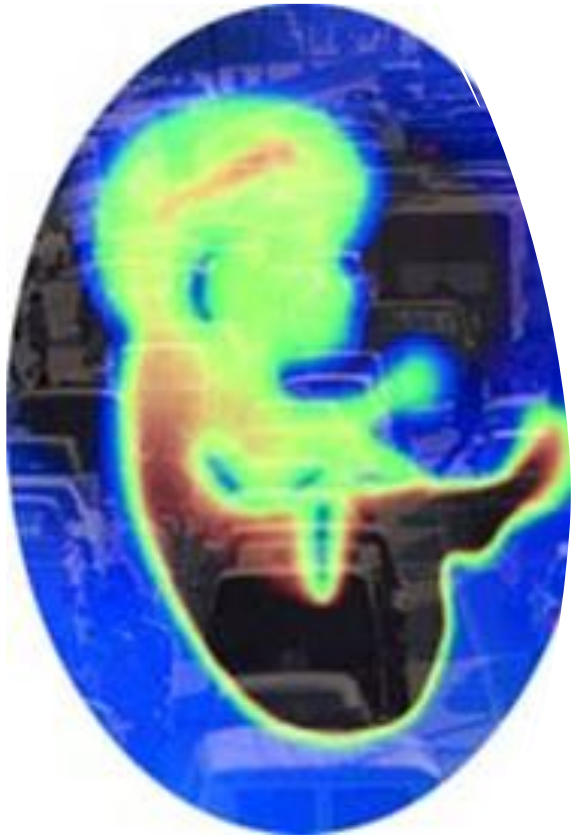

Right tech for improving outcomes in type 1 diabetes pregnancy (T1D)

Professor Helen Murphy
MB BCh BAO, MD, FRACP
Professor of Medicine, University of East Anglia (UEA), Norwich UK
Honorary Consultant Physician, Cambridge University NHS Hospital Trust
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Disclosures

- Board Member/Advisory Panel: UK & European Medtronic Advisory Board, Ypsomed UK
- Research Support: Diabetes UK, National Institute for Health Research (NIHR) Juvenile Diabetes Research Foundation (JDRF), Abbott Diabetes Care, Johnson & Johnson, Medtronic and Dexcom.
- Speaker’s Bureau: Medtronic, Roche, Sanofi-Aventis, Novo Nordisk, Ypsomed

What this session covers

- ✓T1D Pregnancy Outcomes: National Pregnancy in Diabetes (NPID) data
- ✓Evidence for using technology (CSII and CGM) during pregnancy
- ✓Lessons from AiDAPT randomized trial
- ✓Real-world HCL implementation….

What are the chances of a successful pregnancy outcome?

a) 25%
b) 50%
c) 80%
d) 90%

What is success?

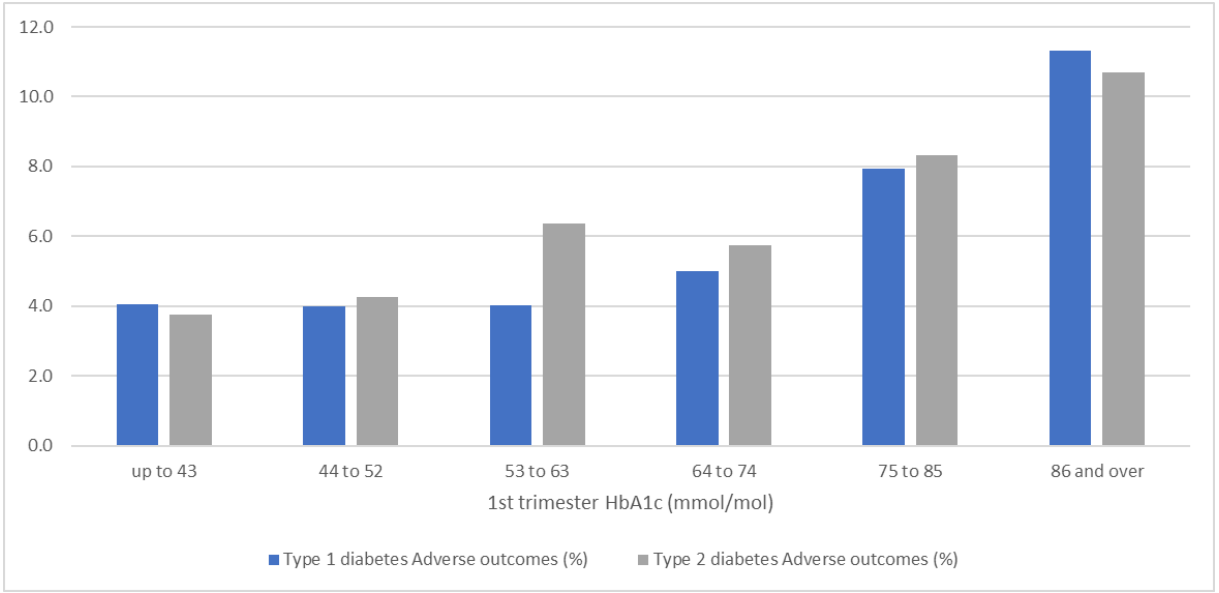
- No congenital malformations
- Live mother + no stillbirth/neonatal death
- No neonatal intensive care
- Baby normal size (<90th centile)
- Uncomplicated delivery
- No neonatal hypoglycaemia, jaundice, respiratory distress

Planning for a safe & healthy pregnancy

Risks and complications

For women with diabetes who do not plan their pregnancy, the risk of a serious complication (e.g. stillbirth, serious heart or birth defect) is about 1 in 10.

Reassuringly, if you do plan your pregnancy with your diabetes team, your risk of serious complications falls closer to that of women without diabetes (1 in 50).



https://www.tommys.org/pregnancy-information/planning-pregnancy/planning-for-pregnancy-tool

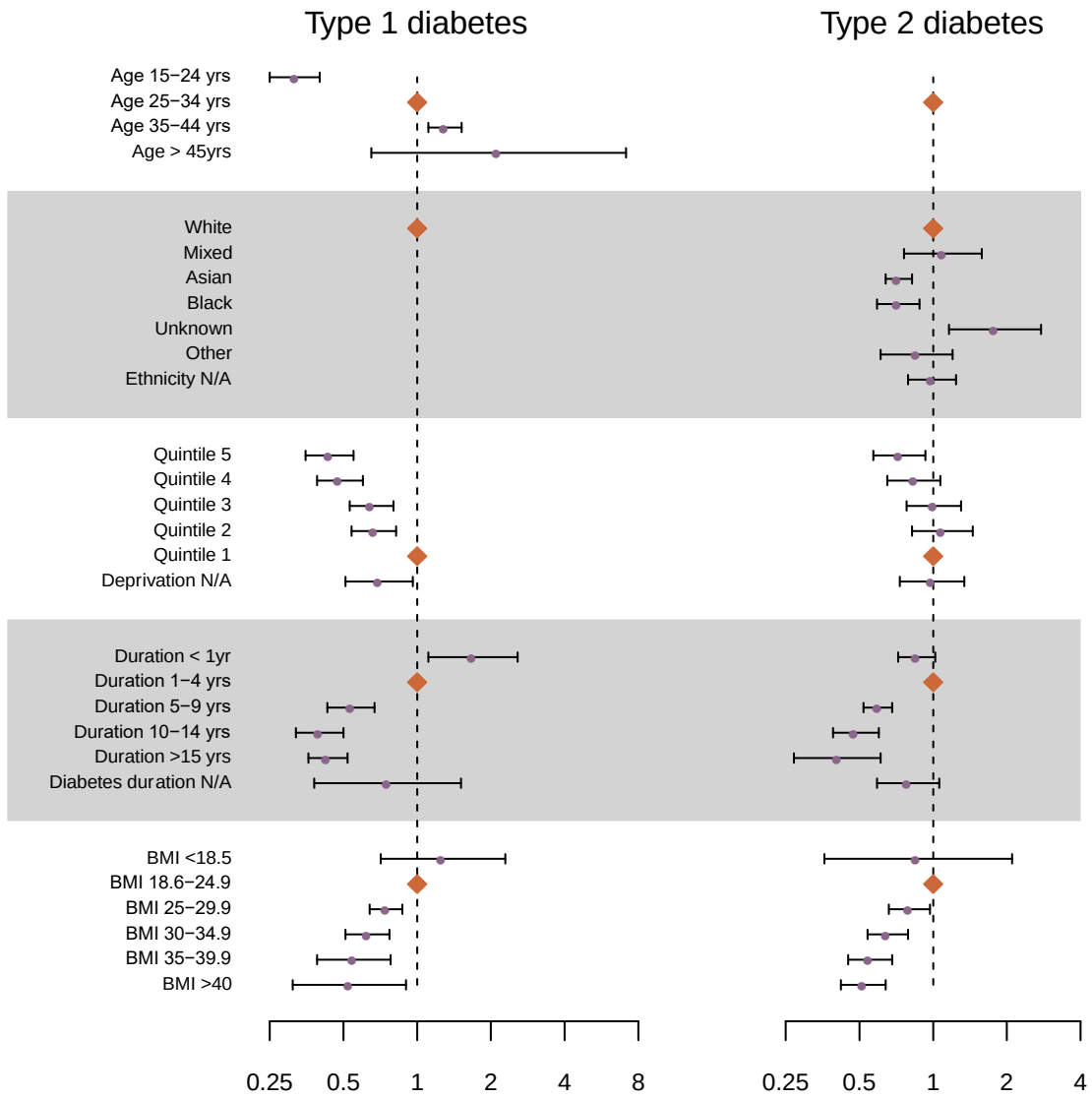
https://abcd.care/resource/planning-pregnancy

ABCD Association of British Clinical Diabetologists

DTN UK collaborate · evolve · support

Are women well prepared for pregnancy?

a) 1 in 2
b) 1 in 3
c) 1 in 5
d) 1 in 8



Odds ratio of first trimester HbA1c <48 mmol/mol (6.5%)

Obstetric complications are common & increasing

LGA

1 in 2 women with **T1D**

1 in 4 women with **T2D**

Caesarean section

3 in 4 of babies of mums with **T1D**

1 in 2 of babies of mums with **T2D**

Preterm birth

1 in 2 women with **T1D**

1 in 4 women with **T2D**

NICU

1 in 2 babies of mums with **T1D**

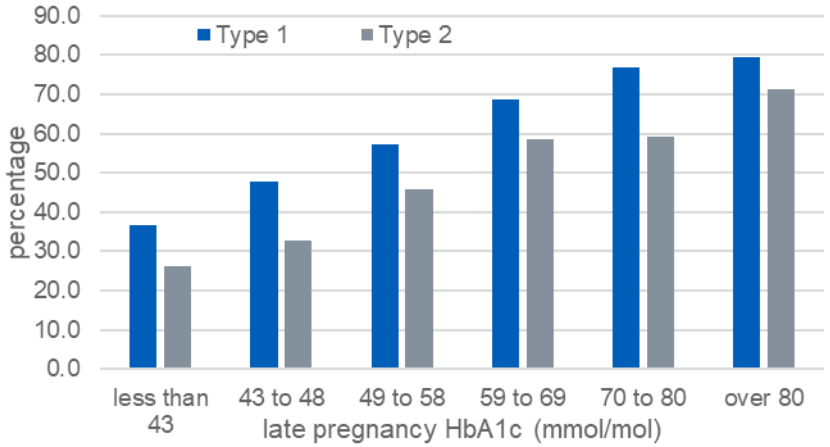
1 in 3 babies of mums with **T2D**

National Pregnancy in Diabetes Audit Report 2020 - NHS Digital

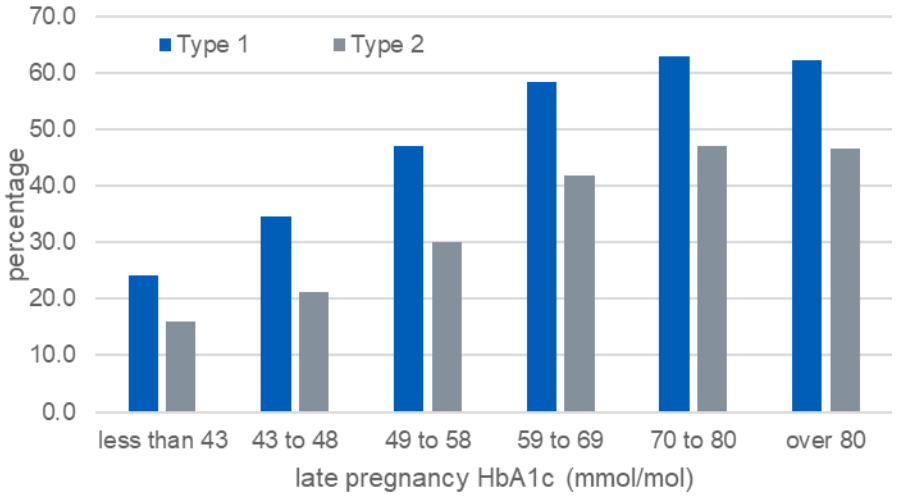
Pregnancy complications & maternal HbA1c during pregnancy

- Preterm births, LGA and neonatal care admissions are lowest with HbA1c <43mmol/mol during pregnancy

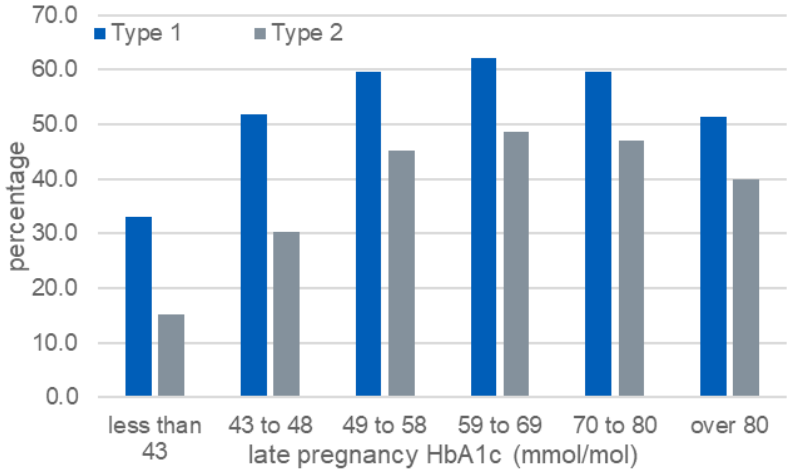
NICU admissions



Preterm births < 37 weeks



Large for gestational age (LGA) babies



CONCEPTT

- To assess the effectiveness of CONTINUOUS real-time CGM on glycemic control in women with T1D who were pregnant or planning pregnancy

Articles

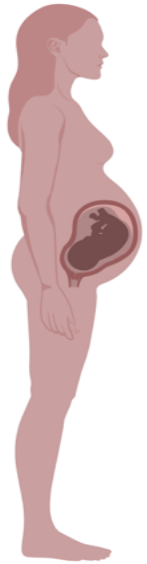
THE LANCET

"Use of continuous glucose monitoring during pregnancy in patients with type 1 diabetes is associated with improved neonatal outcomes, which are likely to be attributed to reduced exposure to maternal hyperglycaemia."

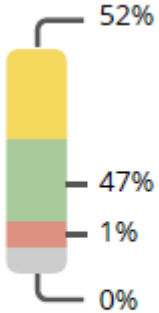
Continuous glucose monitoring in pregnant women with type 1 diabetes (CONCEPTT): a multicentre international randomised controlled trial

*Denice S Feig, Lois E Donovan, Rosa Corcoy, Kellie E Murphy, Stephanie A Amiel, Katharine F Hunt, Elisabeth Asztalos, Jon F R Barrett, J Johanna Sanchez, Alberto de Leiva, Moshe Hod, Lois Jovanovic, Erin Keely, Ruth McManus, Eileen K Hutton, Claire L Meek, Zoe A Stewart, Tim Wysocki, Robert O'Brien, Katrina Ruedy, Craig Kollman, George Tomlinson, Helen R Murphy, on behalf of the CONCEPTT Collaborative Group**

CGM helps in T1D pregnancy (CONCEPTT)



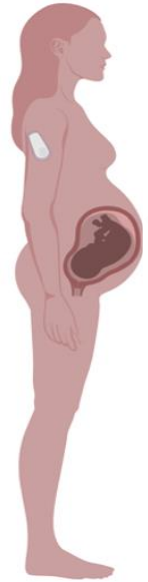
N= 107



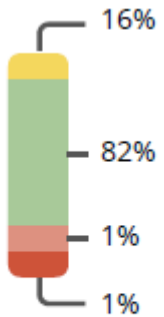
Time in range

Fingerprick users
Higher HbA1c 6.5%
Less TIR (61%TIRp)

Mum's glucose

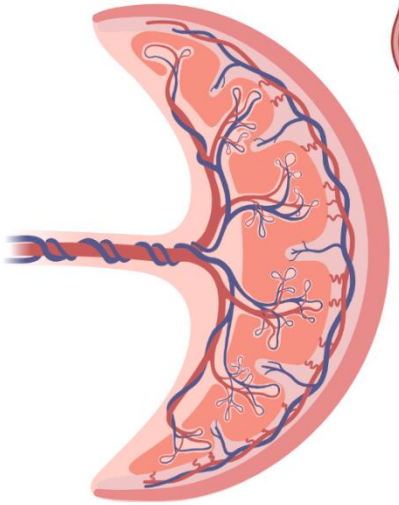


N= 108

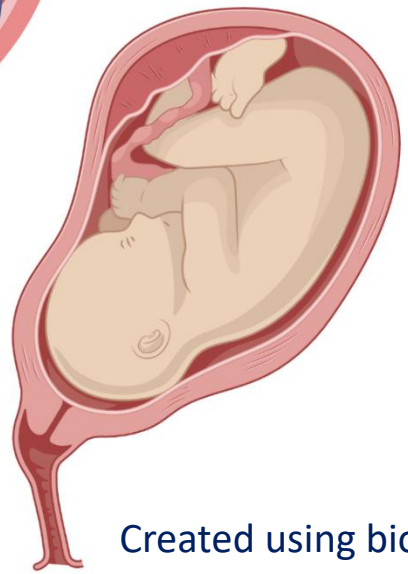


Time in range

CGM users
Lower HbA1c 6.3%
Higher TIR (68% TIRp)



Fingerprick users
More LGA (69%)
More & longer NICU (43%)
More neonatal hypoglycaemia (28%)



CGM users
Fewer LGA (53%)
Fewer shorter NICU (27%)
Less neonatal hypoglycaemia (15%)

Feig DS et al. Lancet 2017

Created using biorender.com

NICE NG3 updated guidance 16th December 2020

Intermittently scanned CGM and continuous glucose monitoring

1.3.17 Offer continuous glucose monitoring (CGM) to all pregnant women with type 1 diabetes to help them meet their pregnancy blood glucose targets and improve neonatal outcomes. **[2020]**

1.3.18 Offer intermittently scanned CGM (isCGM, commonly referred to as flash) to pregnant women with type 1 diabetes who are unable to use continuous glucose monitoring or express a clear preference for it. **[2020]**

1.3.19 Consider continuous glucose monitoring for pregnant women who are on insulin therapy but do not have type 1 diabetes, if:

- they have problematic severe hypoglycaemia (with or without impaired awareness of hypoglycaemia) **or**
- they have unstable blood glucose levels that are causing concern despite efforts to optimise glycaemic control. **[2015, amended 2020]**

1.3.20 For pregnant women who are using isCGM or continuous glucose monitoring, a member of the joint diabetes and antenatal care team with expertise in these systems should provide education and support (including advising women about sources of out-of-hours support). **[2020]**

NATIONAL DIABETES AUDIT

95% of women with **type 1** diabetes wore **continuous glucose monitors** in 2022

95%

NPID Audit data 2023 - Partnership LMS and diabetes networks

Real-world CGM use – N=2055

NATIONAL DIABETES AUDIT

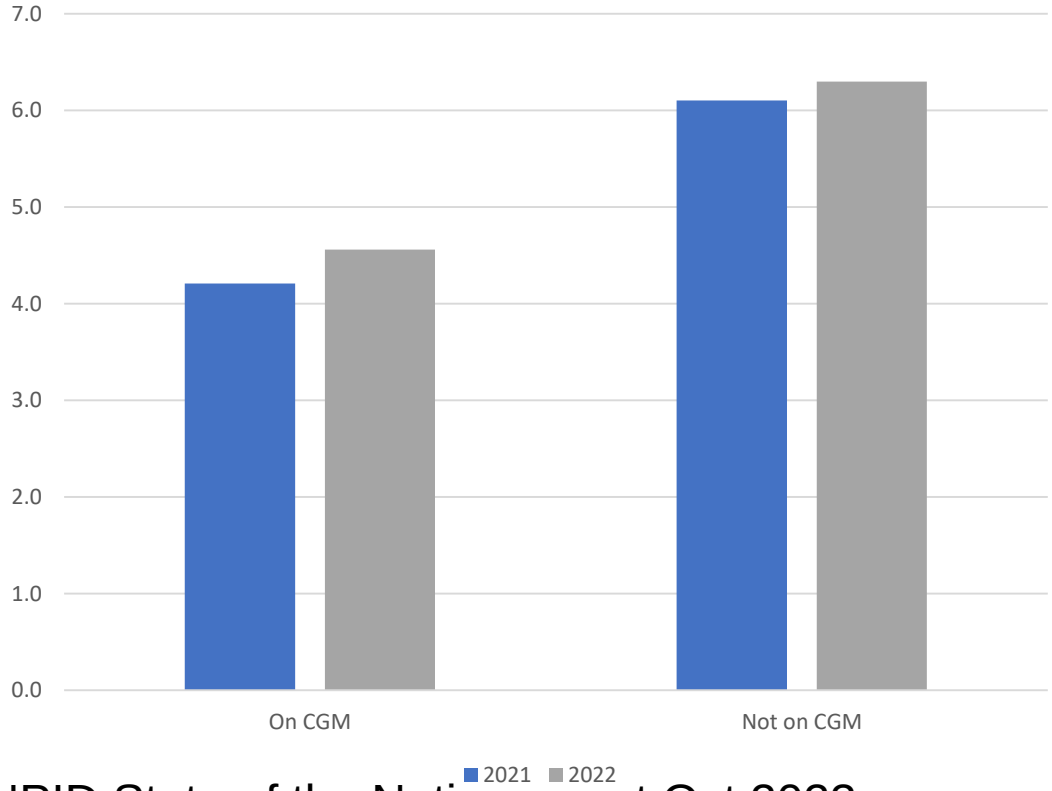
Wearing continuous **glucose montiors** improved:

- **glucose levels** for mothers
- **outcomes** for women and babies

Improved pregnancy glucose levels with:

- ✓ Fewer LGA babies
- ✓ Fewer preterm births
- ✓ Fewer neonatal care admissions

Serious adverse pregnancy outcomes (Birth defects, stillbirth, baby death)

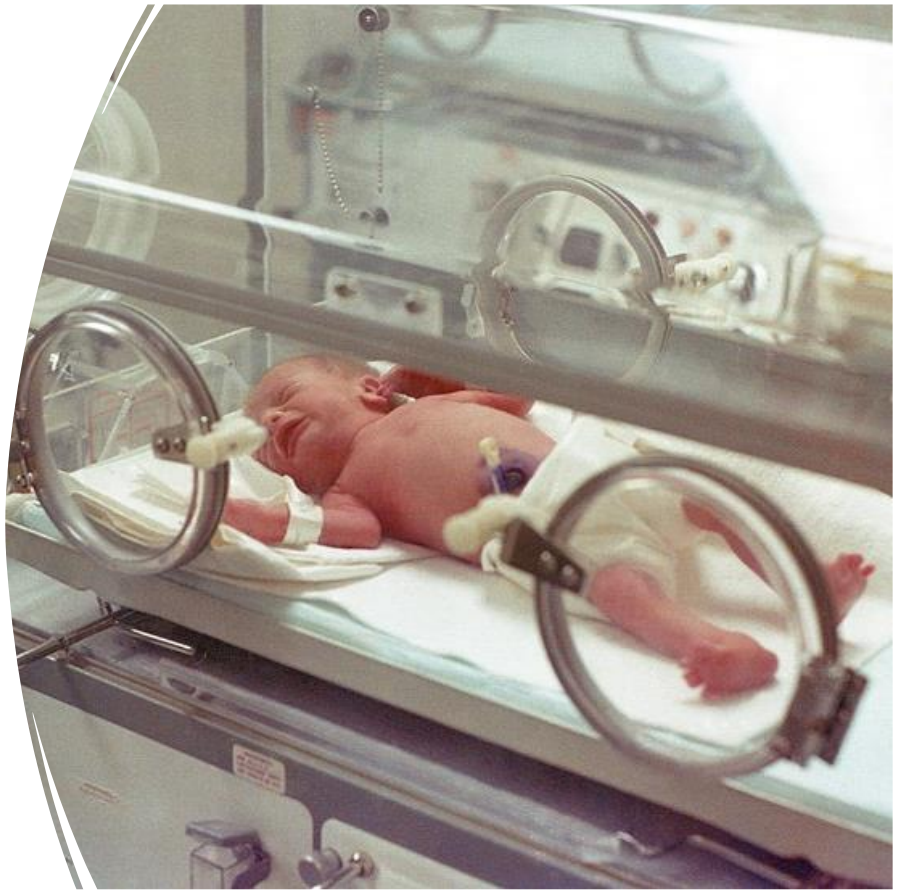


NPID State of the Nation report Oct 2023

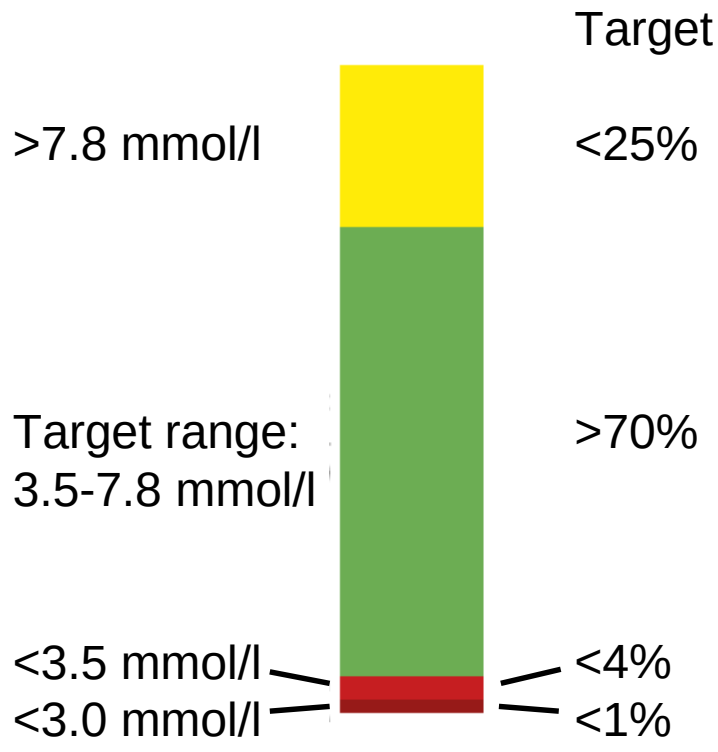
N=2055 (825 in 2021 + 1230 in 2022) CGM users had reduced risk serious adverse outcomes - OR 0.70 95% CI 0.53-0.94; P=0.015

CGM reduces obstetric & neonatal complications

- **Preterm births <37 weeks**: 49 vs 42%
- **Neonatal care admission**: 46 vs 40%
- **Large babies**
- LGA >90th 54 vs 49%
- LGA >97.5th 39 vs 33%



CGM Time in T1D Pregnancy Range



https://abcd.care/dtn/CGM

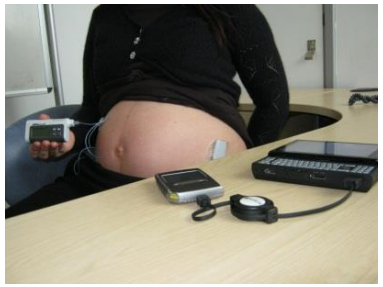
- **Target range 3.5-7.8 mmol/l**
- **Each day aim for:**
  - **> 16 h 48 min in target**
  - **< 6 h above target**
  - **< 1 h < 3.5 mmol/l**
  - **< 15 min < 3.0 mmol/l**

Battelino T et al. *Diabetes Care* 2019;42:1593-1603

Automated insulin Delivery in T1D pregnancy

CLIP-02
Murphy HR et al. (2011)

Crossover RCT
n = 12
24hr closed-loop vs. SAP
2 x 24hr inpatient admissions
Snacks, meals and exercise



CLIP-04
Stewart ZA et al. (2018)

Crossover RCT
n = 16
4 weeks 24hr
HCL vs. SAP
Home setting

Commercialised HCL (2020)

CamAPS Fx
Licensed in pregnancy

CLIP-01
Murphy HR et al. (2011)

Exploratory safety study
n = 10
2 x 24hr inpatient admissions
1st : early pregnancy (12-16 weeks)
2nd : late pregnancy (28-32 weeks)
High carbohydrate meals

CLIP-03
Stewart ZA et al. (2016)

Crossover RCT
n = 16
4 weeks overnight
HCL vs. SAP
Home setting
Optional continuation

Adaptability in labour and delivery
Stewart ZA et al. (2018)

n = 27
Continuation phase of CLIP-03 and CLIP-4 for rest of pregnancy including
home and hospital settings

HCL better glucose control than CGM and Pump

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Closed-Loop Insulin Delivery during Pregnancy in Women with Type 1 Diabetes

Zoe A. Stewart, M.D., Malgorzata E. Wilinska, Ph.D., Sara Hartnell, B.Sc., Rosemary C. Temple, M.D., Gerry Rayman, M.D., Katharine P. Stanley, M.D., David Simmons, M.D., Graham R. Law, Ph.D., Eleanor M. Scott, M.D., Roman Hovorka, Ph.D., and Helen R. Murphy, M.D.

From the Wellcome Trust–Medical Research Council Institute of Metabolic Science, University of Cambridge (Z.A.S., M.E.W., R.H., H.R.M.), and Wolfson Diabetes and Endocrine Clinic, Cambridge University Hospitals NHS Foundation Trust (S.H., D.S., H.R.M.), Cambridge, the Elsie Bertram Diabetes Centre (R.C.T., H.R.M.) and the Department of Obstetrics and Gynaecology (K.P.S.), Norfolk and Norwich University Hospitals NHS Foundation Trust, and the Norwich Medical School, University of East Anglia (H.R.M.), Norwich, the Ipswich Diabetes Centre, Ipswich Hospital NHS Trust, Ipswich (G.R.), and the Division of Epidemiology and Biostatistics, Leeds Institute of Cardiovascular and Metabolic Medicine, University of Leeds, Leeds (G.R.L., E.M.S.) — all in the United Kingdom. Address reprint requests to Dr. Murphy at Norwich Medical School, University of East Anglia, Fl. 2, Bob Champion Research and Education Bldg., Norwich NR4 7UQ, United Kingdom, or at hm386@medschl.cam.ac.uk.

N Engl J Med 2016;375:644-54.
DOI: 10.1056/NEJMoa1602494

ABSTRACT

BACKGROUND
In patients with type 1 diabetes who are not pregnant, closed-loop (automated) insulin delivery can provide better glycemic control than sensor-augmented pump therapy, but data are lacking on the efficacy, safety, and feasibility of closed-loop therapy during pregnancy.

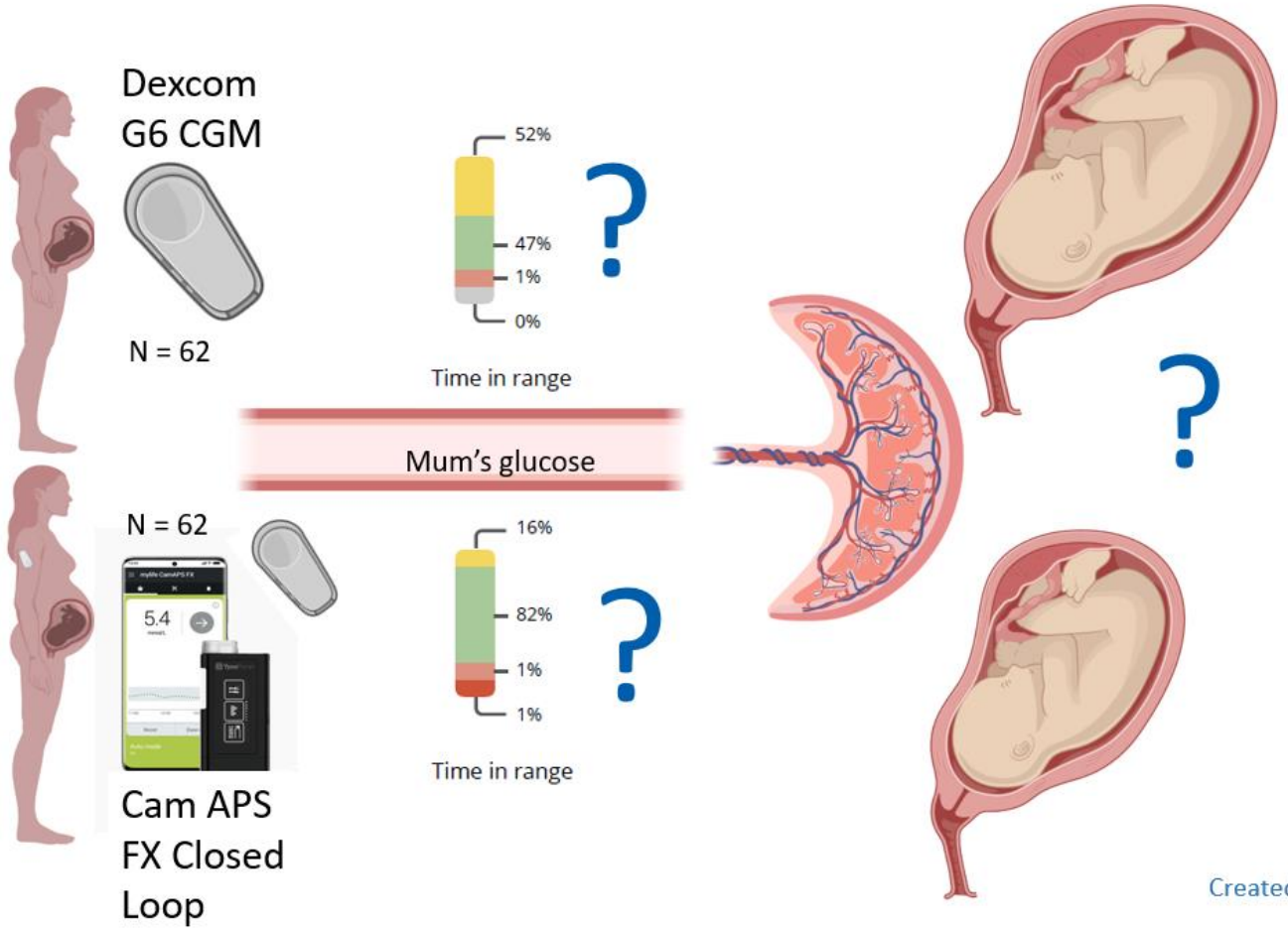
METHODS
We performed an open-label, randomized, crossover study comparing overnight closed-loop therapy with sensor-augmented pump therapy, followed by a continuation phase in which the closed-loop system was used day and night. Sixteen pregnant women with type 1 diabetes completed 4 weeks of closed-loop pump therapy (intervention) and sensor-augmented pump therapy (control) in random order. During the continuation phase, 14 of the participants used the closed-loop system day and night until delivery. The primary outcome was the percentage of time that overnight glucose levels were within the target range (63 to 140 mg per deciliter [3.5 to 7.8 mmol per liter]).

RESULTS
The percentage of time that overnight glucose levels were in the target range was higher during closed-loop therapy than during control therapy (74.7% vs. 59.5%; absolute difference, 15.2 percentage points; 95% confidence interval, 6.1 to 24.2; P=0.002). The overnight mean glucose level was lower during closed-loop therapy than during control therapy (119 vs. 133 mg per deciliter [6.6 vs. 7.4 mmol per liter], P=0.009). There were no significant differences between closed-loop and control therapy in the percentage of time in which glucose levels were below the target range (1.3% and 1.9%, respectively; P=0.28), in insulin doses, or in adverse-event rates. During the continuation phase (up to 14.6 additional weeks, including antenatal hospitalizations, labor, and delivery), glucose levels were in the target range 68.7% of the time; the mean glucose level was 126 mg per deciliter (7.0 mmol per liter). No episodes of severe hypoglycemia requiring third-party assistance occurred during either phase.

CONCLUSIONS
Overnight closed-loop therapy resulted in better glucose control than sensor-augmented pump therapy in pregnant women with type 1 diabetes. Women receiving day-and-night closed-loop therapy maintained glycemic control during a high proportion of the time in a period that encompassed antenatal hospital admission, labor, and delivery. (Funded by the National Institute for Health Research and others; Current Controlled Trials number, ISRCTN71510001.)

Stewart Z et al. NEJM 2016; 375: 644-654

Automated Insulin Delivery Amongst Pregnant women with Type 1 diabetes



Maternal glucose (time in range)

Neonatal outcomes (NICU, LGA)

Qualitative data outcomes

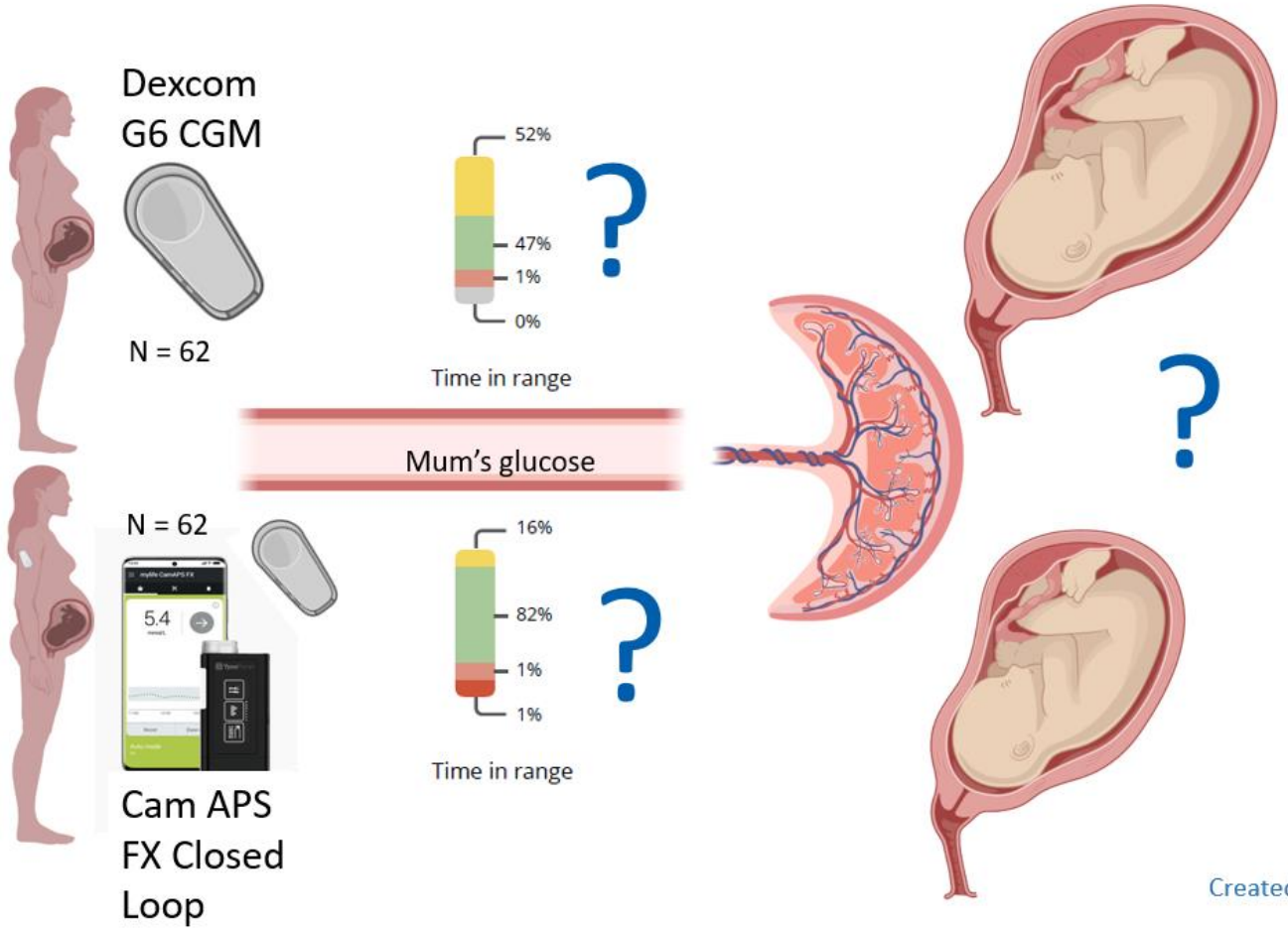
Health economic outcomes

Data informed NICE TA

Lee T et al N Engl J Med 2023; 389:1566-1578

NIHR | National Institute for Health Research

Automated Insulin Delivery Amongst Pregnant women with Type 1 diabetes



Maternal glucose (time in range)

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Health economic outcomes

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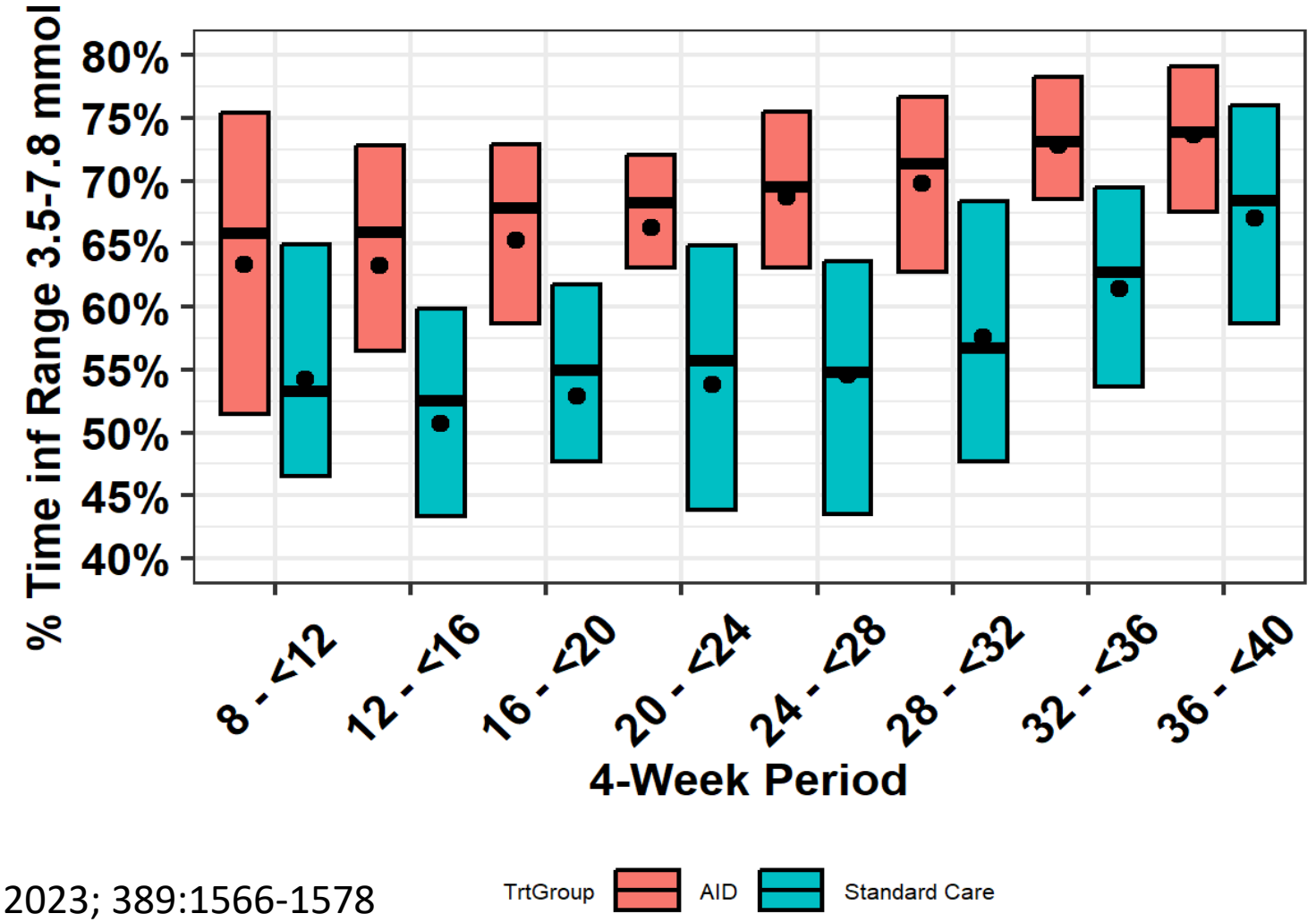
Lee T et al N Engl J Med 2023; 389:1566-1578

NIHR | National Institute for Health Research

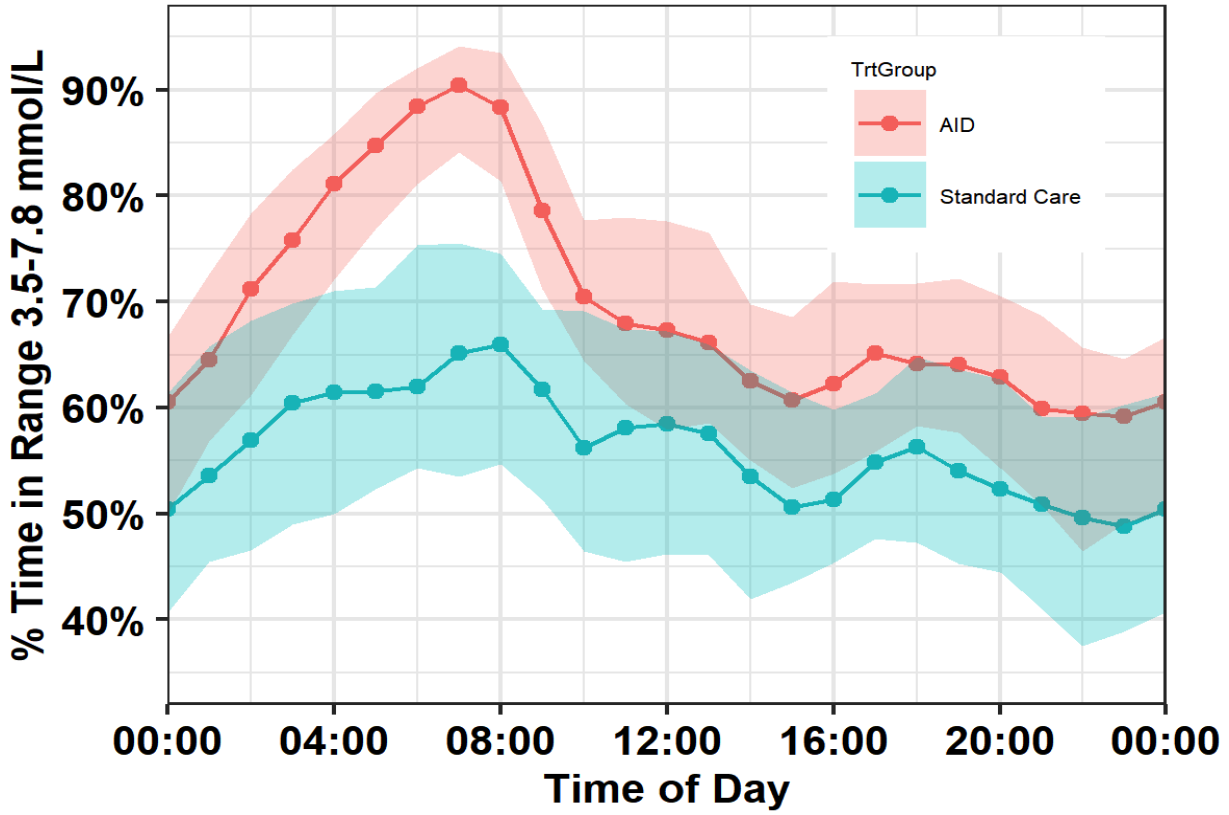
HCL significantly improved time spent in glucose range from early pregnancy



Lee T et al N Engl J Med 2023; 389:1566-1578

AiDAPT

HCL significantly improved time spent in pregnancy target glucose range across 24-hr day, esp. overnight



Lee T et al N Engl J Med 2023; 389:1566-1578

AiDAPT

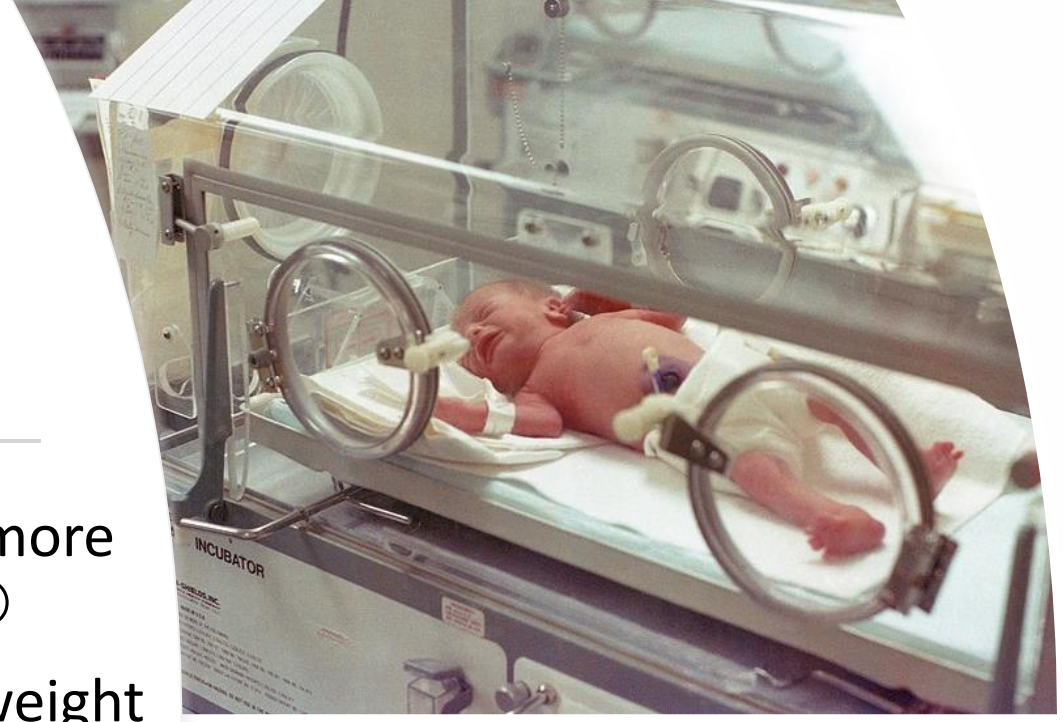
Additional Benefits…..

Less worry, less work, more enjoyable pregnancy ☺

3.7kg less gestational weight gain

Less gestational hypertension

Low rates of LGA/NICU



AiDAPT

Results Summary

- CGM alone (and/or with insulin pump therapy) inadequate for optimal glycaemia
- CamAPS FX associated with 10.5 percentage point increase TIRp in a broadly representative patient population
  - Consistent across maternal HbA1c categories, insulin delivery methods & sites
  - Consistent throughout pregnancy, from first trimester
  - Pregnancy experience (less worry, less work, more enjoyable pregnancy)
  - 3.5kg less gestational weight gain/less gestational hypertension
  - Lowest rates of LGA/NICU admission in representative T1D pregnant population
- HCL (specifically CamAPS FX) should be offered to all pregnant women with T1D

AiDAPT

Hybrid Closed Loop (HCL) recommended for women with Type 1 diabetes who are pregnant or planning

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

In development [GID-TA10845] Expected publication date: TBC Register as a stakeholder

NICE RECOMMENDS LIFE CHANGING TECHNOLOGY IS ROLLED OUT TO PEOPLE WITH TYPE 1 DIABETES

PRESS RELEASE
NICE recommends life changing technology is rolled out to people with type 1 diabetes
An announcement of the recommendations was made today (Tuesday 7 November) at NICE's annual conference in Manchester by NICE chief executive Dr Sam Roberts

Thousands of people with type 1 diabetes could be offered wearable technology to help them manage their condition following the publication of final draft guidance by NICE.

An independent NICE committee has recommended people whose diabetes is not controlled with their current device despite best possible management with an insulin pump, or real-time or intermittently scanned continuous glucose monitoring, are offered a hybrid closed loop system.

ABOUT THE RECOMMENDATIONS

1. Hybrid closed loop systems are recommended as an option for managing blood glucose levels in type 1 diabetes for adults who have an HbA1c of 58 mmol/mol (7.5%) or more, or have disabling hypoglycaemia, despite best possible management with at least 1 of the following:
- continuous subcutaneous insulin infusion (CSII)
  - real-time continuous glucose monitoring
  - intermittently scanned continuous glucose monitoring.

2. Hybrid closed loop systems are recommended as an option for managing blood glucose levels in type 1 diabetes for children and young people.

3. Hybrid closed loop systems are recommended as an option for managing blood glucose levels in type 1 diabetes for people who are pregnant or planning a pregnancy.

07 November 2023

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Automated Insulin Delivery in Women with Pregnancy Complicated by Type 1 Diabetes

Tara T.M. Lee, M.B., B.S., Corinne Collett, B.Sc., Simon Bergford, M.S., Sara Hartnell, B.Sc., Eleanor M. Scott, M.D., Robert S. Lindsay, Ph.D., Katharine F. Hunt, M.D., David R. McCance, M.D., Katharine Barnard-Kelly, Ph.D., David Rankin, Ph.D., Julia Lawton, Ph.D., Rebecca M. Reynolds, Ph.D., Emma Flanagan, Ph.D, Matthew Hammond, M.Sc., Lee Shepstone, Ph.D., Malgorzata E. Wilinska, Ph.D., Judy Sibayan, M.P.H., Craig Kollman, Ph.D., Roy Beck, Ph.D., Roman Hovorka, Ph.D., and Helen R. Murphy, M.D., for the AiDAPT Collaborative Group*

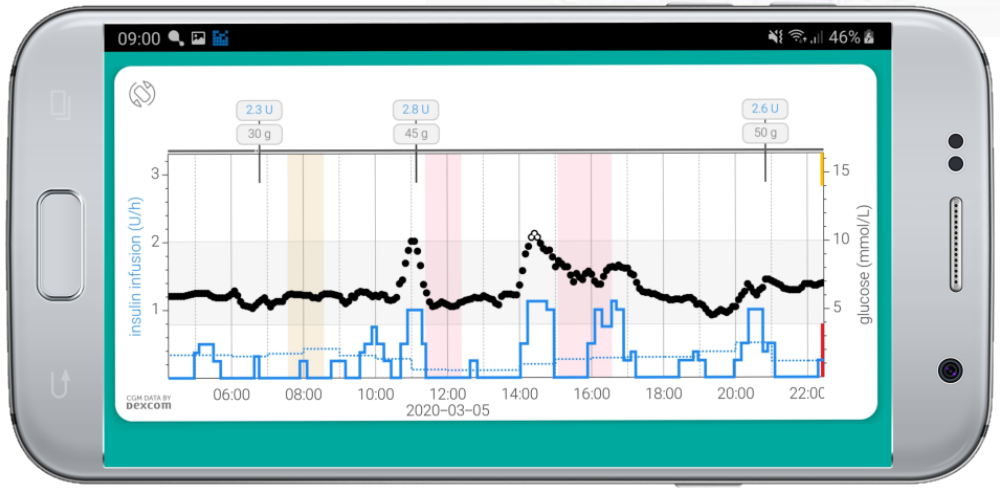
Lee T et al N Engl J Med 2023; 389:1566-1578

How does CamAPS FX work?

Modulates basal insulin delivery by:

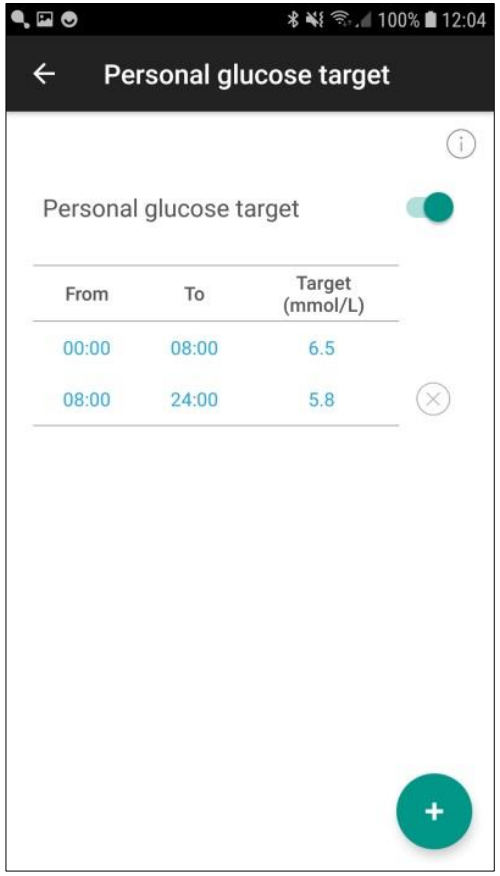
- Adjusting insulin every 8-12 minutes

- Causes for no delivery (occlusion, low reservoir) will result in pump alarm / vibrate
- **Hybrid closed-loop → still requires insulin boluses for carbohydrates**



Personal glucose target – customisable for pregnancy

Algorithm target (default 5.8 mmol/L) adjustable at different times of day & night

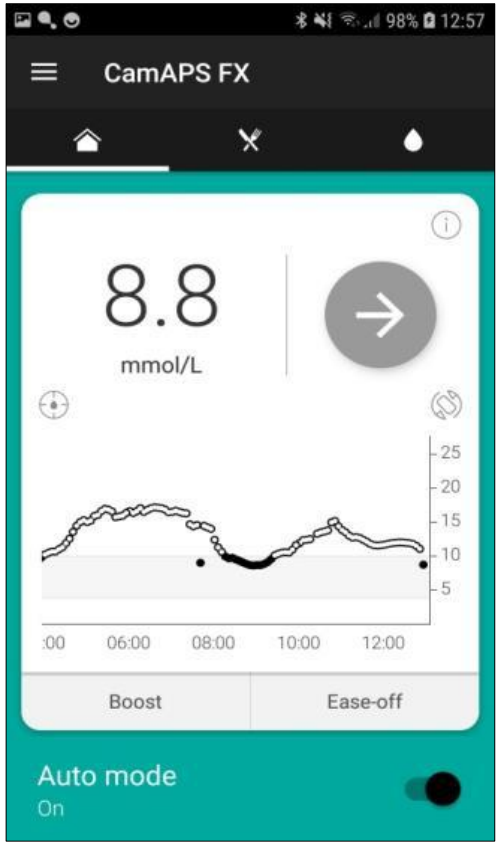


Suggested targets in T1D pregnancy:

- 1st trimester: 5.5 mmol/L
- 2nd trimester (or earlier if hypo risk low): 4.5-5.0 mmol/L

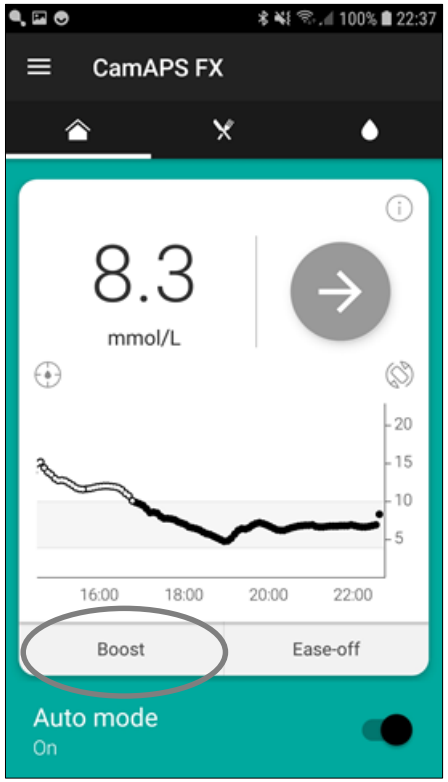
Treat to target:

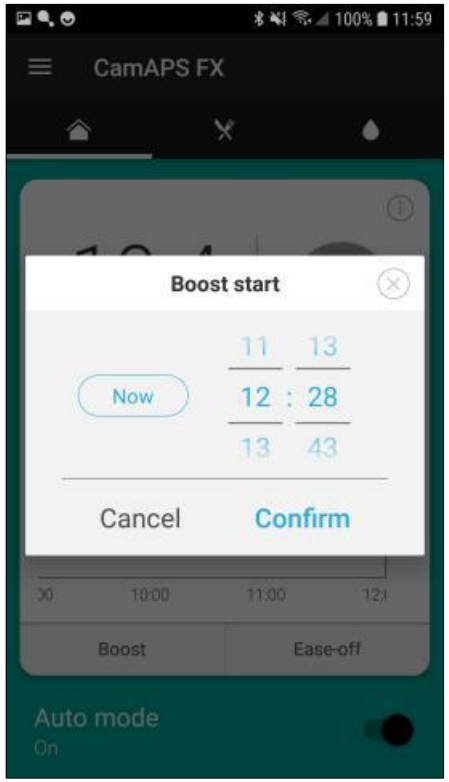
- TIR (3.5-7.8 mmol/L): 70%
- mean glucose: 6.0-6.5 mmol/L

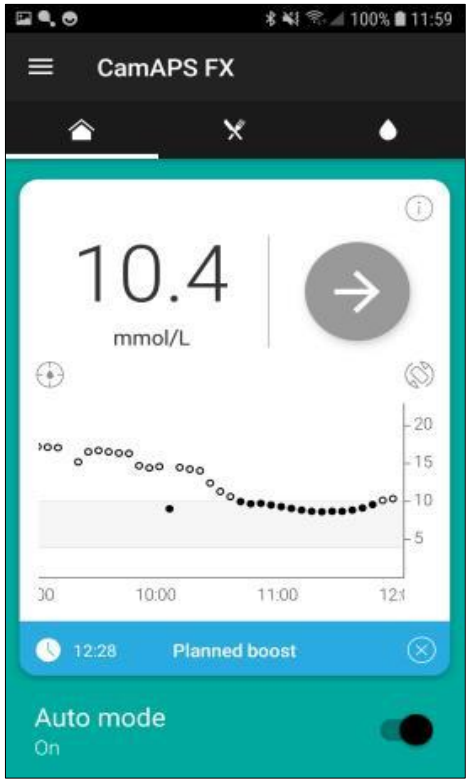


Boost

- Increases basal insulin delivery by ~35%
- Once glucose reaches target, boost **will not** continue to increase insulin delivery





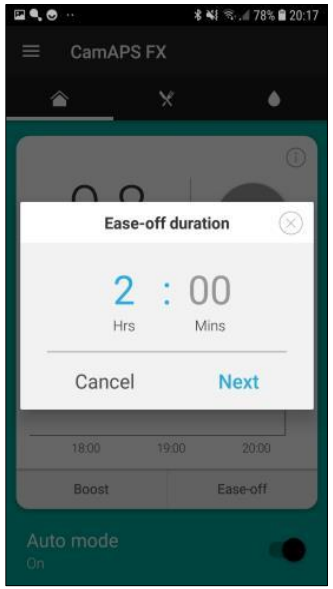


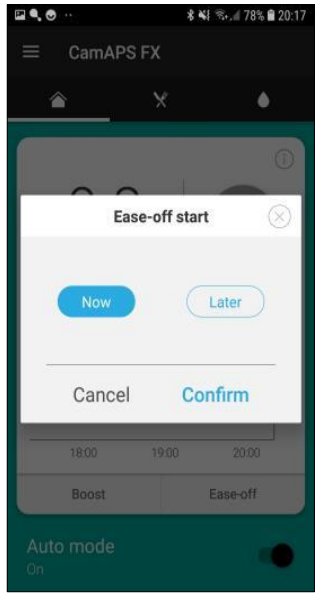
When to use Boost?

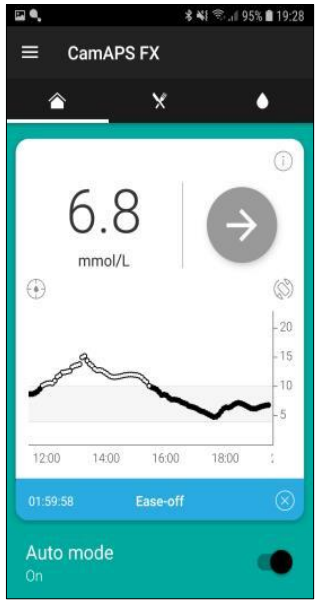
- Post prandial hyperglycaemia
- Antenatal steroids
- Low grade illness (not requiring sick day rules)

Ease-Off

- Tries to prevent glucose falling below 6.1mmol
- Raises glucose target temporarily by 2.5mmol
- Insulin delivery stops if glucose < 7 mmol/L







When to use Ease Off?

- Before, during and/or after exercise/activity
- Following hypoglycaemia
- Labour/birth/post-partum

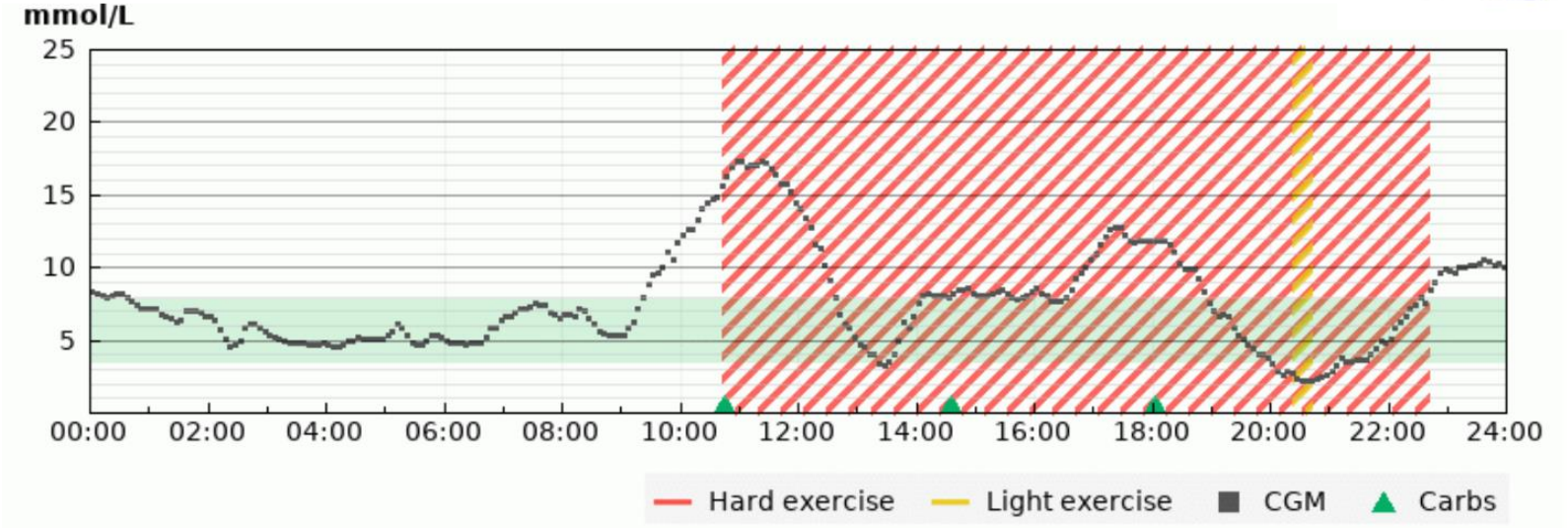
Meals and Pre-bolusing

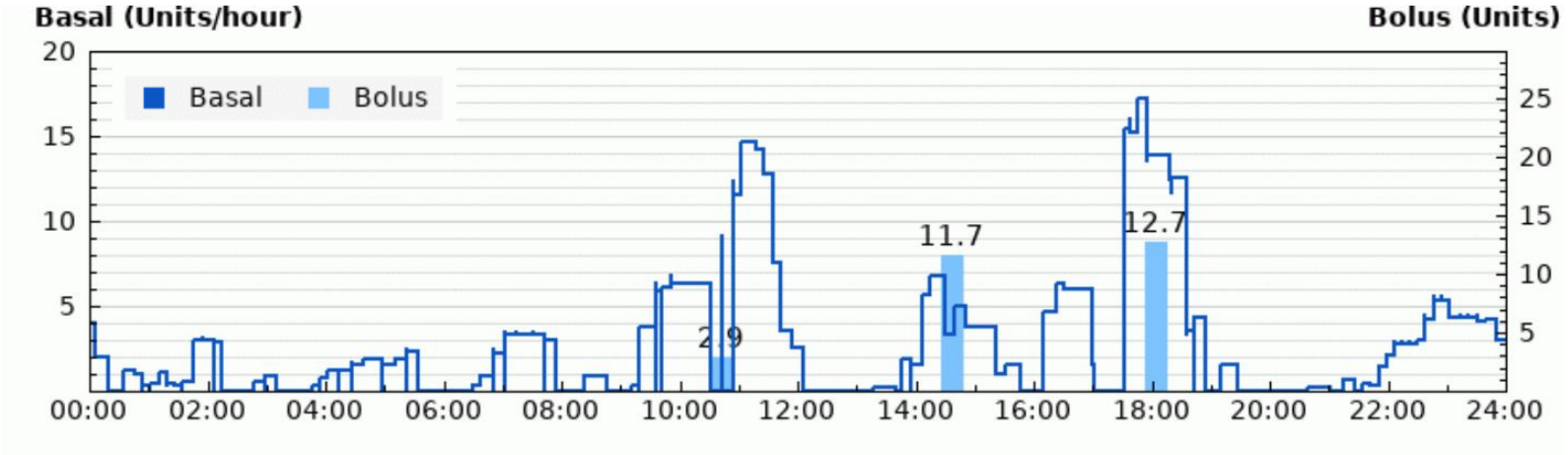
Strengthen insulin-carbohydrate ratios

To keep up with increasing insulin resistance

Mismatch of insulin and carbohydrates

- Exaggerated glucose peak (unannounced)
- Delayed insulin peak
- Insulin stacking
- Uncontrolled drop in BG and likely hypoglycaemia





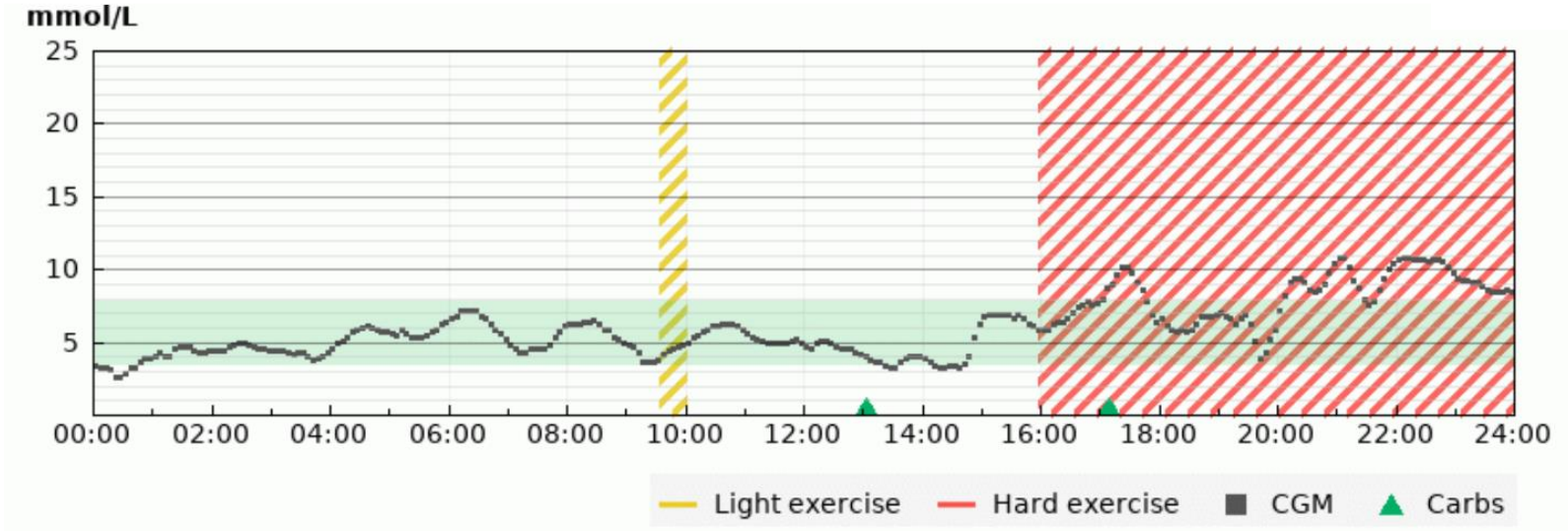
Meals and Pre-bolusing

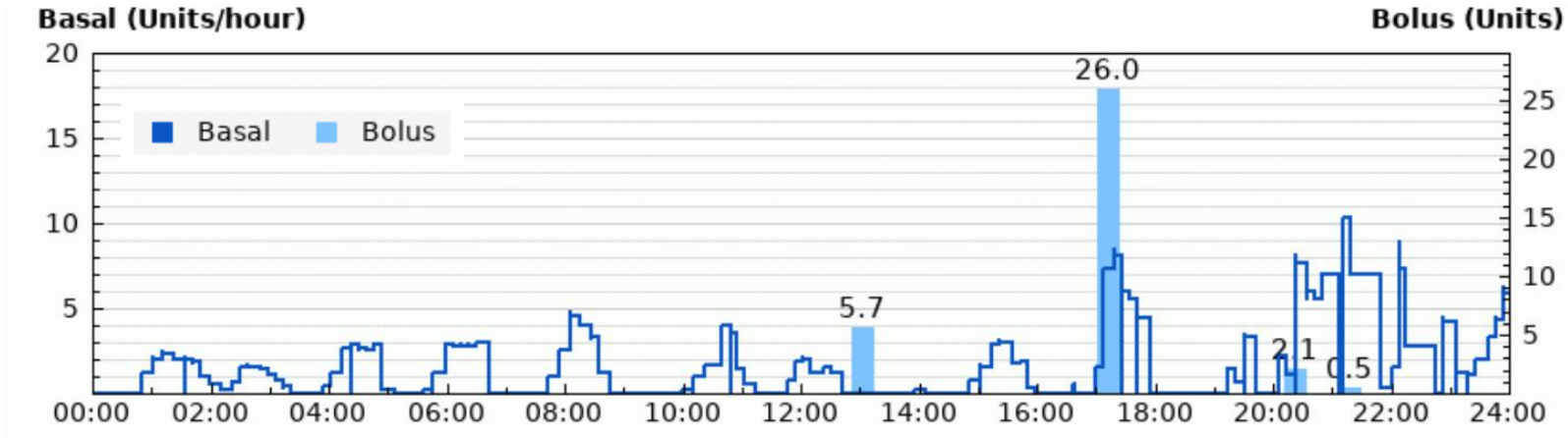
Suggested bolus interval

First trimester:
10-15mins

Second trimester:
20-30mins

Third trimester:
45-60mins





Supporting optimal HCL use?

Starting off → **Optimisation during pregnancy** → Intrapartum and Delivery → Postnatal

- Personal glucose targets
- Meals:
  - Pre-bolus interval
  - Insulin-carbohydrate ratios
- Use of boost and ease-off
- Set changes/check basal rates

Tips and settings for labour

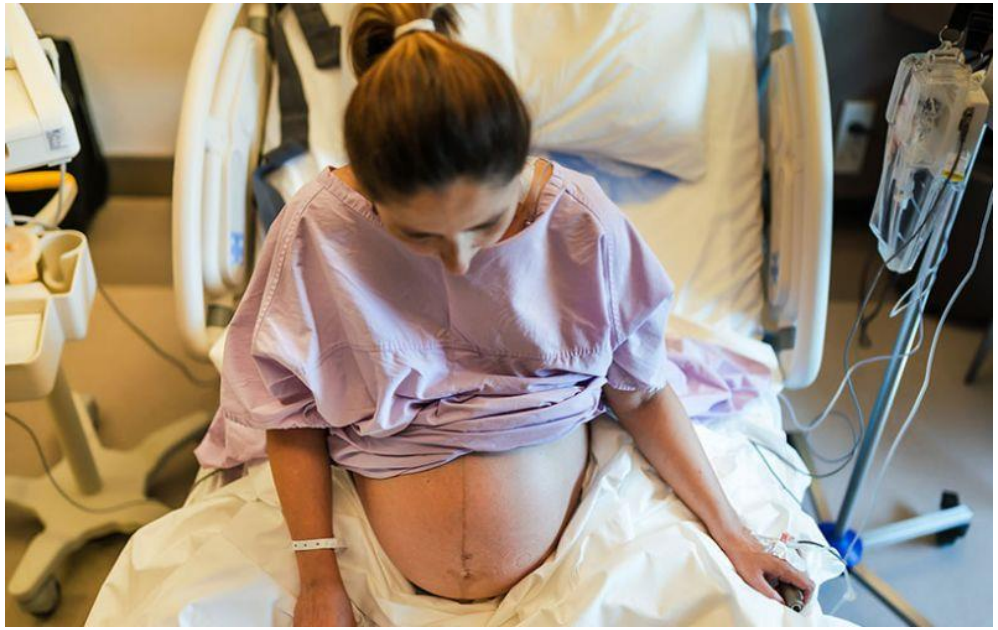


Image: labourpains.org (OAA public information)

Challenges

- Unpredictable
- May not be eating (if on IV oxytocin)
- Varying targets (4-7mmol/mol OR 5-8mmol/mol)
- Maternal steroid administration

Guidance for labour

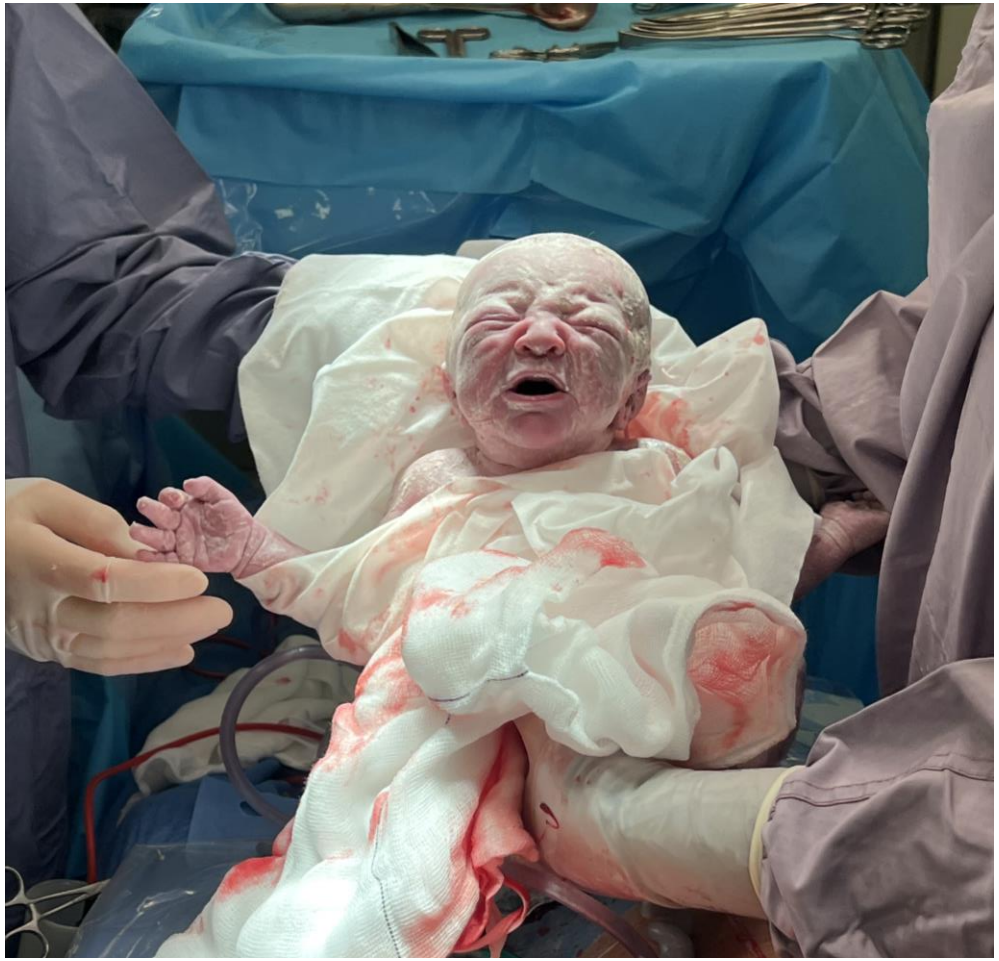
Continue automode

Continue existing PGT programme

Use of boost / ease off

Encourage to use CGM data to guide intake

Tips and settings for caesarean section



Challenges and considerations

- Placement of sensor and pump cannula
- Period of time NBM
- Varying targets (4-7mmol/mol OR 5-8mmol/mol)

Guidance

- Continue automode
- Switch to postnatal settings in anaesthetic room prior
- Use of ease off / boost to further modulate

Tips and immediate postnatal settings

Image: kieferpix/Getty Images

Guidance

- PGT -> 6.0
- Target range (3.9 – 10.0mmol/mol)
- ICR 1:12g or 1:15g
- Adjust basal rates
  (in case out of auto mode)
  - 1/2 end of pregnancy TDD
  - Pre-pregnancy rates

Take home messages

- ✓Use of CamAPS FX HCL improves maternal glucose levels type 1 diabetes pregnancy
- ✓Offer CamAPS FX HCL to all pregnant women T1D
- ✓Rapid optimisation 2-4 days (PGT/CIR)
- ✓Aim for 70% TIRp but every 5% TIR matters
- ✓Post-natal use…..


My super expensive sensor
My state of the art closed loop pump
Me forgetting to bolus for a meal