ISRCTN56898625 https://doi.org/10.1186/ISRCTN56898625

Automated insulin Delivery Amongst Pregnant women with Type 1 diabetes

Submission date
09/04/2018

Recruitment status
No longer recruiting

Registration date
10/04/2018

Overall study status
Completed

Last Edited
31/01/2025

Condition category
Nutritional, Metabolic, Endocrine

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Type 1 diabetes occurs when the body is unable to produce insulin, a hormone that controls the amount of sugar (glucose) in the blood. Closed-loop insulin delivery is a treatment approach for people with type 1 diabetes. It is a medical device consisting of a linked continuous glucose monitor (CGM) and an insulin pump. Previous studies have shown that closed loop insulin delivery may improve glucose control in pregnancy compared to treatment with a standard insulin pump and CGM. These results are important because improving glucose control improves pregnancy outcomes for both mother and baby. However, in the previous studies closed loop insulin delivery was only studied for a short duration in a small number of participants. As a result the aim of this study is to find definitive proof of a benefit to women by using automated closed-loop for about 24 weeks throughout pregnancy in a real-life NHS antenatal care setting.

Who can participate?
Pregnant women between 18 and 45 years of age with type 1 diabetes, between confirmation of and the 13th week of their pregnancy

What does the study involve?
Participants are randomly allocated to receive either the closed loop insulin delivery system or the current standard of care. All participants are asked to wear a continuous glucose monitor which records their glucose levels throughout their pregnancy. Participants attend their routine antenatal visits as usual and study visits can be carried out remotely. Additional blood samples are taken at the 24th and 34th week of pregnancy where possible and questionnaires are also completed by the participant at the 34th week of pregnancy. Following this information on the birth is collected. Eligible participants can continue on the study until 6 months after delivery, with flexible visits at 8-12 weeks and 24 weeks post-delivery. 25 of the woman allocated to the closed loop insulin delivery system are also interviewed to collect more information on, among other things, their existing diabetes management practices, everyday work and family lives and their experience with the device.

What are the possible benefits and risks of participating?
Participating in this study may help participants to better understand what happens to their glucose levels during pregnancy. It will also help research into the development of closed-loop

systems. Participants may also benefit from wearing a CGM and insulin pump. Recent studies suggest that using CGM helps to improve glucose control during pregnancy and reduces newborn complications related to higher glucose levels. Insulin pump use is usually associated with a reduced risk of low blood sugar and improved quality of life. The insulin pump and CGM sensor may produce mild pain when inserted under the skin. There is a low risk for developing a skin infection at the site of the insulin pump or CGM insertion. Itchiness, redness, bleeding, and bruising at the pump and CGM insertion sites may occur as well as tape allergies. Participants are asked to contact the study team if they have any skin problems. Participants are alerted by an alarm if the closed loop stops working or malfunctions in any way, for example loss of connection between the smartphone and insulin pump. If they do not respond to the alarm their usual insulin delivery will be automatically started. During the study participants may experience a 'hypo' as may happen in everyday life. This will be treated according to usual practice. It is possible that there will be a small amount of discomfort or bruising when the blood samples are taken.

Where is the study run from?
Norfolk and Norwich University Hospitals NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
January 2018 to June 2023

Who is funding the study?
National Institute for Health Research (NIHR) (UK)

Who is the main contact?
Corinne Collett, c.collett@uea.ac.uk

Contact information

Type(s)
Public

Contact name
Ms Corinne Collett

Contact details
NCTU
Norwich Medical School
UEA
Norwich
United Kingdom
NR4 7TJ
-
c.collett@uea.ac.uk

Additional identifiers

Integrated Research Application System (IRAS)
240380

Protocol serial number
37660; IRAS Project ID: 240380

Study information

Scientific Title
Evaluation of the biomedical and psychosocial impact of closed-loop (artificial pancreas) insulin delivery in women with type 1 diabetes during pregnancy

Acronym
AiDAPT

Study objectives
Current study hypothesis as of 29/03/2023:

Previous studies have shown that closed loop insulin delivery may improve glucose control in pregnancy compared to treatment with a standard insulin pump/injections and/or continuous glucose monitor without closed loop. These results are important because improving glucose control improves the pregnancy outcomes for both mother and baby. However, in the previous studies closed loop insulin delivery was only studied for a short duration in a small number of participants. As a result this trial focuses on determining the definitive proof of a benefit to women by using automated closed-loop for approximately 24 weeks duration throughout pregnancy in a real-life NHS antenatal care setting.

_____

Previous study hypothesis:

Previous studies have shown that closed loop insulin delivery may improve glucose control in pregnancy compared to treatment with a standard insulin pump and continuous glucose monitor. These results are important because improving glucose control improves the pregnancy outcomes for both mother and baby. However, in the previous studies closed loop insulin delivery was only studied for a short duration in a small number of participants. As a result this trial focuses on determining the definitive proof of a benefit to women by using automated closed-loop for approximately 24 weeks duration throughout pregnancy in a real-life NHS antenatal care setting.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 15/08/2018, NRES Committee East of England - Cambridge Central (Wellcome Trust Clinical Research Facility, Addenbrookes Hospital, Hills Road, Cambridge, CB2 0QQ; 0207 104 8108; NRESCommittee.EastofEngland-CambridgeCentral@nhs.net), ref: 18/EE/0084

Study design
Randomised; Interventional; Design type: Treatment, Device

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Type 1 diabetes pregnancy

Interventions
Current intervention as of 16/02/2022:
The trialists are aiming to recruit 124 pregnant women between 18 and 45 years of age with Type 1 Diabetes of at least 12 months' duration. Participants will be approached between confirmation of a viable pregnancy and the 13th week of their pregnancy and if consent is given they will complete a run-in phase. Following this eligible participants will be randomly allocated to receive either the closed-loop insulin delivery system or the current standard of care. Randomisation will be performed by a computer-based IWRS system on a 1:1 ratio.

The intervention being evaluated in this trial is automated closed-loop insulin delivery. The closed-loop system comprises three components: an insulin pump, a continuous glucose monitor (CGM) and a computer-based model predictive control (MPC) algorithm to compute information from the CGM into a recommended insulin dose. Closed-loop systems are designed to deliver insulin in response to CGM glucose levels and may help to improve glucose control above and beyond what is currently achievable using standard insulin pumps and injections.

All participants will be asked to wear a continuous glucose monitor which will record their glucose levels throughout their pregnancy. Participants will attend their routine antenatal visits. Study visits may be carried out remotely. Additional blood samples for the research will be obtained at the 24th and 34th week of pregnancy where possible and questionnaires will also be completed by the participant at the 34th week of pregnancy. Following this we will collect information on the birth and infant. From December 2021, participants who have consented will continue using their intervention to 6 months post-delivery, with virtual visits and participant descriptive feedback questions at 8-12 and 24 weeks.

25 of the women randomised to the closed-loop insulin delivery system will also be interviewed to gain more information on, among other things, their existing diabetes management practices, everyday work and family lives and their experience with the device.

———

Previous intervention:
The trialists are aiming to recruit 124 pregnant women between 18 and 45 years of age with Type 1 Diabetes of at least 12 months' duration. Participants will be approached between the 8th and 13th week of their pregnancy and if consent is given they will complete initial assessments and safety tests to confirm they are eligible to take part in the study. Following this eligible participants will be randomly allocated to receive either the closed loop insulin delivery system or the current standard of care. Randomisation will be performed by a computer based IWRS system on a 1:1 ratio.

The intervention being evaluated in this trial is automated closed-loop insulin delivery. The closed-loop system comprises of three components: an insulin pump, a continuous glucose monitor (CGM) and a computer-based model predictive control (MPC) algorithm to compute information from the CGM into a recommended insulin dose. Closed-loop systems are designed to deliver insulin in response to CGM glucose levels and may help to improve glucose control above and beyond what is currently achievable using standard insulin pumps and injections

All participants will be asked to wear a continuous glucose monitor which will record their glucose levels throughout their pregnancy. Participants will attend their routine antenatal visits as usual. Additional blood samples for the research will be obtained at the 24th and 34th week of pregnancy and questionnaires will also be completed by the participant at the 34th week of pregnancy. Following this we will collect information on the birth. 25 of the woman randomised to the closed loop insulin delivery system will also be interviewed to gain more information on, among other things, their existing diabetes management practices, everyday work and family lives and their experience with the device.

Intervention Type
Device

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
CamAPS FX app (closed-loop), Dexcom G6 continuous glucose monitor

Primary outcome(s)
Current primary outcome measure as of 16/02/2022:

Percentage of time spent with glucose levels between 3.5-7.8 mmol/L based on CGM levels between 16 weeks gestation and delivery. Data for the intervention group will be collected as part of the data collection from the AiD closed-loop system. Data for the control group will be collected using software provided by the CGM manufacturer.

———

Previous primary outcome measure:
The percentage of time spent with glucose levels between 3.9-7.8 mmol/L based on CGM levels at 24 and 34 weeks gestation. Data for the intervention group will be collected as part of the data collection from the AiD closed-loop system. The control group and those who have withdrawn from the intervention group will have a subcutaneous glucose sensor inserted by the clinical research team and will be instructed to wear it at home for 7-10 days. They will be asked to calibrate the CGM according to manufacturer instructions and to return for CGM sensor downloading within 14 days; Timepoint(s): End of the study

Key secondary outcome(s))
Current secondary outcome measures as of 16/02/2022:

The following will be measured using CGM measures:
1. The time spent with CGM glucose levels above and below target range (TAR>7.8mmol/L, TBR<3.5mmol/L), mean CGM glucose and CGM glucose variability measures (CV, SD)
2. The frequency and severity of hypoglycaemia episodes defined as CGM glucose levels TBR <3.5 mmol/L (level 1 hypoglycaemia) and TBR <3.0 mmol/L (level 2 hypoglycaemia) for at least 15 min. Distinct episodes must be separated for at least 30 min.
3. The international consensus targets for glycaemic assessment; TIR 3.5-7.8 mmol/L >70% (16hr 48 min), TAR >7.8mmol/L <25% (6 h), TBR <3.5 mmol/L <4% (1 h), and TBR <3.0 mmol/L <1% (15 min)
4. The Low Blood Glucose Index (LBGI) and High Blood Glucose Index (HBGI) measures
5. Where possible, blood samples will be collected at baseline, 24-26 weeks, 34-36 weeks for HbA1c testing to assess the change in the maternal level. Samples will be stored for further

metabolic studies (optional).
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 h (midnight to midnight) and overnight time 23.00-07.00

Maternal obstetric outcomes (from hospital records):
1. Gestational weight gain (weight gain from booking visit to 36 weeks)
2. Maternal hypertensive disorders (gestational, worsening of pre-existing hypertension or preeclampsia)
3. Fetal growth (ultrasound estimated fetal weight, head and abdominal circumference measurements)
4. The mode of delivery (vaginal, instrumental, elective caesarean section and emergency caesarean section)
5. The gestational age at delivery and indication for any preterm delivery (<37 weeks)
6. Adverse events including pregnancy loss <24 weeks, stillbirth, neonatal death
7. Maternal hospital admissions (all admissions including the delivery admission)
8. Hospital length of stay (all admissions including the delivery admission)

Infant outcomes (from hospital records):
1. Neonatal morbidity including treatment for neonatal hypoglycaemia, neonatal jaundice and respiratory distress between the time of infant delivery and discharge from hospital
2. Infant birth weight (customised birth weight percentile, incidence of large for gestational age (LGA), and small for gestational age (SGA)
3. Neonatal intensive care unit (NICU) admission >24 h
4. Infant feeding at hospital discharge, 8-12 weeks postpartum, and 24 weeks postpartum (breast, bottle, both)
5. Hospital length of stay (from delivery until hospital discharge), including re-admissions >24 h within the first 7 days from birth

The following safety measures will be recorded on occurrence during the trial (from hospital records):
1. The frequency and severity of diabetic ketoacidosis during the period of inclusion in the trial
2. The number and severity of episodes of severe hypoglycaemia during the period of inclusion in the trial
3. The number and severity of episodes of adverse device effect

Psychosocial outcomes:
1. Questionnaires completed at baseline and 34-36 weeks
2. Qualitative interviews: 25 women randomized to the AiD arm will be interviewed post-randomization and again at 34-36 weeks; up to 25 staff from the trial sites will be interviewed
3. Postpartum: self-reported diabetes and treatment-related experience as described through descriptive writing using free text

Health economic outcomes
1. Cost of the closed-loop (study pump, CGM, and CamAPSCamAPS® FX) and control-arm (CGM and insulin delivery) glucose monitoring and insulin delivery systems including device training costs for intervention and control arm participants
2. Maternity health care use including NHS antenatal clinic visits, and between visit contacts which will be grouped as questions around
2.1. Diabetes management
2.2. Technical device issues
2.3.. Both diabetes and device issues

3. Antenatal hospital admissions (number and total length of hospital stay) including the delivery admission length of hospital stay
4. Neonatal health care use including costs of delivery, costs associated with any complications of delivery, and neonatal complications
5. Neonatal intensive care unit admissions (level of care and duration of admission) and total neonatal length of hospital stay
6. The EQ-5D Health-Related Quality of Life Questionnaire. The cost-effectiveness of the closed loop system will be estimated using the study primary outcome measure of time spent with glucose levels between 3.5-7.8 mmol/L. This cost-effectiveness study will estimate any additional cost per additional week of target glucose control. Additionally, collection of the EQ-5D will enable estimation of quality adjusted life years (QALYs) for a cost-utility analysis.

Key postpartum outcome analysis:
The key analysis will evaluate the change in the time spent in the target glucose range (CGM TIR 3.9 – 10.0 mmol/l) between the intervention and control arm between delivery and 6 months postpartum.

Post-partum exploratory outcomes:
1. Percentage time spent with CGM <3.0 mmol/l to quantify maternal moderate hypoglycaemia
2. Mean CGM glucose
3. Percentage time spent with CGM <3.9 mmol/l to quantify borderline hypoglycaemia
4. Percentage time spent at CGM >10.0 mmol/l to quantify hyperglycaemia
5. Standard deviation (SD) of CGM glucose to quantify the glucose variability
6. Coefficient of variation (CV), of CGM glucose to quantify the glucose variability
7. Insulin delivered (basal, bolus, and total) to assess insulin needs
8. Mild-moderate episodes of hypoglycaemia <3.9 (level 1) and <3.0 (level 2) from CGM data defined as AUC <3.9 or AUC ≤3.0 for 15 minutes duration
9. Nocturnal hypoglycaemia (NH): CGM glucose <3.9 (level 1) and <3.0 (level 2) between 23:00 and 07:00

———

Previous secondary outcome measures:
The following will be measured at 24 weeks and 34 weeks gestation:
1. Time spent with glucose levels between 3.9-7.8 mmol/L
2. Time spent with glucose levels above and below target range
3. Frequency and severity of hypoglycaemia episodes
4. Low and High Blood Glucose Index
5. Change in HbA1c level

The following will be measured following delivery;
1. Gestational weight gain
2. Gestational hypertension or preeclampsia
3. Mode of delivery
4. Gestational age at delivery and indication for any preterm delivery
5. Adverse events
6. Maternal hospital admissions
7. Hospital length of stay (both maternal and neonatal)
8. Neonatal morbidity
9. Infant birth weight
10. Neonatal intensive care unit (NICU) admission >24 hours
11. Infant feeding at hospital discharge (breast, bottle, both)

The following safety measures will be recorded on occurrence during the trial:
1. Frequency and severity of diabetic ketoacidosis
2. Number and severity of episodes of severe hypoglycaemia
3. Number and severity of episodes of adverse device effect

Completion date
30/06/2023

Eligibility

Key inclusion criteria
Current inclusion criteria as of 16/02/2022:
1. Between 18 and 45 years of age (inclusive)
2. A diagnosis of type 1 diabetes (T1D), as defined by WHO (a chronic condition in which the pancreas produces little or no insulin by itself, characterized by deficient insulin production and a requirement for daily administration of insulin), for at least 12 months
3. A viable pregnancy confirmed by ultrasound, up to 13 weeks and 6 days gestation
4. Currently on intensive insulin therapy (≥3 injections or CSII). This includes women using sensor augmented pumps and/or 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. A CGM or Libre GMI (glucose management indicator) ≥48 mmol /mol (≥6.5%) or ≤86 mmol/mol (≤10%) may also be used.
7. Able to provide informed consent
8. Have access to email

———

Previous inclusion criteria:
1. Between 18 and 45 years of age (inclusive)
2. A diagnosis of type 1 diabetes (T1D), as defined by WHO for at least 12 months
3. A viable pregnancy confirmed by ultrasound, at gestational age between 8 weeks and 13 weeks and 6 days
4. Currently on intensive insulin therapy (≥3 injections or CSII)
5. Willingness to use the study devices and complete the CGM assessments
6. HbA1c level ≥48mmol/mol (≥ 6.5%) at booking (first antenatal contact) and <86 mmol/mol (<10%) at point of randomisation
7. Able to provide informed consent
8. Have access to email

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
Female

Total final enrolment
124

Key exclusion criteria
Current exclusion criteria as of 16/02/2022:
1. Non-type 1 diabetes
2. Any other physical or psychological disease which, in the opinion of the investigator, is likely to interfere with the normal conduct and interpretation of the study results e.g. untreated coeliac disease or untreated hypothyroidism
3. Current treatment with drugs known to interfere with glucose metabolism as judged by the investigator such as high dose systemic corticosteroids, non-selective beta-blockers and MAO inhibitors
4. Known or suspected allergy against insulin
5. Women with advanced nephropathy (eGFR <45), severe autonomic neuropathy, uncontrolled gastroparesis or severe proliferative retinopathy, as judged by the investigator, that is likely to interfere with the normal conduct of the study and interpretation of study results
6. Very good or very poor glycaemic control i.e. first antenatal HbA1c <48mmol/mol (<6.5%) and current HbA1c >86mmol/mol (>10%). A CGM or Libre GMI (glucose management indicator) <48 mmol/mol (<6.5%) or >86 mmol/mol (>10%) may also be used. Women who enter pregnancy with HbA1c or GMI >86 mmol/mol (>10%) may participate if they achieve HbA1c or GMI ≤86 mmol/mol (≤10%) before randomization.
7. Total daily insulin dose ≥1.5 IU/kg at recruitment.
8. Severe visual or hearing impairment.
9. Unable to speak and understand English.

_____

Previous exclusion criteria:
1. Non-type 1 diabetes
2. Any other physical or psychological disease which, in the opinion of the investigator, is likely to interfere with the normal conduct and interpretation of the study results e.g. untreated coeliac disease or untreated hypothyroidism
3. Current treatment with drugs known to interfere with glucose metabolism as judged by the investigator such as high dose systemic corticosteroids, non-elective beta-blockers and MAO inhibitors
4. Known or suspected allergy against insulin
5. Women with advanced nephropathy (eGFR< 45), severe autonomic neuropathy, uncontrolled gastroparesis or severe proliferative retinopathy, as judged by the investigator, that is likely to interfere with the normal conduct of the study and interpretation of study results
6. Very good or very poor glycaemic control i.e. first antenatal HbA1c < = 48mmol/mol (< = 6.5%) and current HbA1c > 86mmol/mol (10%) . Women who enter pregnancy with HbA1c > 86mmol /mol (10%) may participate if they achieve HbA1c < 86mmol/mol (10%) before randomisation
7. Total daily insulin dose more than or equal to 1.5 IU/kg at booking
8. Severe visual or hearing impairment
9. Unable to speak and understand English

Date of first enrolment
30/09/2019

Date of final enrolment
31/05/2022

Locations

Countries of recruitment
United Kingdom

England

Northern Ireland

Scotland

Study participating centre
Norfolk and Norwich University Hospital
Colney Lane
Norwich
United Kingdom
NR4 7UY

Study participating centre
Cambridge University Hospitals NHS Foundation Trust
Hills Road
Cambridge
United Kingdom
CB2 0QQ

Study participating centre
Royal Victoria Hospital, Belfast
Belfast
United Kingdom
BT12 6BA

Study participating centre
The Ipswich Hospital NHS Trust
Ipswich
United Kingdom
IP4 5PD

Study participating centre

King's College Hospital NHS Foundation Trust
London
United Kingdom
SE5 9RJ

Study participating centre
NHS Lothian
Edinburgh
United Kingdom
EH10 5HF

Study participating centre
Leeds Teaching Hospitals NHS Trust
Leeds
United Kingdom
LS1 3EX

Study participating centre
Guy's and St Thomas' NHS Foundation Trust
London
United Kingdom
SE1 9RT

Study participating centre
NHS Greater Glasgow and Clyde
J B Russell House
Gartnavel Royal Hospital
1055 Great Western Road Glasgow
Glasgow
United Kingdom
G12 0XH

Sponsor information

Organisation
Norfolk and Norwich University Hospitals NHS Foundation Trust

Funder(s)

Funder type
Government

Funder Name
NIHR Evaluation, Trials and Studies Co-ordinating Centre (NETSCC); Grant Codes: 16/35/01

Results and Publications

Individual participant data (IPD) sharing plan
The data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		05/10/2023	06/10/2023	Yes	No
Results article		27/01/2025	31/01/2025	Yes	No
Protocol article		05/04/2022	07/04/2022	Yes	No
HRA research summary			26/07/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes