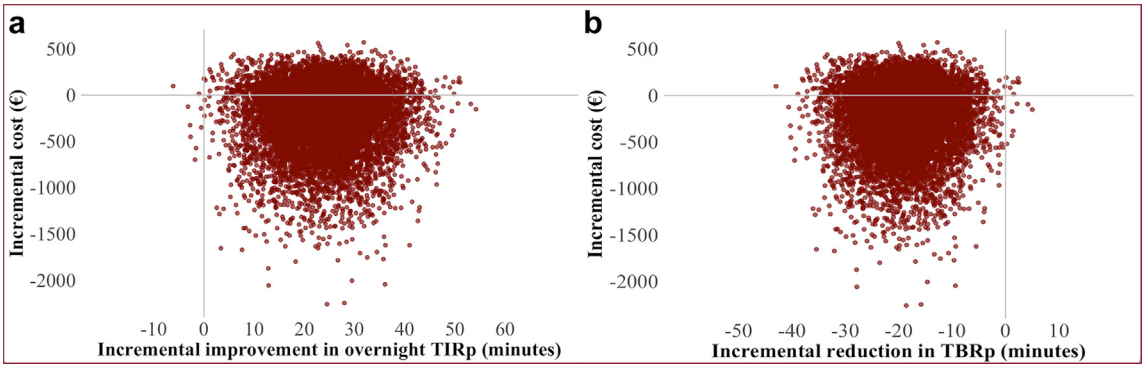

Fig. 3: **Cost-effectiveness planes demonstrating the probability of cost-effectiveness for AHCL compared to SoC in the base-case analysis, based on 10,000 Monte Carlo simulations.**
The y-axis represents the incremental cost of AHCL compared to SoC (€), while the x-axis represents the incremental effects in minutes. In panel a, the incremental effects are defined as the difference in improved overnight pregnancy-specific time in range (TIRp) of AHCL compared to SoC, with positive values indicating increased TIRp (overnight). In panel b, the incremental effects are defined as the difference in reduced pregnancy-specific time below range (TBRp) of AHCL compared to SoC, with negative values indicating a reduction in TBRp. In panel a, 0.02% of the cost–effect pairs fall in the north-west (NW) quadrant (less effective, more costly); 0.07% fall in the south-west (SW) quadrant (less effective, less costly); 72.79% fall in the south-east (SE) quadrant (more effective, less costly); and 27.12% fall in the north-east (NE) quadrant (more effective, more costly). In panel b, where the x-axis measures reductions in TBRp (improvements are negative), 27.07% of the cost–effect pairs fall in the NW quadrant (more effective, more costly); 72.79% fall in the SW quadrant (more effective, less costly); 0.07% fall in the SE quadrant (less effective, less costly); and 0.07% fall in the NE quadrant (less effective, more costly). Both TBRp and overnight TIRp were assumed to be normally distributed. Abbreviations: € euros; TIRp pregnancy-specific time in range; TBRp pregnancy-specific time below range.

In Fig. 5, the deterministic multivariate analysis on the MiniMed™ 780G cost and hospitalisation duration for the SoC group, showed that the threshold number of hospitalisation days for the current MiniMed™ 780G cost of €5,096.24 is approximately 8 days. At the observed hospitalisation duration of 11.5 days in the SoC, the MiniMed™ 780G cost can go as high as €5,331 (from the current cost of €5,096.24) before both treatment options become equally costly. Supplementary Table S4 (Appendix p.7) provides a detailed overview of the considered hospitalisations with indications, and the average durations for each scenario. Similar to the base-case, hospitalisation costs were lower in the AHCL group across all scenarios due to shorter durations.

The estimated costs and cost-effectiveness results under the three scenarios, compared to the base-case analysis, are reported in Table 3. In scenario 1 (base-case with ambiguous hospitalisations), AHCL is dominant in 59% of the simulations, with on average €126.38 in cost savings. The estimated ICERs were €–3.57 per incremental minute of improved overnight TIRp, and €–6.64 per incremental minute of reduced TBRp. Scenario 2 and scenario 3, both fully based on trial data, showed a cost difference of €786.64 and €796.66, respectively. In these scenarios, AHCL is the dominant

Analysis	AHCL cost €	SoC cost €	Incremental cost ΔC (95% CI) €	Incremental effect ΔE: overnight TIRp (95% CI)	Incremental effect ΔE: TBRp (95% CI)	$ICER^{overnight\ TIRp}$ (% dominant simulations)	$ICER^{TBRp}$ (% dominant simulations)
Base-case	13,988.75	14,221.33	−232.57 (−1066.88, 297.08)	24 (8.32, 39.06)	−19 (−31.54, −7.06)	Dominant (72.79%[a])	Dominant (72.79%[a])
Scenario 1	14,209.61	14,335.98	−126.38 (−1066.88, 297.08)	24 (8.32, 39.06)	−19 (−31.54, −7.06)	Dominant (59.18%[a])	Dominant (59.18%[a])
Scenario 2	12,913.79	13,700.43	−786.64 (−2862.1, 894.86)	24 (8.32, 39.06)	−19 (−31.54, −7.06)	Dominant (80.33%[a])	Dominant (80.35%[a])
Scenario 3	13,026.39	13,823.05	−796.66 (−2577.78, 766.68)	24 (8.32, 39.06)	−19 (−31.54, −7.06)	Dominant (78.89%[a])	Dominant (78.94%[a])

The results of the Monte Carlo simulations reflect the impact of sampled parameter uncertainties on the model outcomes. Estimated costs are averages from 10,000 simulations, each employing a 20% standard deviation for all uncertain cost and probability parameters. The 95% confidence interval (CI) represents the variability in simulated costs, providing an estimate of the range within which the true incremental cost could plausibly lie. Incremental effects are represented by changes in pregnancy-specific overnight time in range (TIRp) and reduced time below range (TBRp), expressed in minutes, based on observations from the CRISTAL trial. The 95% CIs of the incremental effects reflect variability observed in the trial. The incremental cost-effectiveness ratio (ICER) is reported for TIRp (overnight) and TBRp separately. $ICER^{overnight\ TIRp}$ is expressed as € per incremental minute of improved TIRp (overnight). $ICER^{TBRp}$ is expressed as € per incremental minute of reduced TBRp. *Dominant* indicates that AHCL is both more effective (higher overnight TIRp, lower TBRp) and less costly than SoC. Abbreviations: AHCL advanced hybrid closed loop; SoC standard insulin therapy; € euros; CI confidence interval. ICER Incremental cost-effectiveness ratio. [a]Percentages show the proportion of simulations where AHCL was estimated to be less costly and more effective, yielding a negative ICER.

Table 3: **Cost-effectiveness analysis of AHCL compared to SoC: estimated costs, incremental effects, and incremental cost-effectiveness ratios (ICERs) across all scenarios.**

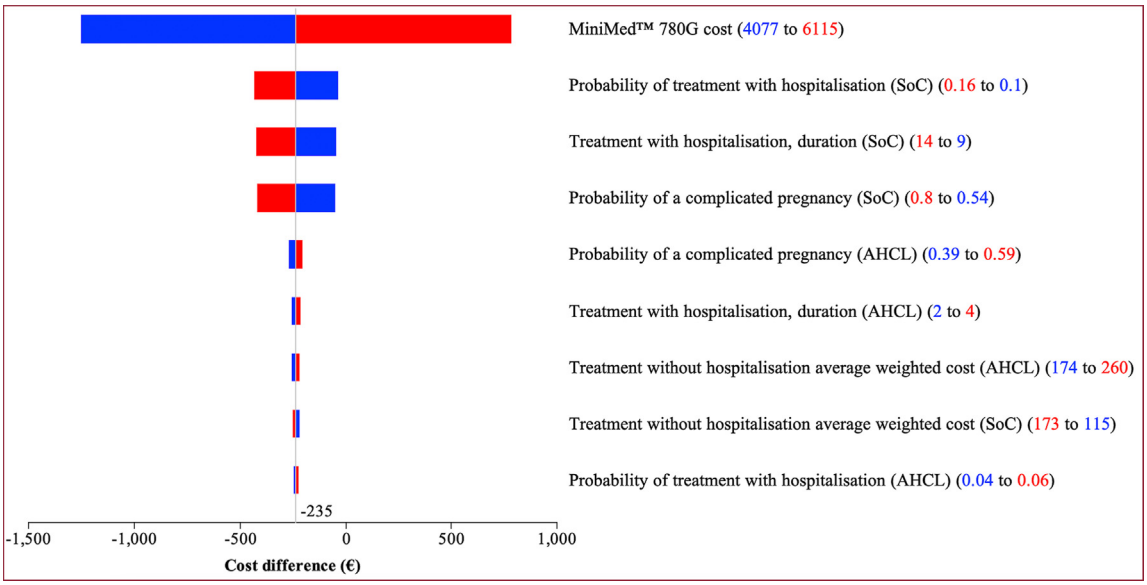

Fig. 4: **Tornado diagram showing the cost difference of AHCL therapy compared to SoC in the base-case analysis.**
This tornado diagram illustrates the sensitivity of the cost difference between AHCL and SoC to variations in key model parameters (univariate sensitivity analysis). The x-axis represents the cost difference in euros (€), with negative values indicating cost savings for AHCL and positive values indicating higher costs for AHCL. Blue bars indicate the decrease in the parameter value, red bars indicate an increase. The extent of each bar shows the impact on the cost difference when the parameter is varied within its specified range. Probability and cost parameters were varied for the MiniMed™ 780G device cost, miscarriages, complicated versus non-complicated pregnancies, and treatment with versus without hospitalisation. Since the same values were consistently applied to both the AHCL and SoC groups, parameters associated with perinatal outcomes did not alter the incremental results in the univariate sensitivity analysis and were therefore excluded from this diagram. Abbreviations: AHCL advanced hybrid closed loop; SoC standard insulin therapy; € euros.

strategy in 80% and 79% of the simulations, respectively. In scenario 2, the estimated ICERs were €–41.21 per incremental minute of improved overnight TIRp, and €–42.58 per incremental minute of reduced TBRp. In scenario 3, the estimated ICERs were €–35.94 per incremental minute of improved overnight TIRp, and €–40.43 per incremental minute of reduced TBRp. Supplementary Figure S1 (Appendix p.9) shows the cost-effectiveness pairs for each scenario analysis, with TIRp (overnight) and TBRp presented as separate outcomes. Supplementary Table S5 (Appendix p.8) provides a summary of the cost-effectiveness pairs within the quadrants of the cost-effectiveness planes for each scenario.

Discussion

AHCL therapy leads to improved glycaemic control in non-pregnant individuals with T1D.[3–5] In addition, recent studies have demonstrated benefit of AHCL use in pregnancies complicated by T1D.[1,8,22] The CRISTAL trial, evaluating an AHCL system (MiniMed™ 780G) not approved for use in pregnancy, has demonstrated clinical benefits of AHCL therapy compared to SoC in pregnant people with T1D, such as improved glycaemic control overnight (an additional 24 min per night) and reduced hypoglycaemia (19 min less per day and 7 min less per night).[1] Additionally, an increase in treatment satisfaction with AHCL therapy was observed, aligning with findings from Lawton et al., which show positive pregnancy experiences associated with AHCL use.[23] However, there is a lack of data on the cost-effectiveness of AHCL compared to SoC in pregnant individuals with T1D. This is the first study evaluating the cost-effectiveness of AHCL use in pregnancy compared to SoC. Our analysis found that although the cost of the AHCL system (MiniMed™ 780G) was €554 higher than that for SoC (MiniMed™ 640G) on the Belgian market, AHCL therapy was associated with fewer and shorter hospitalisations during pregnancy due to complications such as dysregulated diabetes, hyperglycaemia, severe maternal hypoglycaemia, and DKA. According to this analysis, the prevented healthcare costs offset the initial higher cost of the MiniMed™ 780G, resulting in net cost savings ranging from approximately €232.57 per patient in the conservative base-case analysis, to €796.66 per patient in the most inclusive scenario (scenario 3). In the base-case analysis, these net cost savings, combined with improved overnight TIRp and reduced TBRp, make AHCL the dominant intervention in 73% of simulations.[1] In 27% of simulations, AHCL was more effective but also more

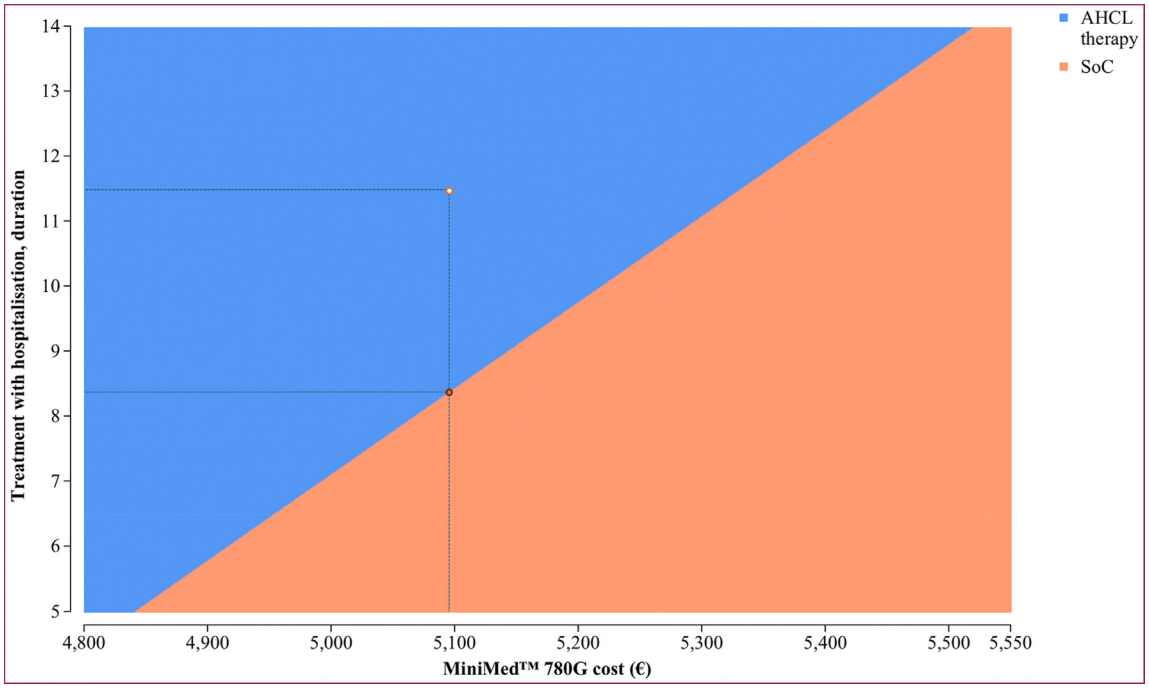

Fig. 5: **Multivariate sensitivity analysis on the MiniMed™ 780G cost in euros (€) and the number of hospitalisation days in the SoC group.**
The figure illustrates how changes to the MiniMed™ 780G cost in euros (x-axis) and the hospitalisation days in the SoC group (y-axis) affect the estimated cost difference. The orange area represents the combinations of the MiniMed™ 780G cost and hospitalisation days where SoC is the cost-saving choice, while the blue area indicates combinations where AHCL therapy is cost-saving. The intersection between the areas represents the combinations where the costs of AHCL and SoC are equal. At the observed average number of hospitalisation days in the SoC group (11.5 days) and the current cost of the MiniMed™ 780G (€5,096 on the Belgian market), AHCL therapy is more economical since this combination falls in the blue area, as indicated by the white circle. Given the current MiniMed™ 780G cost of €5,096, the threshold number of hospitalisation days is approximately 8.4 days. If the hospitalisation duration falls below this value, SoC becomes the cost-saving strategy, as indicated by the dark circle, which lies on the threshold. All combinations of fewer than 8.4 days fall below the dark circle and within the orange area.

costly. Even if AHCL does not result in cost savings, it could still be considered cost-effective if the clinical benefits are deemed worth the additional costs of the MiniMed™ 780G.[21]

In this analysis, TIRp overnight and TBRp are treated as separate effectiveness measures, assuming independence between these outcomes. This may underestimate cost-effectiveness, as these outcomes are correlated in clinical practice and collectively enhance clinical benefits. Furthermore, while the observed glycaemic improvements in the AHCL group may appear modest, even small improvements can have a meaningful clinical impact in pregnant women with T1D.

Although the CRISTAL trial demonstrated the safety and efficacy of AHCL use in pregnancy compared to SoC, caution is warranted regarding the modelled cost savings due to the limited reliability of prevalences derived from the clinical trial. The results suggest that AHCL is dominant compared to SoC. However, as the CRISTAL trial was not powered for the modelled outcomes, this dominance should be interpreted descriptively rather than inferentially. The Monte Carlo simulations accounted for this uncertainty by assuming a 20% standard deviation around each parameter's point estimate, allowing for variation within the defined distributions. Although the majority of simulations suggest cost savings with AHCL, there were instances where AHCL therapy was found to be more costly than SoC. These were primarily driven by changes in the prevalence rates of complications during pregnancy and the durations of maternal hospitalisations in the SoC group, as revealed by the univariate sensitivity analysis. When the differences in complication prevalences and hospital durations between the AHCL and SoC groups are minimised, the financial burden of hospitalisations in the SoC group (being the most costly outcomes modelled) may no longer fully offset the initial higher cost of AHCL therapy. Given the previously discussed data limitations, formal significance tests on cost differences were not feasible; thus, the Monte Carlo simulation results should not be misconstrued as results of formal hypothesis testing. Furthermore, by

sampling costs and effects independently from their respective distributions, the Monte Carlo simulations may generate cost-effectiveness pairs showing high costs combined with improved outcomes. This potentially underestimates the cost-effectiveness of AHCL therapy, as improved glycaemic control is typically associated with fewer cost-intensive pregnancy outcomes (e.g., hospitalisations, C-sections, and NICU stays). The analyses reveal that potential cost savings with AHCL therapy are indeed closely tied to its effectiveness in reducing the hospitalisation burden due to diabetes-related complications during pregnancy.

Since the CRISTAL study did not collect detailed data on maternal intensive care unit (ICU) admissions, hospitalisation costs were estimated based on regular inpatient care. Although this approach does not account for higher potential ICU costs for events like DKA or severe hypoglycaemia, the longer admission duration for such events in the SoC group suggest that this likely results in conservative estimates, favouring SoC.

Given the uncertainty surrounding hospitalisation duration, a threshold analysis for hospitalisation days in the SoC group was performed. Additionally, the multivariate analysis explored how changes in hospitalisation duration in the SoC group and the fixed cost of the MiniMed™ 780G device in the AHCL group influence cost savings. Given the higher initial cost of the device, as this cost decreases, the difference in hospitalisation burden between AHCL and SoC required for AHCL to be cost-saving also decreases.

An important strength of the study is that analyses could (partly) be based on data derived from the CRISTAL trial, a large RCT evaluating AHCL in pregnancies complicates by T1D. This allowed us to model the potential economic implications of improved diabetes control during pregnancy. Secondly, by bundling outcomes or complications during pregnancy according to the type of care required (with or without hospitalisation), the model acknowledges that healthcare costs are influenced by both the occurrence of complications and their severity, which dictates the level of care required. Moreover, grouping patients based on healthcare needs allowed for the use of aggregated cost estimates, such as the daily cost of hospitalisation, rather than detailed micro-costs (e.g., specific tests, medications, and healthcare provider fees). This approach is more pragmatic and may enhance the generalisability of the findings to healthcare systems similar to the Belgian system.

This study also has limitations. A key limitation is that a long-term economic analysis (including indirect costs) could not be performed, as it would rely, given the current data, on projections of outcomes that are already uncertain in the short term. The exclusion of indirect costs, such as work absenteeism, simplifies the analysis by relying on straightforward direct cost data. However, this approach may underestimate the total economic burden of suboptimal diabetes management during pregnancy. Certain assumptions also had to be made for modelling purposes. For instance, bundling hospitalisations may have obscured some clinically relevant outcomes, such as differences in the severity or duration of NICU admissions across groups. The base-case model assumes no such differences, although the CRISTAL trial reported that NICU admissions due to neonatal hypoglycaemia occurred less frequently in the AHCL therapy group compared to the SoC group (14.3% vs. 63.6%, respectively).[1] As a result, using the same duration for NICU stays in the base-case analysis and scenario analysis 1 may have obscured this clinically relevant difference. In contrast, scenarios 2 and 3, which incorporate CRISTAL trial data, show a slightly longer NICU duration in the SoC group than in the AHCL group. These differences might have indirectly addressed the obscuring effect seen in the base-case analysis. It is also important to note that some clinically relevant outcomes, such as neonatal hypoglycaemia, may not always translate clearly into monetary terms. For instance, even short NICU stays for neonatal hypoglycaemia can have substantial long-term health impacts that are not fully captured in cost estimates.[24] Finally, to ensure the most reliable estimates possible, the base-case analysis adopted the same prevalence rates from literature for pregnancy outcomes in both groups. This may underestimate the true cost difference by implying no effect of the treatment (AHCL vs. SoC) on these outcomes. To address this concern, scenario analyses were performed to capture a range of possible and more inclusive outcomes by gradually incorporating more CRISTAL trial data. The greater certainty in scenarios 2 and 3 regarding the potential cost-effectiveness of AHCL therapy suggests that incorporating a broader range of trial data, including differences in pregnancy complications influenced by diabetes management, may provide a more realistic view of the economic impact. In these scenarios, 80% and 79% of the simulations suggest that AHCL is the dominant strategy, respectively.

The use of the lower-cost MiniMed™ 640G was assumed for the entire SoC group to provide a conservative cost-effectiveness estimation. However, it is important to note that a large proportion of patients in the SoC group also used the MiniMed™ 780G, albeit in manual mode. This reflects real-world practice, where many women become pregnant while already using the MiniMed™ 780G or other alternatives that may also be more costly than the MiniMed™ 640G. It is therefore possible that the actual cost savings associated with AHCL therapy may be larger than estimated in this study, given that the comparison was based on the least expensive option in the SoC group (with the exclusion of insulin injections due to the very small numbers involved). Furthermore, to align most closely with the CRISTAL trial data, the use of the Guardian 3 CGM was

assumed for both AHCL therapy and SoC, as it was the most frequently used CGM system in both groups. This is a realistic assumption for SoC, given the incompatibility of Guardian 4 with the MiniMed™ 640G. While the Guardian 4 CGM is more commonly used with the MiniMed™780G in current practice, assigning its costs explicitly in the base case and scenario 1 would be methodologically flawed, as these scenarios deliberately restrict differences between AHCL and SoC to outcomes during pregnancy only. In scenarios 2 and 3, which allow for broader outcome differences, assigning Guardian 4 costs would reduce estimated cost savings by approximately 40% but would not alter dominance of AHCL. Explicitly modelling these costs in scenarios 2 and 3 was deemed unnecessary, as the estimated cost savings already exceed the additional costs of Guardian 4 usage, allowing us to infer its impact indirectly. Future studies with larger datasets could further explore the impact of CGM choice on cost-effectiveness.

While the CRISTAL trial data on pregnancy outcomes had insufficient statistical power, it is noteworthy that the observed parameters showed a numerically higher overall C-section rate and numerically higher LGA rate in the SoC group compared to the AHCL group (64.4% vs. 48.8% and 67% vs. 56%, respectively).[1] This additional clinical burden in the SoC group suggests more severe complications during pregnancy, although no definitive conclusions can be drawn. Additionally, the clinical benefits of AHCL-therapy that were demonstrated in the CRISTAL trial could potentially lead to improved long-term quality of life for both mother and neonate. In this study, AHCL appears to be a dominant intervention, offering cost savings along with demonstrated clinical benefits.[1] However, the Monte Carlo simulations indicated that in some cases, when parameter values are varied, AHCL could be more costly than SoC. A 20% standard deviation was assumed for probabilities and costs to define the distributions used in the simulations, as a pragmatic approach to model uncertainty. This approach may either underestimate or overestimate true uncertainty, as data-driven standard deviations are not currently available and would require other studies, e.g., meta-analyses of multiple RCTs comparing AHCL to SoC in T1D pregnancies.

It is important to acknowledge that conducting a RCT like the CRISTAL or AiDAPT study with sufficiently large sample sizes to ensure adequate power for pregnancy outcomes is not feasible, as this would probably require tripling the sample size. Furthermore, as the number of women with childbearing potential already using AHCL before pregnancy continues to increase, the willingness to be randomised will likely be limited due to the advantages associated with AHCL. The results of this short-term economic evaluation offer valuable insights into the cost-effectiveness of AHCL therapy during T1D pregnancies, providing a foundation for future research. It is imperative that more robust data be collected through meta-analyses and (inter)national data registries to gain a more comprehensive understanding of the effectiveness of AHCL therapy. This would pave the way for future research to explore the long-term cost-effectiveness and health outcomes associated with AHCL therapy, offering valuable insights for healthcare decision-making.

In conclusion, MiniMed™ 780G AHCL therapy in T1D complicated pregnancies is associated with some clinical benefits, which might make it cost-effective from a Belgian healthcare payer perspective, despite the higher initial cost of the device. However, more robust data are needed on the potential impact of AHCL therapy on pregnancy and long-term health outcomes.

Contributors

KBeu, NVW, DB, GV, YT, XPA, FN, LVH, JM, DL, JC, VP, SES, RCP, AL, PG, CM, and KBen contributed to the conception and/or development of the CRISTAL trial and to data collection. SA, KBeu, AL, JL, and KBen contributed to data and/or statistical analyses. SA, KBeu, JL, and KBen co-wrote the original draft of the manuscript. SA contributed to figure and table creating. All authors read and approved the final version of the manuscript. The authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Data sharing statement

Selected anonymous data and samples collected in the study and additional documents can be made available to others not involved in the CRISTAL trial, on the basis of a reasonable request. Please contact Prof. Dr. Katrien Benhalima for any inquiry: katrien.benhalima@uzleuven.be.

Declaration of interests

KBeu is the recipient of a PhD fellowship strategic basic research (FWO-SB) from FWO. GV reported service on an advisory board for Eli Lilly and receiving honoraria for speaking, writing, or education and support for attending conferences/meetings from Boehringer Ingelheim, Eli Lilly, and Novo Nordisk. YT has a fiduciary role in the Diabetes Liga (no financial compensation), reported receiving honoraria for speaking, writing, or education from Boehringer Ingelheim and Eli Lilly, and support for attending conferences/meetings from Bayer and Sanofi. XPA reported receiving speaker honoraria from AstraZeneca, Menarini, and Novo Nordisk and support for attending conferences/meetings from Novo Nordisk. FN is the president of the Belgian Diabetes Forum; reported service on advisory boards for Eli Lilly and Novo Nordisk; reported receiving a grant from AstraZeneca to organize a symposium; reported receiving honoraria for speaking, writing, or education from AstraZeneca, Boehringer Ingelheim, Eli Lilly, Novo Nordisk, and Sanofi; and reported receiving support for attending conferences/meetings from AstraZeneca and Novo Nordisk. LVH reported service on an advisory board for Abbott, Dexcom, and Roche, and reported receiving honoraria for speaking, writing, or education, and support for attending conferences/meetings from Medtronic. JM reported receiving honoraria for speaking from Novo Nordisk and Sanofi, and support for attending conferences/meetings from Novo Nordisk. DL reported receiving honoraria for speaking, writing, or education from Menarini. SES reported receiving honoraria for speaking, writing, or education from Eli Lilly and Medtronic and service on advisory boards for Roche, Medtronic, and Ypsomed (all financial compensation received by her institution and used for investigator-initiated research). RCP reported receiving a grant from ZonMw for "Leading the Change". PG reported service on advisory boards for Insulet and Ypsomed; grants from Dexcom, Medtronic, Novo Nordisk, Sanofi, Tandem, and Roche; consulting fees for Abbott, Bayer, and Medtronic; honoraria for speaking, writing, or education from Abbott, Bayer, Dexcom, Insulet, Medtronic, Novo Nordisk, VitalAire, Ypsomed; and support for attending conferences/meetings from

Medtronic, Novo Nordisk, Sanofi Aventis, and Roche (all financial compensation received by KU Leuven); and receipt of study equipment from Dexcom. CM reported service on advisory boards for ActoBio Therapeutics, AstraZeneca, Bayer, Biomea Fusion, Boehringer Ingelheim, Eli Lilly, Imcyse, Insulet, Medtronic, Novo Nordisk, Roche, SAB Bio, Sanofi, and Vertex; and reported receiving honoraria for speaking, writing, or education from ActoBio Therapeutics, Boehringer Ingelheim, Eli Lilly, Insulet, Medtronic, Novo Nordisk, Sanofi, and Vertex; and being president of the European Association for the Study of Diabetes for which all external support is given at https://www.easd.org. UZ/KU Leuven received research support for KBen from AstraZeneca (financial), the Diabetes Liga Research Fund (financial), Dexcom (nonfinancial), Eli Lilly (financial), Medtronic (financial and nonfinancial), Metagenics (financial), and Novo Nordisk (financial and nonfinancial). KBen reported receiving consulting fees from AstraZeneca and Eli Lilly and honoraria for speaking, writing, or education from AstraZeneca, Mundipharma, and Novo Nordisk and support for attending conferences/meetings from AstraZeneca and Novo Nordisk. KBen is the recipient of a senior clinical research fellowship from FWO, the Flemish Research Council. No other potential conflicts of interest relevant to this article were reported.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.eclinm.2025.103106.

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