Supplementary Appendix

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Methods

Closed-Loop System

This study used the CamAPS FX (CamDiab, Cambridge, UK) hybrid closed-loop system. It is an app that runs the Cambridge model predictive control algorithm (version 0.3.71) and was hosted by an unlocked android smartphone (Galaxy S8-12, Samsung). The smartphone communicated via Bluetooth with the insulin pump (Dana Diabecare RS, Sooil, South Korea) and continuous glucose monitor (Dexcom G6, Dexcom, CA, USA). A glucose-responsive basal rate as calculated by the algorithm in response to continuous glucose monitor levels, is delivered as extended boluses by the insulin pump every 8-12 minutes.

When starting on CamAPS FX the participant's weight and total daily insulin dose were provided to the system and their insulin-to-carbohydrate ratios and insulin sensitivity / correction factors were programmed into the pump bolus calculator. If already a pump user, their previous pre-programmed basal rate was programmed into the insulin pump in case Auto Mode was not available (e.g. loss of communication between the pump and smartphone; if glucose data were not available to the smartphone and algorithm for > 30minutes including during sensor warm up or loss of power of the smartphone) at which point the insulin pump would revert to the pre-programmed basal profile (Manual Mode). For those previously on multiple daily injections, their total daily insulin dose was standardised to 70±10% of their injection total daily dose and a pre-programmed flat basal rate of half their injection total daily insulin dose split evenly over 24 hours. Closed-loop participants were advised to adjust the maternal weight setting in each trimester to accommodate gestational weight gain.

Training Resources for Trial Staff and Participants

Ongoing training was available to all participants and trial staff in the form of online resources. CGM training modules and "Top Tips" patient education leaflets from the Association for British Clinical Diabetologists' Diabetes Technology Network were available to participants and staff (https://abcd.care/dtn-education/diabetes-tech-in-pregnancy, https://abcd.care/dtn-uk-top-tips)

A further "Top Tips" leaflet for using the pump and closed-loop system was provided to intervention arm participants. In addition, CamDiab training webinars for both participants and trial staff were available from https://camdiab.cdep.org.uk/view/20/Webinars.htm.

Insulin Dose Adjustment

Pregnant patients were reviewed by their local clinical teams at 2-4 weekly intervals in accordance with national guidelines for management of type 1 diabetes during pregnancy. Healthcare teams and participants on both groups were given standardized information regarding pregnancy glucose targets, aiming for pre-meal 63-100 mg/dL [3.5-5.5mmol/L] and one-hour post meal <140 mg/dL [7.8mmol/L]) with an emphasis on the expected increases in insulin doses during the second and third trimesters. Participants were encouraged to administer pre-meal insulin at least 15 minutes before eating during the first trimester, increasing to 30 ±10 mins in trimester 2, and 45 ± 15 mins in trimester 3, in line with best practice guidelines.

Participant Technical Support

All participants had access to support from their study teams and Dexcom technical support in case of technical problems with their continuous glucose monitor devices and connectivity. Those randomized to closed-loop insulin delivery were also signposted to Advanced Therapeutics in case of pump related problems and had access to a telephone helpline to contact the research study team for any concerns about their closed-loop function and device connectivity.

Inclusion / Exclusion criteria

Eligibility Criteria

Participants were eligible if they fulfilled the following inclusion criteria:

1. Between 18 and 45 years of age
2. Type 1 diabetes for at least 12 months
3. Viable pregnancy confirmed by ultrasound, up to 13 weeks and 6 days gestation
4. On intensive insulin therapy (≥3 injections/day or insulin pump). This includes sensor augmented insulin pumps and hybrid closed-loop systems other than CamAPS FX
5. Willingness to use the study devices throughout the trial
6. HbA1c level ≥48 mmol/mol (≥6.5%) at booking (first antenatal contact) and ≤86 mmol/mol (≤10%) at point of randomization
7. Provide informed consent
8. Have access to email

Exclusion Criteria

1. Non-type 1 diabetes
2. Other physical or psychological disease which, is likely to interfere with the normal conduct and interpretation of the study results, as per investigator judgement
3. Current treatment with drugs known to interfere with glucose metabolism (e.g. high dose corticosteroids)
4. Known or suspected insulin allergy
5. Advanced nephropathy (eGFR <45), severe autonomic neuropathy, uncontrolled gastroparesis or severe proliferative retinopathy, as per investigator judgement
6. Target glycaemia or very high HbA1c i.e. first antenatal HbA1c <48mmol/mol (<6.5%) and HbA1c >86mmol/mol (>10%). Those with HbA1c >86 mmol/mol (>10%) may participate if they achieve HbA1c ≤86mmol/mol (≤10%) before randomization.
7. Total daily insulin dose ³ 1.5 units/kg
8. Severe visual or hearing impairment
9. Unable to speak and understand English

Summary of Study Outcomes

Maternal Glucose Outcomes

1. The percentage of time spent with sensor glucose levels above and below target range (>7.8mmol/L and <3.5mmol/L), mean sensor glucose and glucose variability measures; glucose standard deviation (SD) and glucose coefficient of variation (CV)
2. The frequency and severity of hypoglycaemia episodes <3.5 mmol/L (mild) and <3.0 mmol/L (moderate) for more than 15 minutes duration
3. The international CGM time in range consensus targets; CGM glucose levels 3.5-7.8mmol/L >70% (16hr 48 min), >7.8mmol/L <25% (6hr), <3.5mmol/L <4% (1hr), and <3.0mmol/L <1% (15min)
4. The Low Blood Glucose Index (LBGI) to quantify the risk of hypoglycemia
5. Change in maternal HbA1c based on blood samples collected at baseline, 24-26 weeks, 34-36 weeks
6. CGM glucose levels during the first (<12 weeks 6 days gestation), second (13-27 weeks 6 days gestation) and third trimesters (28 weeks until delivery)
7. CGM glucose levels during the 24 hours (midnight to midnight) and overnight time 23.00- 07.00hr

Maternal Obstetric Outcomes

1. Gestational weight gain
2. Maternal hypertensive disorders
3. Mode of delivery
4. Gestational age at delivery
5. Preterm delivery (<37 weeks)
6. Adverse events including pregnancy loss <24 weeks, stillbirth, neonatal death
7. Maternal hospital admissions and length of hospital stay

Neonatal Outcomes

1. Neonatal morbidity including treatment for neonatal hypoglycemia, neonatal jaundice and respiratory distress
2. Infant birth weight (customized birth weight percentile, incidence of large and small for gestational age)
3. Neonatal care unit admission >24 hours
4. Hospital length of stay (from delivery until hospital discharge), including re-admissions >24h within the first seven days from birth

Safety Outcomes

1. Diabetic ketoacidosis events
2. Severe hypoglycemia events (defined as requiring third party assistance)
3. Adverse device effect

Psychosocial Outcomes

1. Questionnaires during early and late pregnancy; Insulin Delivery Systems: Perspectives, Ideas, Reflections and Expectations (INSPIRE)[1], Euroqol Five Dimensions Health-Related Quality of Life Questionnaire (EQ-5D)[2], Diabetes Distress Scale[3], Hypoglycemia Fear Survey II (worry scale only)[4], and Pittsburgh Sleep Quality Index[5]
2. Qualitative interviews: 23 women randomized to the intervention group and 19 trial staff (trial staff interviews are reported separately[6,7])

Additional Statistical Methods Details

Calculation of CGM-measured Outcomes

Baseline: CGM variables were calculated based on data obtained in the run-in period prior to randomization. Each recruited participant wore a study CGM sensor at home during run-in for up to 10 days. At least 96 hours of CGM glucose values with 24 hours of glucose values during 11pm-7am were required for randomization. To avoid large gaps in the data, CGM data in the 14 days prior to randomization date was included, and if less than 96 hours of data was obtained, additional days were added 1 at a time until 96 hours or 28 days prior to randomization were reached, whichever came first.

Follow up: For both AiD arm and control arm, CGM data from the 16 weeks' gestation until delivery was used to calculate all CGM metrics for the intervention phase. If a participant miscarried or had a termination of pregnancy, CGM data until that day was included for calculating CGM metrics. A minimum of 96 hours of CGM data was required for the calculation, otherwise, values would have been considered missing and imputed in the analysis. CGM metrics were also calculated overnight, defined as 23:00 to 07:00, with a minimum of 24 hours of CGM data required.

CGM metrics were also calculated for each trimester, with a minimum of 24 hours of data required for the calculation. The first trimester is from the day after randomization until 12 weeks 6 days gestation, the second trimester is from 13 weeks until 27 weeks 6 days, and the third trimester is from 28 weeks until delivery.

HbA1c and Insulin Outcomes

HbA1c values were collected at baseline, 24 weeks, and 34 weeks. The analysis window for 24 weeks was 20 to <30 weeks' gestation, and the analysis window for 34 weeks was 30 weeks' gestation to delivery. If no HbA1c value was available in the window, GMI estimates were used instead.[8] GMI was calculated from CGM data during gestation weeks 23 to <26 and weeks 33 to <36. Insulin data was recorded via CRF at visits. Baseline insulin data came from the earliest visit before 14 weeks. Insulin data at weeks 24 and 34 had the same window as HbA1c values. If no value was available within the analysis window, the corresponding outcome was treated as missing.

Questionnaires

Several questionnaires were administered at baseline and 34-36 weeks. The EQ-5D Health-Related Quality of Life Questionnaire, the Diabetes Distress Scale, the Hypoglycemia Fear Survey Questionnaire II, and the Pittsburgh Sleep Quality Index were administered to all participants. The INsulin delivery Systems: Perspectives, Ideas, Reflections and Expectations questionnaire was administered to the intervention group only.

Analysis of Outcomes

For CGM outcomes, insulin outcomes, and questionnaires that were approximately normally distributed, a linear mixed effects regression model was fit with time in range from 16 weeks' gestation until delivery as the dependent variable adjusting for baseline time in range, insulin delivery modality at baseline, and clinical center and subject as random effects.

For the CGM targets, a mixed effects logistic regression model was fit adjusting for baseline value, insulin delivery modality at baseline, and clinical center and subject as random effects. Subject effects would have accounted for correlated data if some participants were enrolled for multiple pregnancies, however, no participants had multiple enrollments, so the models did not include a random subject effect.

Missing data were handled using multiple imputation with pattern mixture models assuming the dropout trajectory of the treatment subjects was that of the control arm. If we let R denote the indicators (or "pattern") for which data are missing (R=0) and which are observed, let Y_1 represent the observed data values, and Y_0 the missing data values, then we can express the joint likelihood as $P(Y_0,Y_1,R) = P(Y_0 \mid Y_1,R)*P(Y_1,R)$. If we were to assume the data were missing at random, then we would have $P(Y_0 \mid Y_1,R=0) = P(Y_0 \mid Y_1,R=1)$. However, if we assume the data are missing not at random, then in general we may have $P(Y_0 \mid Y_1,R=0) \neq P(Y_0 \mid Y_1,R=1)$. To reflect this, the missing values from the treatment group were imputed generated from the distribution of the control group. That is, we take $P(Y_0 \mid Trt=1,Y_1,R=0) = P(Y_0 \mid Trt=0,Y_1,R=1)$. All randomized subjects were included in the imputation.

A direct likelihood model was used for the HbA1c outcome adjusting for insulin delivery modality at baseline and clinical center as a random effect. HbA1c values were not imputed as direct likelihood was used to handle missing HbA1c values.

Subgroup Analyses

The treatment effect for the primary outcome in the following subgroups was assessed: insulin modality at baseline, baseline HbA1c, maternal age, and clinical site.

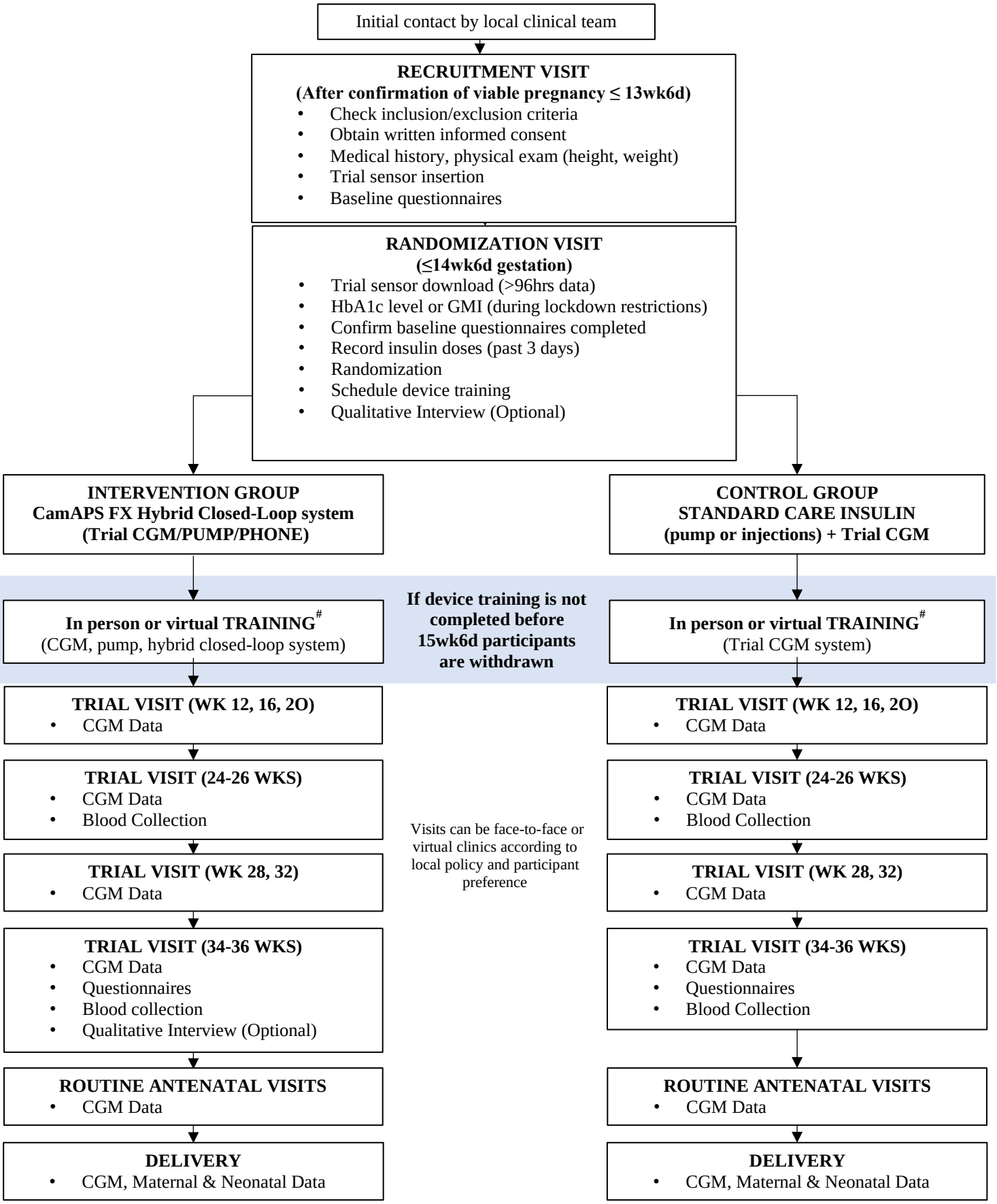
Per-Protocol Analysis

A per-protocol analysis was performed, using inverse probability of treatment weighting for whether a participant met the per-protocol analysis requirements. A logistic regression model for a participant's fulfilment of per-protocol requirements was fitted with baseline time in range and age as the explanatory variables. Participant weights were used in the same linear mixed effects regression model described above, with participants included if they completed the 34-36 week visit or delivered prior to the 34-36 week visit, had a minimum of 96 hours of CGM data from 16 weeks' gestation to delivery, and had ≥60% closed-loop use if they were in the AID group.

Multiple Comparisons

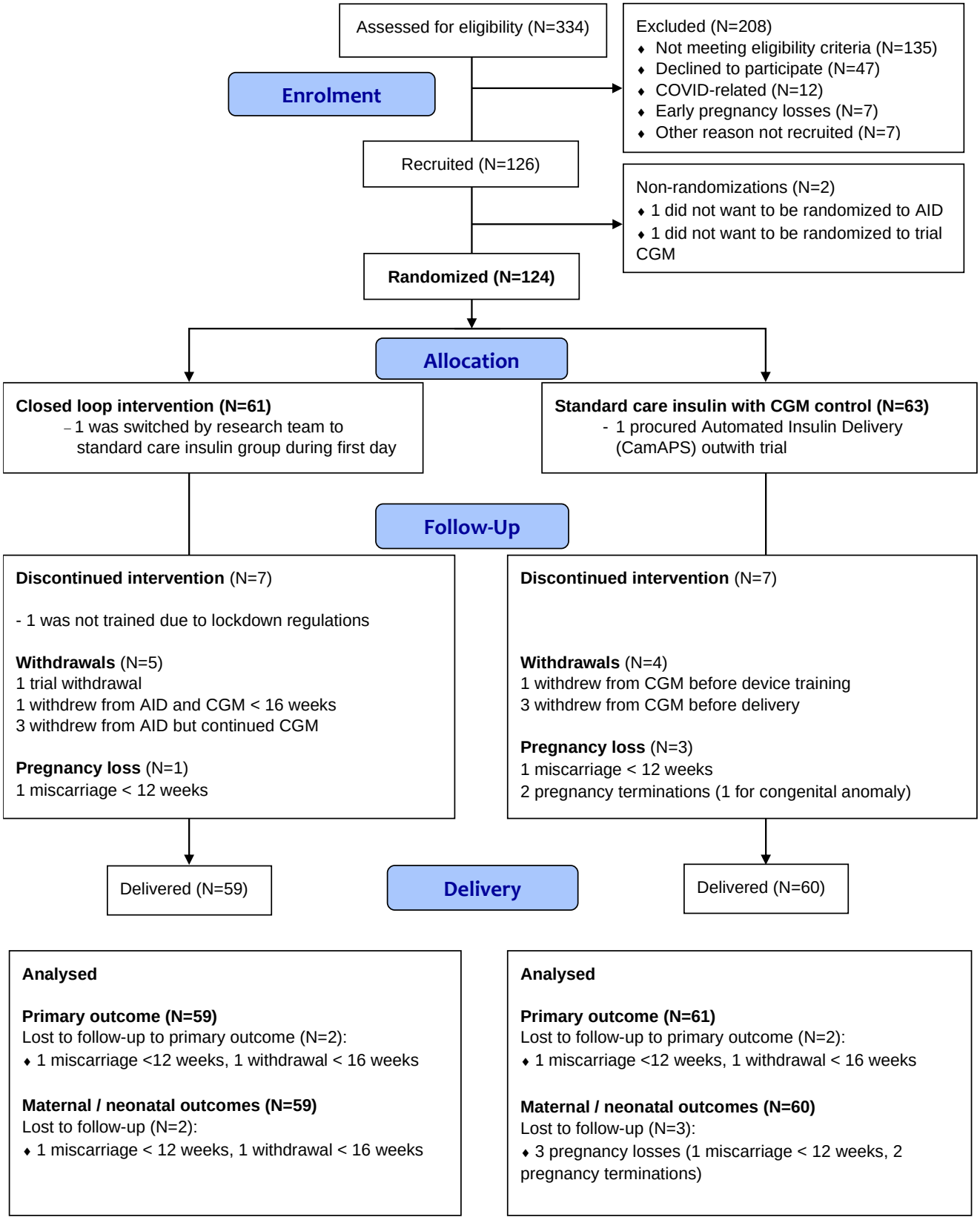
For the primary outcome and key secondary outcomes, the Holm step-down method was used to control the Type 1 Error. Confidence intervals for the other secondary outcomes were not adjusted.

Figure S1: Flow of Participants Through the Trial



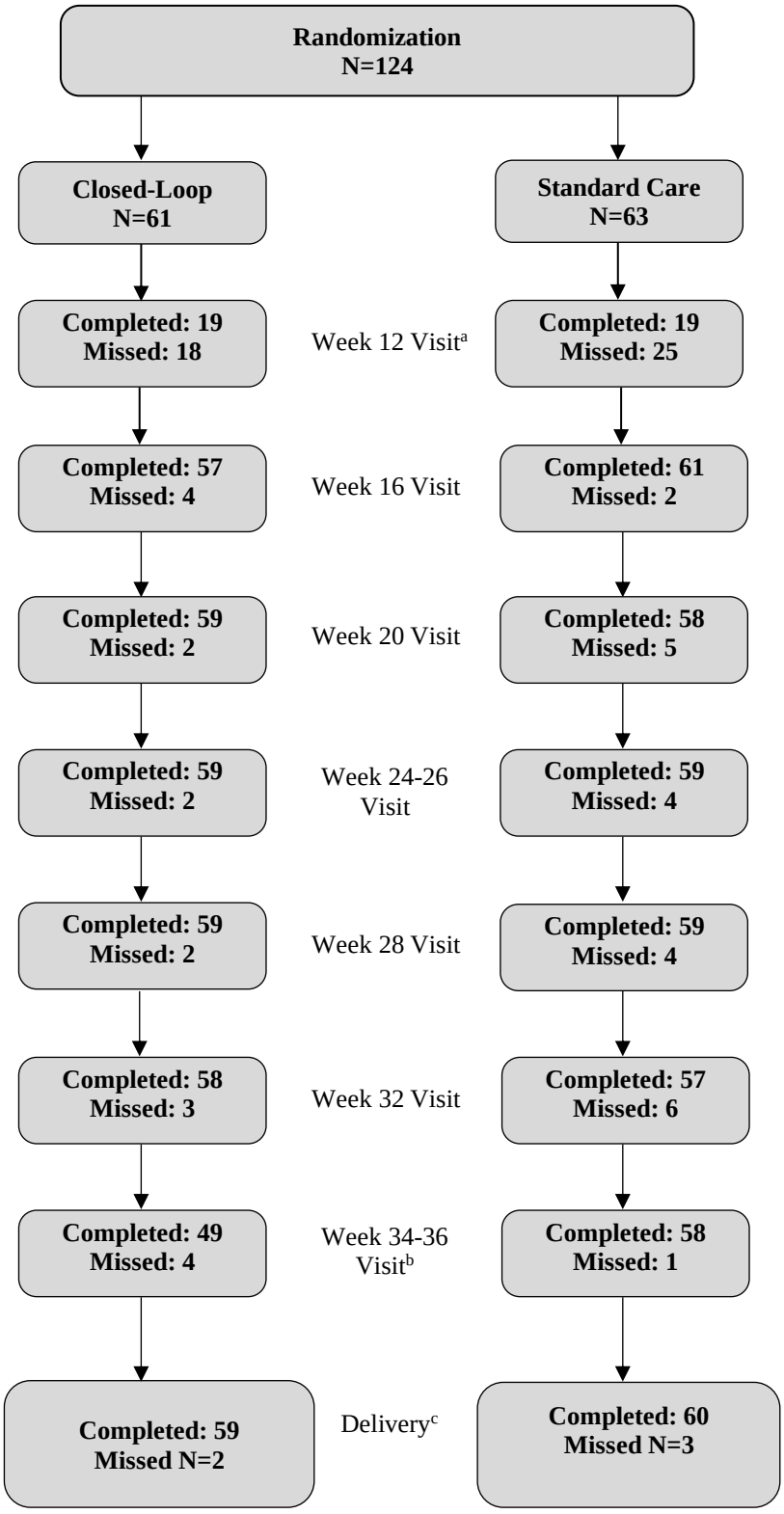
#Virtual device training procedures and visits were implemented following the Covid-19 lockdown restrictions

Figure S2: Consort Diagram



Reasons for not meeting trial eligibility criteria (N=135) were: HbA1c out of range (N=60), unwilling to use study devices/switch from current treatment methods (N=32), outside of gestational age window (>13wks 6days) (N=24), other reasons (N=19).

Figure S3: Completion of trial visits



a. participants who were randomized before 12 weeks. Study visits were 4-weekly so those randomized at 9-11 weeks did not require an additional 12 week visit.
b. participants who had not delivered prior to the 34 -36 weeks visit
c. 5 participants (2 intervention, 3 control) did not have 96 hours of sensor data between 16 weeks - delivery
There were 5 out of window visits in the intervention group and 9 in the standard care group.

Figure S4: CGM Use by Treatment Group Throughout Pregnancy

Supplemental Figure S3 shows side by side boxplots of the continuous glucose monitoring (CGM) use for each treatment group, by 4-week antenatal period following device training. Black bars denote medians and black dots denote means.

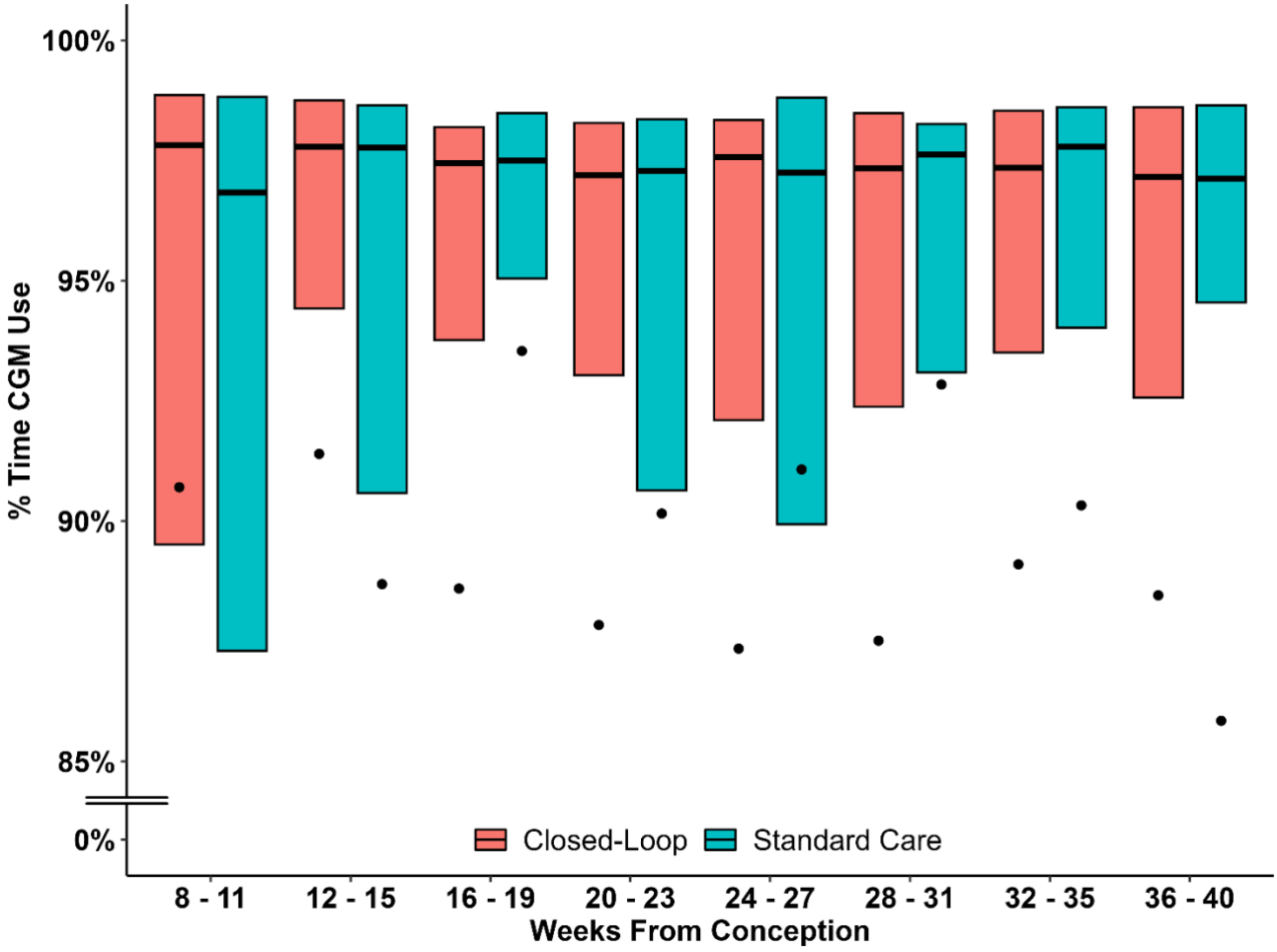


Figure S5: Frequency of Closed-Loop use throughout pregnancy

Supplemental Figure S5 shows boxplots of the CamAPS FX closed-loop (CL) system use in the intervention group, by 4-week antenatal period following device training. Black bars denote medians and black dots denote means.

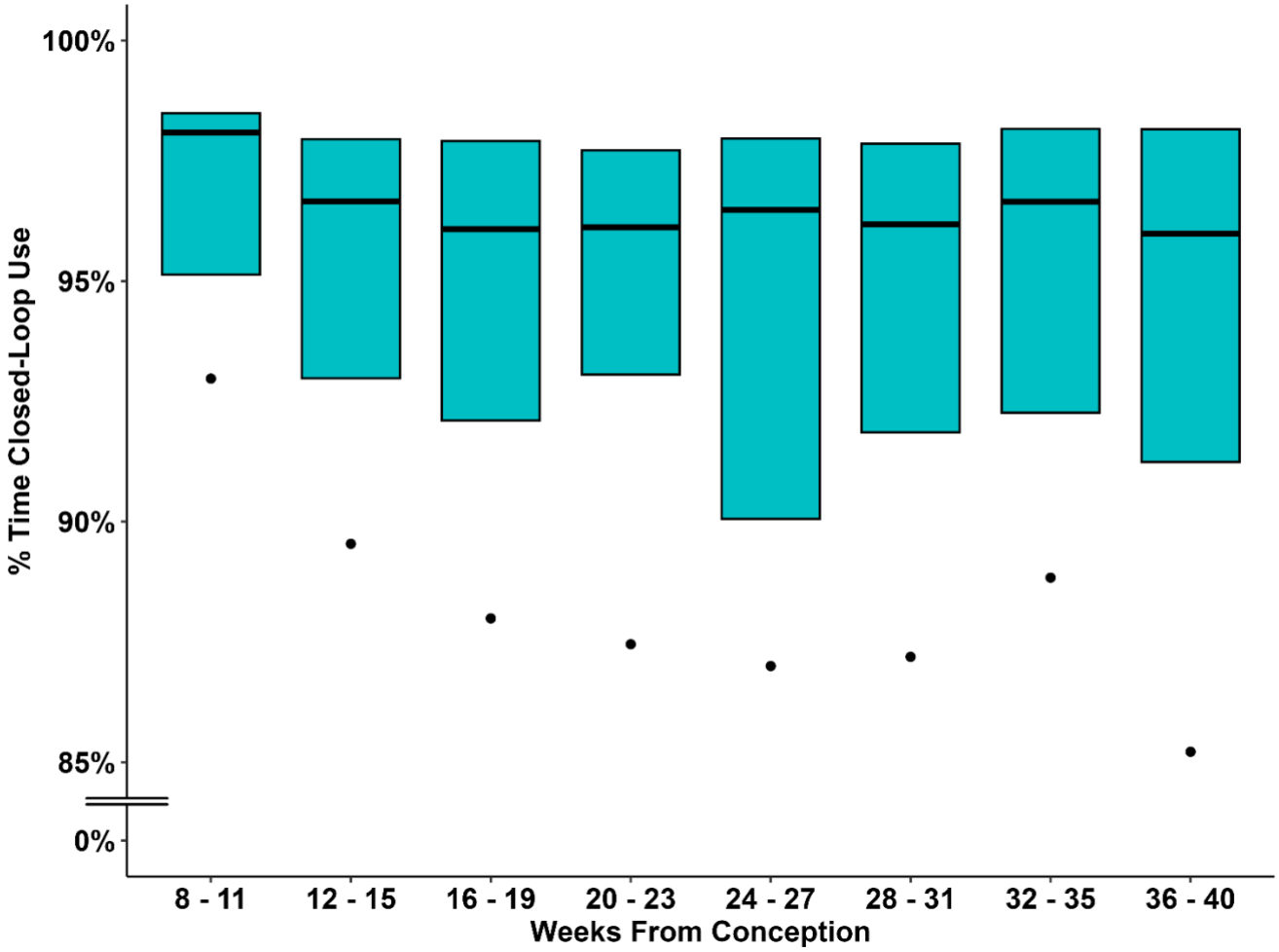


Figure S6: Percentage Time Spent in the Pregnancy Target Glucose Range

Supplemental Figure S8 shows the cumulative distribution of the percentage of time that the glucose level was within the pregnancy-specific target glucose range of 63-140mg/dL (3.5-7.8 mmol/L), as measured by continuous glucose monitoring, for each treatment group from 16 weeks' gestation to delivery.

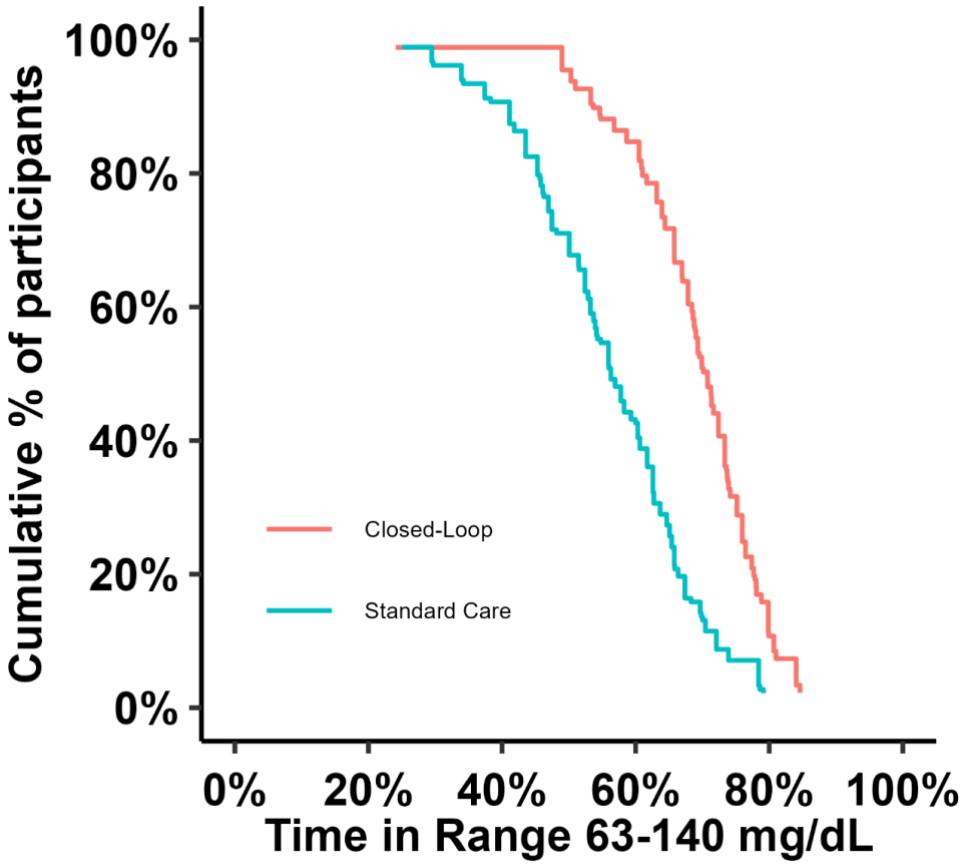
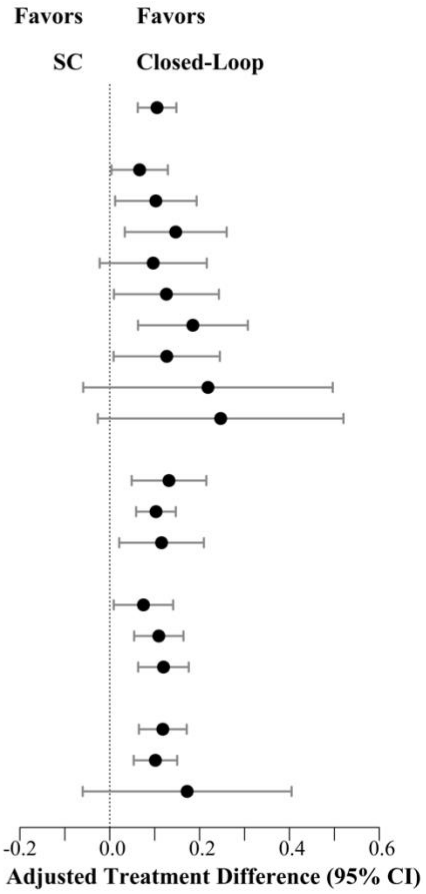


Figure S7: Subgroup Analyses for Primary Outcome (% Time in Range 63-140 mg/dL)

	Closed-Loop		Standard Care		
Group	**N**	**Mean ± SD**	**N**	**Mean ± SD**	**Adjusted Treatment Difference (95% CI)**
Overall	59	68.2% ± 10.5%	61	55.6% ± 12.5%	10.5% (6.2%, 14.8%)
SiteID					
A	19	66.9% ± 13.2%	21	56.8% ± 11.1%	6.6% (0.4%, 12.9%)
B	10	68.9% ± 11.7%	10	53.9% ± 11.9%	10.3% (1.2%, 19.3%)
C	6	67.8% ± 7.0%	6	57.4% ± 14.5%	14.7% (3.3%, 26.0%)
D	6	66.2% ± 7.2%	5	59.6% ± 6.0%	9.7% (-2.3%, 21.6%)
E	5	73.1% ± 11.5%	6	60.5% ± 16.8%	12.6% (0.9%, 24.3%)
F	5	64.4% ± 9.7%	5	42.8% ± 17.1%	18.5% (6.3%, 30.7%)
G	5	69.5% ± 5.0%	6	56.3% ± 11.9%	12.7% (0.8%, 24.5%)
H	2	73.6% ± 7.4%	1	58.3%	21.8% (-5.9%, 49.6%)
I	1	77.8%	1	45.8%	24.7% (-2.7%, 52.0%)
Age					
18 - <26 years	9	70.1% ± 7.0%	15	50.6% ± 13.0%	13.2% (4.9%, 21.5%)
26 - <36 years	41	68.1% ± 11.3%	37	56.8% ± 12.4%	10.3% (5.9%, 14.7%)
≥ 36 years	9	66.9% ± 9.9%	9	59.0% ± 11.3%	11.5% (2.1%, 20.9%)
Baseline HbA1c (%)					
<7%	22	72.2% ± 7.7%	12	63.6% ± 9.9%	7.5% (0.9%, 14.1%)
7% to <8%	20	68.8% ± 9.7%	23	59.5% ± 8.8%	10.9% (5.4%, 16.4%)
≥ 8%	17	62.3% ± 12.2%	26	48.5% ± 13.0%	11.9% (6.3%, 17.6%)
Insulin Modality at Baseline					
Pump	30	70.1% ± 8.6%	24	57.7% ± 10.3%	11.8% (6.5%, 17.1%)
MDI	27	65.2% ± 11.7%	36	54.2% ± 13.9%	10.2% (5.3%, 15.0%)
AID	2	80.0% ± 5.7%	1	58.3%	17.2% (-6.0%, 40.5%)



MDI – Multiple Daily Injections

Table S1: Trial Site Recruitment

Sites	Closed-Loop (N=61)	Standard Care (N=63)
Cambridge University Hospitals NHS Foundation Trust	11	11
St Thomas' Hospital, London	6	7
Norfolk and Norwich University Hospital NHS Foundation Trust	19	21
King's College Hospital NHS Foundation Trust	6	6
NHS Greater Glasgow and Clyde	6	5
Royal Infirmary of Edinburgh	5	5
Belfast Health and Social Care Trust	2	1
Leeds Teaching Hospitals NHS Foundation Trust	1	1
East Suffolk and North Essex NHS Foundation Trust	5	6
Total	61	63

Table S2. Representativeness of study participants[9]

Condition under investigation	Pregnancy complicated by Type 1 Diabetes (T1D)
Special considerations related to	
Sex and gender	Pregnant women
Age	Women of reproductive years aged 18-45years
Race or ethnic group	The T1D pregnant population are predominantly White, with 91% White ethnicity based on population-based data in the UK.[10]
Geography	Prevalence of T1D is higher in Northern Europe, with approximately 2,000 T1D pregnancies per year in the UK. The onset of T1D at a lower age is increasing so women are now entering pregnancy with longer duration of T1D.
Other considerations	Maternal age, parity (number of previous pregnancies), BMI and duration of T1D are important factors in relation to diabetes and pregnancy complications. Although women with T1D are advised to plan for pregnancy (take 5mg folic acid, and aim for HbA1c <6.5%), approximately 50% of T1D pregnancies are unplanned. Most women (85%) do not achieve HbA1c <6.5%. The mean HbA1c during early pregnancy, is 7.6% at 7 weeks' gestation, at the first contact with specialist diabetes pregnancy teams. Complications in babies of mothers with T1D are common, with population-based data from the UK showing that 57% of babies are large for gestational age, 47% are delivered preterm <37 weeks' gestation, and 51% are admitted to neonatal care units.[11]
Overall representativeness of this trial	Our age range was from 19.7 to 44.7 (mean 31.1) years reflecting the pregnant population with T1D. Participants were predominantly White (92.7%), with smaller numbers self-identifying as Asian (3.9%), Black (2.1%) and Mixed/Other racial or ethnic groups (2.9%). The duration of T1D ranged from 2 to 33 (mean 17) years, meaning that our T1D duration was 4 years longer than the population average of 13 years. Our participants' BMI ranged from 18.0 to 48.9 kg/m^2 with 37% having a healthy BMI category, 37% overweight and 26% obese, reflecting high rates of maternal overweight and obesity. We included women across maternal glucose categories with entry HbA1c ranging from 6.0% to 14.0% (mean 7.7%). Our study population had longer duration of T1D, and higher rates of diabetes complications (57% vs 37% retinopathy). However, overall maternal age, ethnicity, pregnancy planning and baseline HbA1c characteristics are very similar to the national UK T1D pregnant population during 2019-2020.

Table S3: Detailed Participants Characteristics

	Closed-Loop (N=61)	Standard Care (N=63)
Age (years)		
18-25	9 (15%)	15 (24%)
26-35	41 (67%)	38 (60%)
≥ 36	11 (18%)	10 (16%)
Mean ±SD	32.0 ± 5.0	30.2 ± 5.5
Range	19.9 to 42.7	19.7 to 44.7
White race/ethnicity	58 (95%)	57 (90%)
Diabetes duration (years)		
1-<5	4 (7%)	5 (8%)
5-<10	8 (13%)	9 (14%)
≥ 10	49 (80%)	49 (78%)
Mean ±SD	18 ± 8	16 ± 7
Range	2 to 31	2 to 33
Maternal weight (kg)		
Mean ±SD	76.0 ± 16.4	73.3 ± 14.0
Range	49.0 to 138.0	53.9 to 117.8
Higher education[a]	36 (59%)	33 (52%)
Maternal BMI (kg/m^2)		
Mean ±SD	27.9 ± 5.9	26.9 ± 4.8
Range	18.0 to 48.9	19.9 to 41.2
Recruitment gestation (weeks)		
Median (IQR)	10.3 (8.0-11.7)	10.0 (8.4-11.3)
Range	6.7 to 13.7	6.1 to 14.3
Randomization gestation (weeks)		
Median (IQR)	11.3 (9.6-13.0)	11.0 (9.6-12.4)
Range	7.7 to 15.0	7.7 to 16.3
Past diabetes/medical history		
Diabetes complications	35 (57%)	35 (56%)
Retinopathy	35 (57%)	34 (54%)
Nephropathy	4 (7%)	5 (8%)
Neuropathy	4 (7%)	2 (3%)
Prior diabetic ketoacidosis[b]	1 (2%)	10 (16%)
Prior severe hypoglycaemia[c]	4 (7%)	5 (8%)
Chronic hypertension	4 (7%)	2 (3%)
Systolic BP	117.8 ± 11.9	117.3 ± 12.9
Diastolic BP	69.4 ± 9.3	68.3 ± 9.4
Pregnancy history		
Primiparous[d]	21 (34%)	38 (60%)
Previous pregnancy loss[e]	21 (34%)	20 (32%)
Pre-pregnancy factors		
Folic acid	38 (62%)	34 (54%)
Alcohol	36 (59%)	36 (57%)
Smoking	10 (16%)	14 (22%)
HbA1c during early pregnancy[f]		
≥ 6.0% -<7.0%	23 (38%)	13 (21%)
≥ 7.0% - <8.0%	21 (34%)	24 (38%)
≥ 8.0%	17 (28%)	26 (41%)
Mean ±SD	7.6 ± 1.1	7.9 ± 1.3
Range	6.0 to 11.6	6.5 to 14.0
Continuous glucose monitoring	59 (97%)	62 (98%)
Abbott Freestyle Libre	43 (73%)	47 (75%)

Dexcom CGM	12 (20%)	14 (23%)
Medtronic CGM	4 (7%)	1 (2%)
Insulin delivery		
Insulin pump	32 (52%)	25 (40%)
Multiple daily injections	27 (44%)	37 (59%)
Automated insulin delivery[g]	2 (3%)	1 (2%)
Total daily insulin (U/kg/day)		
Mean ±SD	0.7 ± 0.2	0.7 ± 0.2
Range	0.3 to 1.3	0.3 to 1.4

a- Higher education refers to university undergraduate or vocational equivalent.
b- Participants in standard care had more self-reported diabetic ketoacidosis (DKA) events in the 12 months before enrolment. 9 standard care participants reported 1 DKA event and 1 reported >10 DKA events.
c- Severe hypoglycemia (SH) events defined as requiring third party assistance as self-reported in the 12 months before enrolment. 4 standard care participants reported 1 SH event and 1 reported 3 SH events. 3 closed-loop participants reported 1 SH and 1 reported 2 SH events.
d- 23 (38%) closed-loop participants had 1 previous birth, 14 (23%) had 2 births, and 3 (5%) had 3 or more births. 21 (33%) standard care participants had 1 previous birth, 3 (5%) had 2 births and 1 (2%) had 3 or more births.
e- Includes previous miscarriages and pregnancy terminations. 15 participants in each group reported 1 pregnancy loss, 6 closed-loop and 5 standard care participants reported 2 or more pregnancy losses.
f- 1 participant with HbA1c 6.0% was entered during the pandemic (Mar 2020) whilst experiencing frequent hypoglycemia using an alternative closed-loop (Tandem Control IQ) system.
g- Participants using alternative hybrid closed-loop systems were eligible. Two (1 DIY loop Android APS via Accuchek Insight, 1 Tandem Control IQ) were randomized to the intervention group and 1 to standard care (Medtronic 780G).

Table S4: Compliance with Treatment Protocol

Reason[a]	Closed-Loop (N=61 randomized)	Standard Care (N=63 randomized)
<96 hours CGM data from 16 weeks until delivery[b]	2	2
Participants who did not complete the 34-36 weeks visit[c]	2	4
Intervention group: CL active for <60% of the time[d]	7	NA
Included in Per Protocol analysis	54	59

a- Participants may have several reasons for exclusion

b- Reasons for <96 hours' CGM data in intervention group were 1 miscarriage <12 weeks, 1 withdrawal of a previous CL user 17 days post training. Reasons in Standard care were 1 miscarriage <12 weeks, 1 withdrawal of previous Freestyle Libre user before CGM training.

c- Reasons for not completing the 34-36 weeks visit (if not delivered by then) in the closed-loop group were 1 miscarriage <12 weeks, 1 withdrawal of a previous CL user 17 days post training. Reasons in Standard care were 1 miscarriage <12 weeks, 1 withdrawal of previous Freestyle Libre user before CGM training, 2 pregnancy terminations (one for congenital anomaly). 3 Standard care participants who completed the 34-36 weeks visit but discontinued CGM in late pregnancy are included.

d- Reasons for CL active <60% of the time in the intervention group were,

- 1 miscarriage <12 weeks' gestation.
- 1 intervention group participant was re-allocated to standard care by research team day 1 post randomization due to the covid-19 lockdown restrictions which prevented training.
- 4 withdrawals at days 15, 17, 17 and 21 post device training from participants who stated that CL was not sufficiently aggressive/responsive. These included 1 previous CL user (Tandem Control IQ) with entry HbA1c 6.0%.
- 1 withdrawal with no closed-loop use from 16 weeks' gestation until delivery due to deteriorating medical co-morbidities (20 hyperemesis and severe ketosis events).

Table S5: Additional Unscheduled Visits and Contacts by Treatment Group

	Closed-Loop (N=61)	Standard Care (N=63)
Number of Unscheduled Visits	**68**	**94**
Visits per participant Median (quartiles)	0 (0, 2)	0 (0, 2)
Visits per participant		
0	35 (57%)	34 (54%)
1	9 (15%)	13 (21%)
2	5 (8%)	4 (6%)
3	7 (11%)	4 (6%)
4	2 (3%)	3 (5%)
5	0 (0%)	1 (2%)
6	1 (2%)	1 (2%)
7	2 (3%)	1 (2%)
15	0 (0%)	1 (2%)
16	0 (0%)	1 (2%)
Number of Unscheduled Contacts[a]	**371**	**605**
Contacts per participant Median (quartiles)	2 (1, 4)	1 (0, 9)
Contacts per participant		
0	8 (13%)	24 (38%)
1-9	45 (74%)	24 (38%)
10-19	2 (3%)	3 (5%)
20-29	1 (2%)	3 (5%)
30-39	3 (5%)	4 (6%)
40-49	1 (2%)	2 (3%)
≥50	1 (2%)	3 (5%)

a- Includes any phone call, email, text or video chat contact.

Table S6: Reasons for Additional Unscheduled Visits and Contacts

Reason for additional unscheduled visits	Closed-Loop	Standard Care
Additional CGM training	4	2
Additional insulin pump training	3	2
Additional closed-loop training	2	0
Additional protocol/procedure training or advice	0	0
Question or problem relating to diabetes management	15	25
Question or problem relating to pregnancy	35	51
Potential adverse event	2	3
Potential device deficiency	4	3
Needed study supplies	3	1
Other	14	21

The same visit can have multiple reasons

Reason for additional unscheduled contacts[a]	Closed-Loop	Standard Care
Additional CGM training	19	35
Additional insulin pump training	29	8
Additional closed-loop training	61	1
Additional protocol/procedure training or advice	0	1
Question or problem relating to diabetes management	124	331
Question or problem relating to pregnancy	26	76
Potential adverse event	18	20
Potential device deficiency	29	29
Needed study supplies	43	48
Other	88	128

Includes any phone call, email, text or video chat contact. The same contact can have multiple reasons.

Table S7: CGM Use by Treatment Group

Frequency of CGM use in the Closed-Loop intervention group (N=61)

	24 Hours	Daytime	Nighttime
% Time CGM Use [*median (Q_1, Q_3)*]	97% (93%, 98%)	97% (92%, 98%)	98% (93%, 99%)
>90%	47 (77%)	47 (77%)	48 (79%)
80%-90%	2 (3%)	2 (3%)	2 (3%)
70%-80%	3 (5%)	3 (5%)	2 (3%)
60%-70%	2 (3%)	2 (3%)	2 (3%)
50%-60%	2 (3%)	2 (3%)	2 (3%)
<50%	3 (5%)	3 (5%)	3 (5%)
0%	2 (3%)	2 (3%)	2 (3%)

Frequency of CGM use in the Standard Care control group (N=63)

	24 Hours	Daytime	Nighttime
% Time CGM Use [*median (Q_1, Q_3)*]	97% (91%, 98%)	96% (91%, 98%)	96% (90%, 99%)
>90%	47 (75%)	47 (75%)	44 (70%)
80%-90%	8 (13%)	8 (13%)	9 (14%)
70%-80%	3 (5%)	3 (5%)	2 (3%)
60%-70%	1 (2%)	1 (2%)	2 (3%)
50%-60%	1 (2%)	1 (2%)	1 (2%)
<50%	1 (2%)	1 (2%)	3 (5%)
0%	2 (3%)	2 (3%)	2 (3%)

Table S8: Closed-Loop System Use in the Intervention Group

Frequency of CamAPS FX Closed-Loop (CL) system use in the intervention group (N=61)

	24 Hours	Daytime	Nighttime
% Time CL Use [*median (Q_1, Q_3)*]	96% (94%, 98%)	96% (93%, 97%)	97% (95%, 99%)
>90%	49 (80%)	48 (79%)	52 (85%)
80%-90%	5 (8%)	5 (8%)	2 (3%)
70%-80%	0 (0%)	1 (2%)	0 (0%)
60%-70%	0 (0%)	0 (0%)	0 (0%)
50%-60%	0 (0%)	0 (0%)	0 (0%)
<50%	2 (3%)	2 (3%)	2 (3%)
0%	5 (8%)	5 (8%)	5 (8%)

Table S9: Per-Protocol Analysis

End Points	Baseline		Intervention Phase[a]		P-value[b]
	Closed-Loop (N=54)	Standard Care (N=57)	Closed-Loop (N=54)	Standard Care (N=59)	
Hours of Sensor Data	151 (128, 162)	149 (124, 168)	3,381 (3,087, 3,562)	3,421 (3,169, 3,510)	
% Time 63-140 mg/dL	48.7% ± 16.4%	45.4% ± 13.9%	69.5% ± 8.5%	56.4% ± 12.0%	NA
Change from Baseline	NA	NA	20.8% ± 14.2%	10.9% ± 11.8%	NA
Adjusted Treatment Difference[b,c] *mean (95% CI)*	NA		12.1% (8.6%, 15.6%)		<0.001

Data are Mean ± SD or median (Quartiles).

a- CGM data calculated from 16 weeks' gestation until delivery

b- Model adjusted for baseline %time 63-140 mg/dL, insulin delivery modality, and site as a random effect. Model used inverse probability of treatment weighting. See Additional Details of the Statistical Methods section above in this supplement.

c- Difference is Closed-Loop – Standard Care. Excludes 7 participants from the Closed-Loop group and 4 participants from the Standard Care group. The timings and reasons for per-protocol analysis exclusions are outlined in Table S2.

Table S10: Detailed secondary endpoints

Secondary Endpoints	Baseline		Antenatal Intervention Phase[b]		Adjusted Treatment Difference[c] (95% CI)
	Closed-Loop (N=59)	Standard Care (N=59)	Closed-Loop (N=59)	Standard Care (N=61)	
Hours of Sensor Data	150 (128, 156)	149 (124, 171)	3,361 (2,996, 3,561)	3,417 (3,112, 3,507)	NA
Secondary endpoints					
% Time 63-180 mg/dL	70.6% ± 15.6%	68.2% ± 14.7%	86.6% ± 8.6%	79.7% ± 10.5%	5.8% (2.9%, 8.8%)
Mean Glucose (mg/dL)	149 ± 28	151 ± 24	125 ± 14	136 ± 16	-9 (-14, -5)
Glycated Hemoglobin (HbA1c) %	7.6 ± 1.1	7.9 ± 1.3	6.0 ± 0.5	6.4 ± 0.5	-0.31 (-0.50, -0.12)
Glucose SD (mg/dL)	54 ± 14	55 ± 12	42 ± 11	47 ± 10	-4 (-7, -2)
Glucose CV (%)	36% ± 5%	37% ± 6%	33% ± 5%	34% ± 5%	-1.1% (-2.5%, 0.3%)
Hyperglycemia					
%Time >180 mg/dL	25.9% ± 16.8%	28.1% ± 15.6%	10.8% ± 8.5%	17.3% ± 10.5%	-5.5% (-8.4%, -2.5%)
Glucose AUC >120 mg/dL	39.5 ± 23.7	41.3 ± 19.7	19.3 ± 12.2	27.9 ± 12.9	-7 (-11, -4)
Hypoglycemia					
% Time <63 mg/dL	2.75% (0.86%, 4.87%)	2.22% (0.72%, 6.00%)	2.26% (1.54%, 3.31%)	2.02% (1.25%, 4.37%)	-0.4% (-1.0%, 0.2%)
% Time <54 mg/dL	1.05% (0.07%, 2.37%)	0.79% (0.18%, 2.28%)	0.71% (0.49%, 1.19%)	0.73% (0.36%, 1.67%)	-0.2% (-0.5%, 0.1%)
Low Blood Glucose Index (LBGI)	1.5 ± 1.2	1.5 ± 1.3	1.5 ± 0.5	1.4 ± 0.8	0.0 (-0.2, 0.2)
Mild Hypoglycemia[e]	6.4 (2.2, 11.5)	5.5 (2.4, 11.1)	6.7 (4.6, 9.4)	5.7 (3.1, 9.4)	0.1 (-1.1, 1.3)
Moderate Hypoglycemia[f]	2.2 (0.0, 5.7)	2.2 (0.0, 5.9)	2.3 (1.6, 3.8)	2.1 (1.1, 4.4)	-0.0 (-0.7, 0.7)
Overnight Endpoints[g]					
Hours of Sensor Data	48 (41, 49)	49 (40, 56)	1,135 (1,017, 1,194)	1,127 (1,039, 1,179)	NA
Mean Glucose (mg/dL)	149 ± 33	150 ± 26	125 ± 14	135 ± 17	-9 (-14, -4)

% Time >140 mg/dL	48.8% ± 22.1%	51.5% ± 18.1%	27.3% ± 11.1%	40.0% ± 13.9%	-11.0% (-15.0%, -7.0%)
% Time <63 mg/dL	1.40% (0.00%, 5.27%)	2.33% (0.51%, 5.67%)	1.56% (1.10%, 2.51%)	2.57% (1.04%, 4.41%)	-1.4% (-2.1%, -0.6%)
Glucose SD (mg/dL)	52 ± 17	54 ± 14	40 ± 12	47 ± 12	-6 (-9, -2)
Glucose CV (%)	35% ± 8%	36% ± 8%	32% ± 5%	35% ± 6%	-2.4% (-4.2%, -0.5%)
Mild Hypoglycemia[e]	3.5 (0.0, 10.2)	6.4 (0.0, 11.9)	4.3 (2.9, 5.5)	5.3 (2.8, 8.7)	-1.7 (-3.0, -0.5)
Moderate Hypoglycemia[f]	0.0 (0.0, 4.7)	0.0 (0.0, 6.9)	1.7 (1.0, 2.5)	2.1 (0.8, 4.3)	-0.7 (-1.4, -0.0)

Data are mean ± SD or median (Quartiles).

a- Baseline CGM metrics calculated using data from the pre-randomization run-in. 2 participants were missing baseline CGM data. The 4 participants who were missing intervention CGM data (due to miscarriage and/or pregnancy terminations) are not tabulated

b- Antenatal intervention phase is from 16 weeks' gestation until delivery. Endpoints are calculated using Continuous Glucose Monitoring (CGM) sensor data except for glycated hemoglobin which was measured at trial sites. The glycated hemoglobin level at 34-36 weeks reflects maternal glycemia over the preceding 10-12 weeks. 4 participants were missing intervention CGM data.

c- Difference is Closed-Loop – Standard Care. Model adjusted for baseline value, insulin delivery modality, and site as a random effect. P-values are adjusted using the Holm step-down method to control the type 1 error.

d- The results were similar when adjusting for the number of DKA events in the previous 12 months and the number of previous pregnancies as covariates in the model

e- Mild hypoglycemia is defined as consecutive CGM glucose <63 mg/dL for at least 15 consecutive minutes. Episodes separated by 30 minutes.

f- Moderate hypoglycemia is defined as consecutive CGM glucose <54 mg/dL for at least 15 consecutive minutes. Episodes separated by 30 minutes.

g- 23:00-07:00

Table S11: Secondary Maternal Glucose Outcomes by Trimester

End Points	Baseline		First Trimester		Second Trimester		Third Trimester	
	Closed-Loop (N=61)	**Standard Care (N=61)**	**Closed-Loop (N=40)**	**Standard Care (N=44)**	**Closed-Loop (N=60)**	**Standard Care (N=61)**	**Closed-Loop (N=57)**	**Standard Care (N=58)**
Hours of Sensor Data	150 (128, 156)	149 (124, 168)	371 (219, 519)	378 (214, 567)	2,380 (2,066, 2,463)	2,418 (2,151, 2,462)	1,442 (1,181, 1,597)	1,494 (1,356, 1,572)
% Time 63-140 mg/dL	47.7% ± 16.2%	44.8% ± 14.6%	59.2% ± 14.8%	53.3% ± 12.9%	65.8% ± 10.3%	52.6% ± 12.5%	71.2% ± 8.7%	59.7% ± 12.8%
Adjusted treatment difference *mean (95% CI)*			5.4% (0.9%, 9.9%)		11.9% (8.6%, 15.1%)		10.6% (7.1%, 14.2%)	
Mean Glucose (mg/dL)	149 ± 28	150 ± 24	135 ± 20	139 ± 19	128 ± 14	140 ± 18	121 ± 10	131 ± 15
Adjusted treatment difference *mean (95% CI)*			-4.6 (-10.8, 1.6)		-10.2 (-14.9, -5.6)		-9.5 (-13.7, -5.4)	
% Time >140 mg/dL	48.9% ± 17.8%	51.5% ± 16.3%	38.0% ± 15.5%	43.5% ± 13.9%	31.6% ± 10.6%	44.2% ± 13.4%	26.2% ± 9.0%	37.5% ± 13.3%
Adjusted treatment difference *mean (95% CI)*			-4.7% (-9.5%, 0.1%)		-11.1% (-14.6%, -7.6%)		-10.4% (-14.2%, -6.6%)	
% Time <63 mg/dL	2.5% (0.8%, 4.8%)	2.2% (0.7%, 5.1%)	2.2% (1.1%, 4.0%)	2.1% (1.2%, 3.6%)	2.2% (1.6%, 3.6%)	2.1% (1.3%, 4.8%)	2.2% (1.4%, 3.3%)	2.7% (1.2%, 3.9%)
Adjusted treatment difference *mean (95% CI)*			-0.3% (-1.4%, 0.7%)		-0.6% (-1.2%, 0.1%)		-0.2% (-0.8%, 0.4%)	
Glucose SD (mg/dL)	54 ± 14	55 ± 12	48 ± 12	50 ± 10	44 ± 11	49 ± 10	38 ± 8	43 ± 9
Adjusted treatment difference *mean (95% CI)*			-1.9 (-5.2, 1.4)		-4.6 (-7.5, -1.6)		-4.4 (-7.0, -1.8)	
Glucose CV (%)	36% ± 5%	37% ± 6%	35% ± 5%	36% ± 6%	34% ± 5%	35% ± 5%	31% ± 4%	33% ± 5%
Adjusted treatment difference *mean (95% CI)*			-0.3% (-2.2%, 1.6%)		-0.9% (-2.3%, 0.5%)		-1.1% (-2.6%, 0.4%)	

Data are Mean ± SD or Median (Quartiles).

Difference is Closed-Loop – Standard Care adjusted for baseline value, insulin delivery modality, and site as a random effect.

Table S12: Attainment of Type 1 Diabetes Pregnancy Glucose Targets

End Points	Baseline		Pregnancy Intervention Phase[a]	
	Closed-Loop (N=59)	Standard Care (N=59)	Closed-Loop (N=59)	Standard Care (N=61)
Hours of Sensor Data	150 (128, 156)	149 (124, 171)	3,361 (2,996, 3,561)	3,417 (3,112, 3,507)
HbA1c ≤ 6.5%			48 (83%)	36 (59%)
% Time In Range 63-140 mg/dL >70%			28 (47%)	7 (11%)
% Time > 140 mg/dL <25%			22 (37%)	7 (11%)
% Time <63 mg/dL <4%			47 (80%)	44 (72%)
% Time <54 mg/dL <1%			38 (64%)	37 (61%)

a- CGM data calculated from 16 weeks' gestation until delivery.

The type 1 diabetes pregnancy sensor glucose targets are: Time In Range 63-140 mg/dL for >70% (16hr 48 min), Time Above Range > 140 mg/dL for <25% (6hr), Time <63 mg/dL for <4% (1hr), and Time <54 mg/dL <1% (15min). The NICE HbA1c target is ≤ 6.5%**.**

Data are Mean ± SD or Median (Quartiles).

Table S13: Personal Glucose Target in the Closed-Loop Group

Trimester[a]	**N**[b]	**Mean Target** *(mmol/mol)*	**Mean Target** *(mg/dL)*
1	34	5.7 ± 0.1	102 ± 2
2	58	5.4 ± 0.3	97 ± 6
3	53	5.1 ± 0.3	93 ± 5

a – The first trimester is from the day after randomization until 12 weeks 6 days gestation, the second trimester is from 13 weeks until 27 weeks 6 days, and the third trimester is from 28 weeks until delivery.
b - 27 participants without 1st trimester data, 3 participants without 2nd trimester data, 8 participants without 3rd trimester data
Data are Mean ± SD

Table S14: Maternal Insulin Outcomes

	Baseline		Week 24-26		Week 34-36		Adjusted Treatment Difference (95% CI)
	Closed-Loop	**Standard Care**	**Closed-Loop**	**Standard Care**	**Closed-Loop**	**Standard Care**	
Total Daily Insulin (U/kg/day) N=#	61	60	58	54	56	56	
Mean ± SD	0.69 ± 0.23	0.69 ± 0.23	0.79 ± 0.30	0.81 ± 0.31	0.97 ± 0.43	1.06 ± 0.47	-0.10 (-0.25, 0.06)
% change from baseline N=#	NA	NA	58	52	56	55	
Mean ± SD	NA	NA	18% ± 35%	21% ± 42%	44% ± 52%	61% ± 69%	
Daily Basal Insulin (U/kg/day) N=#	61	61	59	59	57	56	
Mean ± SD	0.37 ± 0.16	0.37 ± 0.15	0.40 ± 0.15	0.37 ± 0.18	0.47 ± 0.21	0.43 ± 0.23	0.04 (-0.03, 0.12)
% change from baseline N=#	NA	NA	59	58	57	56	
Mean ± SD	NA	NA	18% ± 48%	5% ± 42%	36% ± 61%	21% ± 60%	
Daily Bolus Insulin (U/kg/day) N=#	61	61	58	54	56	56	
Median (Quartiles)	0.31 (0.23, 0.37)	0.30 (0.22, 0.40)	0.32 (0.23, 0.51)	0.41 (0.30, 0.50)	0.42 (0.28, 0.65)	0.55 (0.40, 0.84)	-0.13 (-0.26, 0.01)
% change from baseline N=#	NA	NA	58	52	56	55	
Median (Quartiles)	NA	NA	9% (-11%, 50%)	42% (2%, 92%)	44% (-2%, 100%)	91% (35%, 208%)	

Difference is Closed-Loop – Standard Care adjusted for baseline value, insulin delivery modality, and site as a random effect.

Table S15: Patient Reported Outcomes

End Points	Baseline ~12/40				Follow-up Phase ~34/40				Adjusted Treatment Difference
	Closed-Loop		Standard Care		Closed-Loop		Standard Care		(95% CI)
INSPIRE[a]	57	80 ± 10	NA	NA	34	82.9 ± 9.4	NA	NA	NA
EQ-5D[b]	57	0.88 ± 0.15	59	0.89 ± 0.14	34	0.85 ± 0.16	44	0.76 ± 0.19	0.09 (0.02, 0.17)
Diabetes Distress Scale (DDS) total[c]	57	2.1 ± 0.9	58	2.0 ± 0.8	34	1.5 ± 0.5	43	1.5 ± 0.4	-0.07 (-0.26, 0.11)
DDS Emotional	57	1.8 ± 0.8	58	1.7 ± 0.7	34	1.4 ± 0.5	43	1.4 ± 0.4	0.00 (-0.18, 0.19)
DDS Physician	57	2.1 ± 0.9	58	2.1 ± 0.7	34	1.5 ± 0.5	43	1.6 ± 0.4	-0.1 (-0.3, 0.1)
DDS Regimen	57	2.4 ± 1.0	58	2.4 ± 1.1	34	1.5 ± 0.5	43	1.8 ± 0.6	-0.3 (-0.5, 0.0)
DDS Interpersonal	57	1.9 ± 0.9	58	1.7 ± 0.8	34	1.6 ± 0.8	43	1.3 ± 0.6	0.1 (-0.2, 0.4)
HFSQ II – Worry[d]	55	34 ± 12	58	32 ± 10	34	28 ± 10	43	29 ± 7	-0.9 (-4.8, 3.1)
PSQI[e]	42	9.2 ± 3.6	45	8.9 ± 3.1	28	11.3 ± 3.2	29	10.7 ± 3.4	1.8 (-0.2, 3.8)

Difference is Closed-loop – Standard Care adjusted for baseline value of the metric, insulin delivery modality, and site as a random effect. Data are Mean ± SD.

[a]The INsulin delivery Systems: Perspectives, Ideas, Reflections and Expectations (INSPIRE) questionnaire (intervention group only) with higher scores indicating more positive experiences

[b]EQ-5D Health-Related Quality of Life Questionnaire: total EQ-5D score, the maximum score of 1 indicates the best health state

[c]Diabetes Distress Score – higher scores indicating more total, emotional, physician, treatment-related, and interpersonal diabetes distress.

[d]Hypoglycemia Fear Survey Questionnaire II (HFSQ II) (Worry scale only)

[e]Pittsburgh Sleep Quality Index (PSQI) with higher scores indicating worse sleep quality

Table S16: Adverse Device Effects in the Closed-Loop Group

Related to Closed-Loop[a]	Related to CGM[a]	Serious Adverse Event	Event	Severity	Notes
Possibly	Unlikely	No	Hyperglycemia – highest glucose 259mg/dL	Mild	Device deficiency – CamAPS app required re-installation. Participant reported anxiety, nausea, and lethargy (unrelated to device). No impact on pregnancy outcome.
Probably	Unlikely	**Yes**	Severe Hypoglycemia (miscarriage, epilepsy, stress, sleep deprivation)	Severe	Closed-loop 'user error' reported – participant forgot to change her insulin carbohydrate ratio and gave incorrect bolus dose post-miscarriage. Post miscarriage ADE – no impact on pregnancy outcome.
Possibly	Unrelated	No	Self-treated hypoglycemia – lowest glucose 52mg/dL	Mild	Resolved prior to admission for covid infection with abdominal pain/vomiting. No impact on pregnancy outcome.
Unrelated	Definitely	No	Dermatitis allergic	Mild	No impact on glycemic/pregnancy outcome.
Definitely	Unrelated	No	Moderate non-acidotic ketosis. Ketones 2.5, glucose 320mg/dL, pH 7.4, bicarb 14.1. Spontaneous onset of preterm labor	Moderate	Closed-loop went out of auto-mode (loss of Bluetooth connectivity) whilst asleep. Auto-mode reconnected when she woke and closed-loop was reinstated. Admitted later same day with preterm labor at 35^{+2} week's gestation and was delivered by repeat cesarean section. Participant was seen for reduced fetal movements on the day before ADE but a potential impact on pregnancy outcome cannot be excluded.
Unrelated	Definitely	No	Sensor bled at insertion site. Settled with compression.	Mild	No impact on glycemic/pregnancy outcome
Unrelated	Definitely	No	Bruising at sensor insertion site.	Mild	No impact on glycemic/pregnancy outcome
Unrelated	Definitely	No	Sensor bled at insertion site. Sensor replaced	Mild	No impact on glycemic/pregnancy outcome
Probably	Definitely	No	Hyperglycemia – highest glucose 320mg/dL	Moderate	Sensor failed to report glucose levels from 4am whilst sleeping. The pump continued to deliver insulin but did not adequately control glucose levels, resulting in discontinuation of her assigned CamAPS closed-loop treatment. Participant resumed her prior Tandem control IQ closed-loop system 17 days post-device training.

Unrelated	Possibly	**Yes**	Hyperglycemia – highest glucose 362mg/dL. Moderate non-acidotic ketosis: Ketones 3.3. pH 7.4, Bicarb 17	Moderate	Sensor stopped working intermittently 28 days after randomization. Moderate non-acidotic ketosis - admitted and treated with variable rate iv insulin infusion No impact on pregnancy outcome
Definitely	Definitely	No	Mild ketosis. Ketones 0.7, resolved at presentation to Emergency Department, not admitted	Moderate	Hyperglycemia induced by set failure compounded by loss of glucose sensing ~3 hrs. Resolved once glucose sensing and closed loop recommenced. No impact on pregnancy outcome
Definitely	Unrelated	No	Mild ketosis. Hyperglycemia – highest glucose 390mg/dL. Medium urinary ketones. Not admitted.	Moderate	Participant reported sensor came loose /infusion cannula kinked – pump did not alert participant. No impact on pregnancy outcome

a-Possibly, probably, or definitely related (or unlikely / unrelated) to device as determined by local site investigator

Table S17: Primary and Secondary Maternal Glucose Outcomes with Site as Fixed Effect

Endpoints	Baseline[a]		Antenatal Intervention Phase[b]		Adjusted Treatment Difference[c] (95% CI)	P-value[c]
	Closed-Loop (N=59)	Standard Care (N=59)	Closed-Loop (N=59)	Standard Care (N=61)		
Hours of Sensor Data	150 (128, 156)	149 (124, 171)	3361 (2996, 3561)	3417 (3112, 3507)	NA	NA
Primary Endpoint						
% Time in Range 63-140mg/dL	**47.8% ± 16.4%**	**44.5% ± 14.4%**	**68.2% ± 10.5%**	**55.6% ± 12.5%**	**10.6% (7.0%, 14.1%)**	**<0.001**
Key Secondary Endpoints						
%Time >140mg/dL	**48.7% ± 18.0%**	**51.8% ± 16.2%**	**29.2% ± 10.6%**	**41.4% ± 13.2%**	**-10.3% (-14.0%, -6.7%)**	
%Overnight Time in Range 63-140mg/dL (23.00-0700)[a]	**47.4% ± 20.8%**	**44.5% ± 16.6%**	**70.8% ± 11.2%**	**56.7% ± 13.6%**	**12.4% (8.4%, 16.4%)**	
Secondary Endpoints						
% Time 63-180mg/dL	71% ± 16%	68% ± 15%	87% ± 9%	80% ± 10%	6% (3%, 9%)	
%Time >180mg/dL	26% ± 17%	28% ± 16%	11% ± 9%	17% ± 11%	-6% (-8%, -3%)	
Glucose AUC >120 mg/dL	39.5 ± 23.7	41.3 ± 19.7	19.3 ± 12.2	27.9 ± 12.9	-8 (-11, -4)	
Mean Glucose (mg/dL)	149 ± 28	151 ± 24	125 ± 14	136 ± 16	-9.3 (-13.8, -4.8)	
Glycated Hemoglobin (HbA1c) %	7.6 ± 1.1	7.9 ± 1.3	6.0 ± 0.5	6.4 ± 0.5	-0.31 (-0.50, -0.12)	
Glucose SD (mg/dL)	54 ± 14	55 ± 12	42 ± 11	47 ± 10	-4.4 (-7.3, -1.4)	
Glucose CV (%)	36% ± 5%	37% ± 6%	33% ± 5%	34% ± 5%	-1.0% (-2.4%, 0.4%)	
Hypoglycemia						
% Time <63mg/dL	2.75% (0.86%, 4.87%)	2.22% (0.72%, 6.00%)	2.26% (1.54%, 3.31%)	2.02% (1.25%, 4.37%)	-0.4% (-1.0%, 0.2%)	
% Time <55mg/dL	1.05% (0.07%, 2.37%)	0.79% (0.18%, 2.28%)	0.71% (0.49%, 1.19%)	0.73% (0.36%, 1.67%)	-0.2% (-0.5%, 0.1%)	
Mild Hypoglycemia[d]	6.4 (2.2, 11.5)	5.5 (2.4, 11.1)	6.7 (4.6, 9.4)	5.7 (3.1, 9.4)	0.2 (-1.0, 1.4)	
Moderate Hypoglycemia[e]	2.2 (0.0, 5.7)	2.2 (0.0, 5.9)	2.3 (1.6, 3.8)	2.1 (1.1, 4.4)	-0.0 (-0.7, 0.7)	
Overnight Endpoints (23.00-07.00 hours)						
Mean Glucose (mg/dL)	149 ± 33	150 ± 26	125 ± 14	135 ± 17	-9.1 (-13.9, -4.4)	
% Time >140mg/dL	49% ± 22%	52% ± 18%	27% ± 11%	40% ± 14%	-11% (-15%, -7%)	
% Time <63mg/dL	1.40% (0.00%, 5.27%)	2.33% (0.51%, 5.67%)	1.56% (1.10%, 2.51%)	2.57% (1.04%, 4.41%)	-1.3% (-2.1%, -0.6%)	
Glucose SD (mg/dL)	52 ± 17	54 ± 14	40 ± 12	47 ± 12	-5.8 (-9.4, -2.2)	
Glucose CV (%)	35% ± 8%	36% ± 8%	32% ± 5%	35% ± 6%	-2.3% (-4.2%, -0.5%)	
Mild Hypoglycemia[d]	3.5 (0.0, 10.2)	6.4 (0.0, 11.9)	4.3 (2.9, 5.5)	5.3 (2.8, 8.7)	-1.7 (-3.0, -0.4)	
Moderate Hypoglycemia[e]	0.0 (0.0, 4.7)	0.0 (0.0, 6.9)	1.7 (1.0, 2.5)	2.1 (0.8, 4.3)	-0.7 (-1.4, -0.0)	

Data are mean ± SD or median (Quartiles).

a- Baseline CGM metrics calculated using data from the pre-randomization run-in phase. Two participants were missing baseline CGM data. Four participants were missing follow-up CGM data (due to miscarriage and/or pregnancy terminations) are not tabulated.

b- Antenatal intervention phase is from 16 weeks' gestation until delivery. Endpoints are calculated using Continuous Glucose Monitoring (CGM) sensor data except for glycated hemoglobin which was measured at trial sites. 4 participants were missing intervention CGM data. The glycated hemoglobin level at 34-36 weeks reflects maternal glycemia over the preceding 10-12 weeks.

c- Difference is Closed-Loop – Standard Care. Model adjusted for baseline value, insulin delivery modality, and site as a random effect. P-values are adjusted using the Holm step-down method to control the type 1 error.

d- Mild hypoglycemia is defined as consecutive CGM glucose <63mg/dL (3.5 mmol/L) for at least 15 consecutive minutes. Episodes separated by 30 minutes.

e- Moderate hypoglycemia is defined as consecutive CGM glucose<55mg/dL (3.0 mmol/L) for at least 15 consecutive minutes. Episodes separated by 30 minutes.

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