



Right Technology, Right Person, Right Timing: pregnancy, technology and type 1 diabetes

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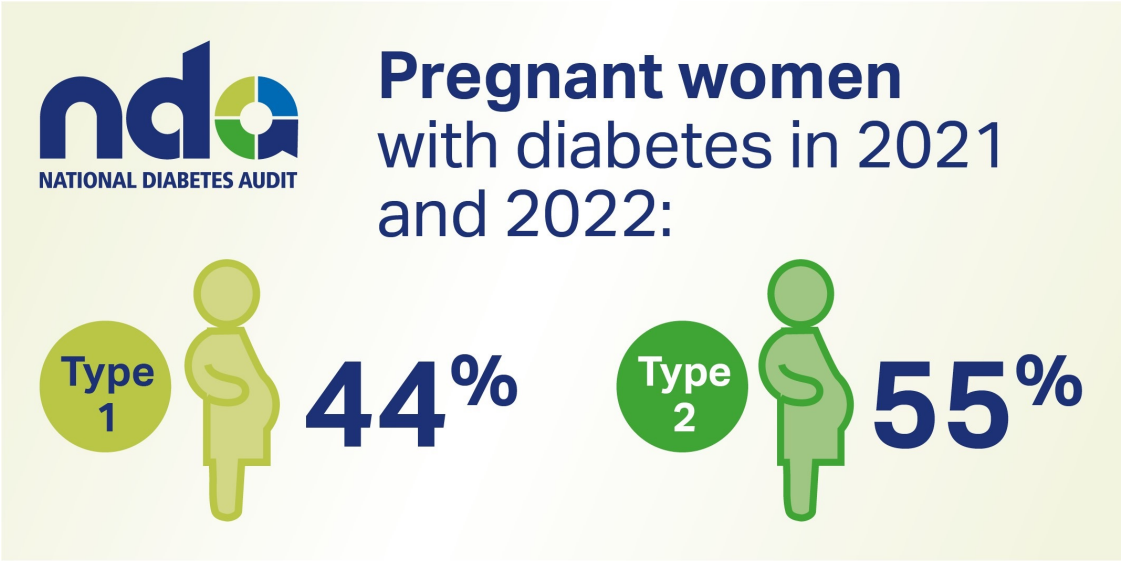
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A close-up photograph of a pregnant woman's belly, which is the central focus of the image. Her hands are gently cupping and holding her belly from the sides. She is wearing a dark-colored top. The background is a plain, light color.

What this session covers

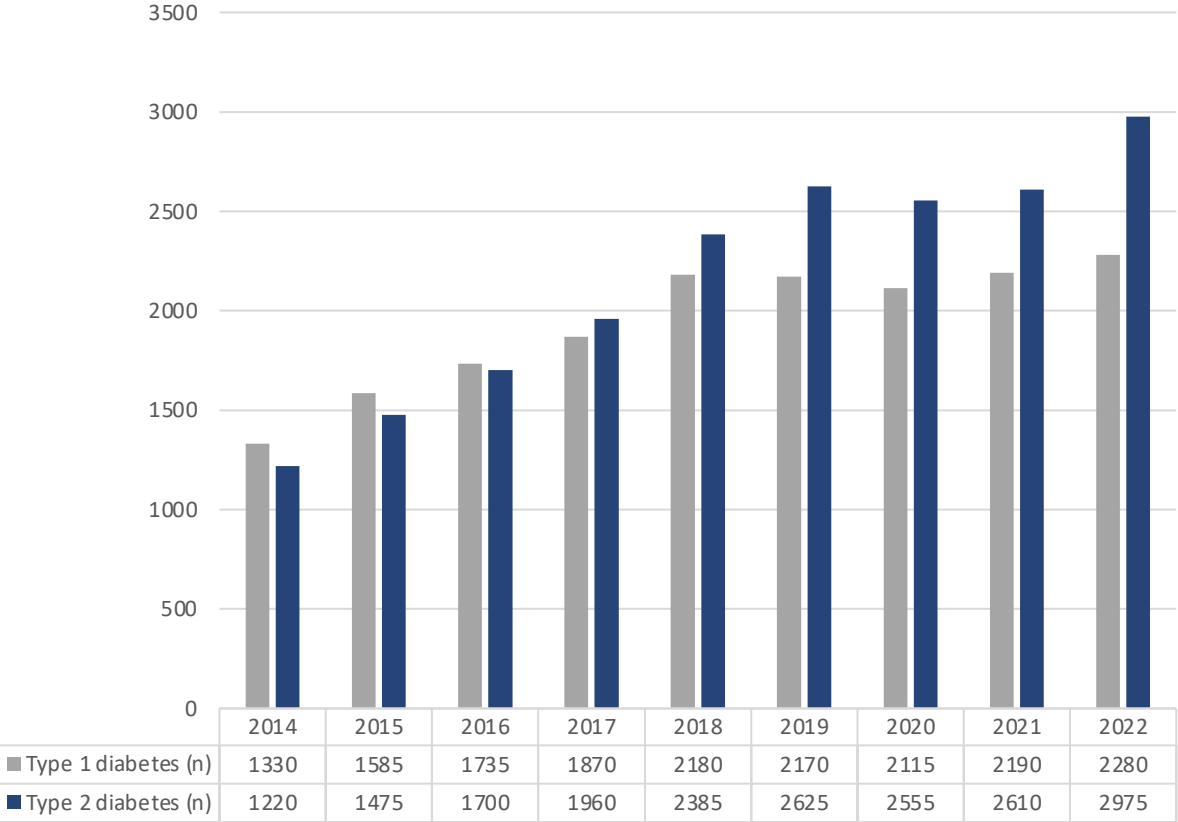
- ✓ Pregnancy Outcomes: National Pregnancy in Diabetes (NPID) data
- ✓ Evidence for using CGM in pregnancy
- ✓ Evidence for HCL including AiDAPT RCT
- ✓ Tips for real-world HCL implementation

NPID 34,770 pregnancies: 15,265 T1D & 19,505 T2D



N= 4,290 T1D and N= 5,415 EOT2D

Prevalence (n) of type 1 and type 2 diabetes in England and Wales



What is a successful pregnancy outcome?



- Live mother & baby - no stillbirth/neonatal death (98.8% vs 99.6%)
- No congenital anomaly
- Uncomplicated delivery
- Baby normal size (<90th centile)
- No neonatal hypoglycaemia, jaundice, respiratory distress
- No neonatal intensive care unit (NICU)

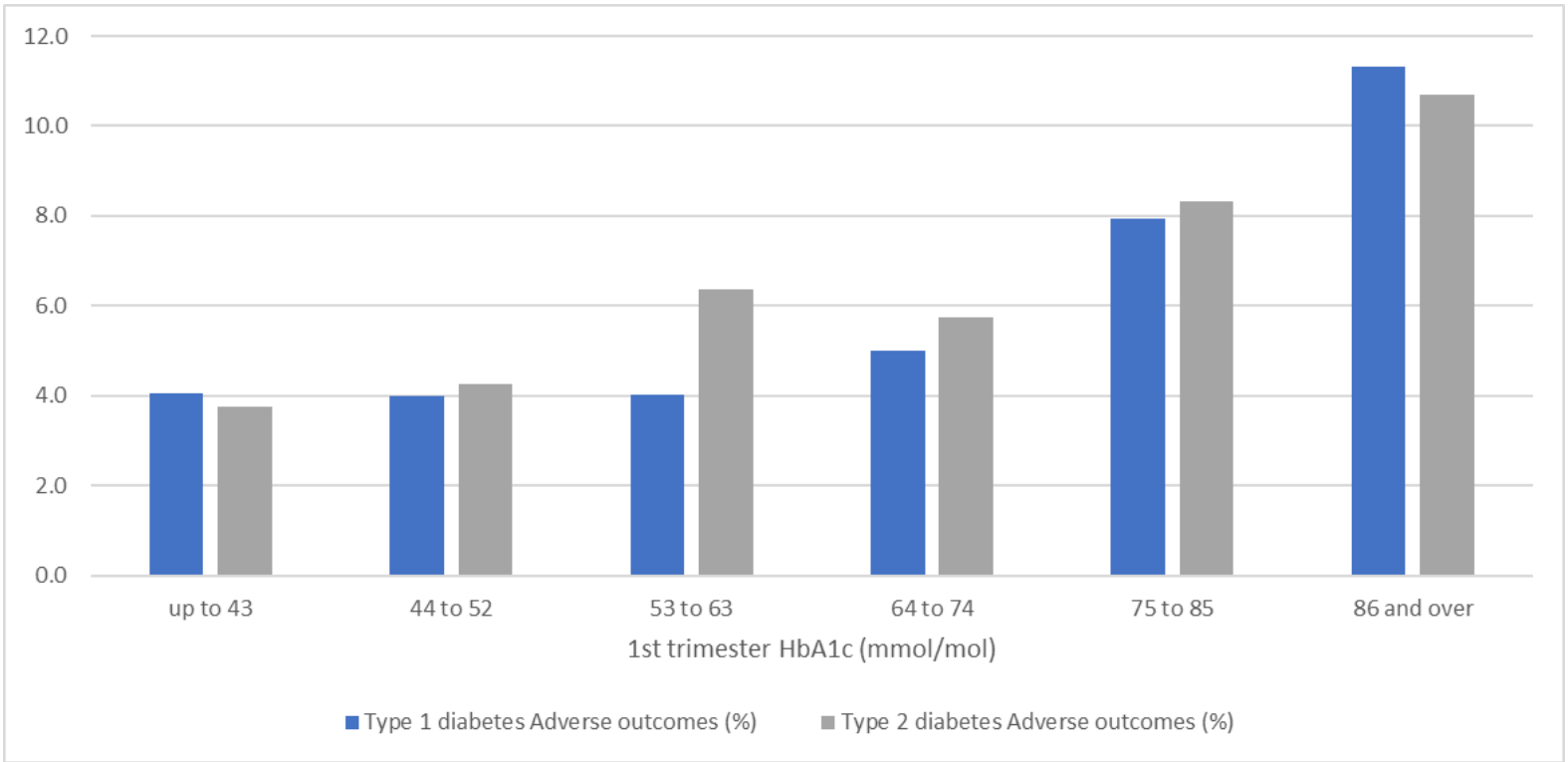
Effective Communication About Pregnancy, Birth, Lactation, Breastfeeding and Newborn Care: The Importance of Sexed Language

Gribble KD et al, Front Glob Womens Health. 2022 Feb 7;3:818856.

<https://www.frontiersin.org/articles/10.3389/fgwh.2022.818856/full>

Early pregnancy HbA1c

Serious adverse outcomes

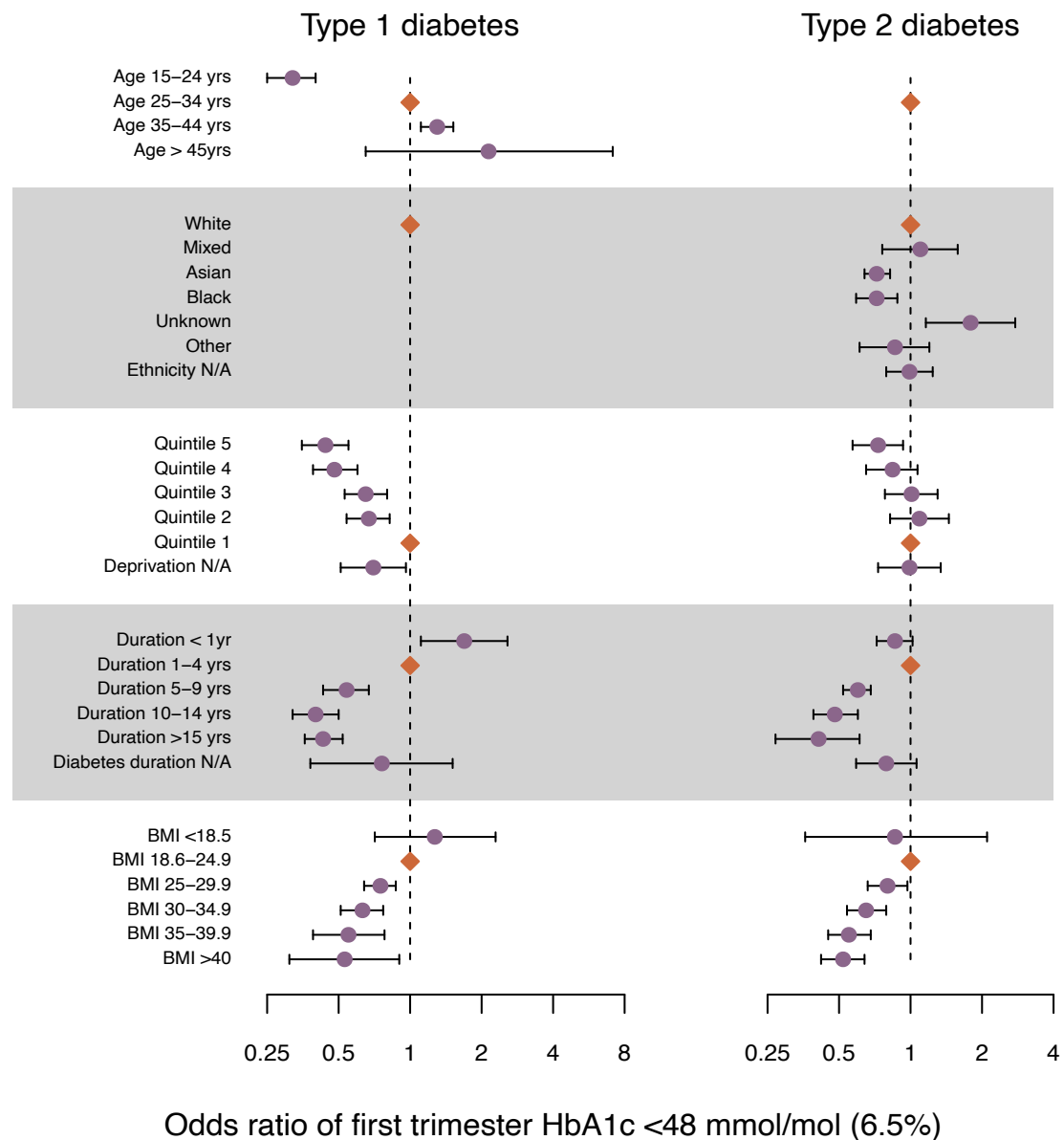


Risks and complications



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.

HbA1c depends (almost entirely) on patient characteristics



Complications are common & increasing 2014- 20

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**

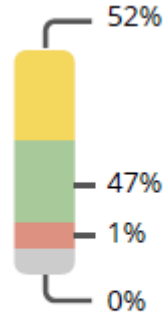
1 in 3 babies of mums with **T2D**



CGM helps in T1D pregnancy (CONCEPTT)



N= 107

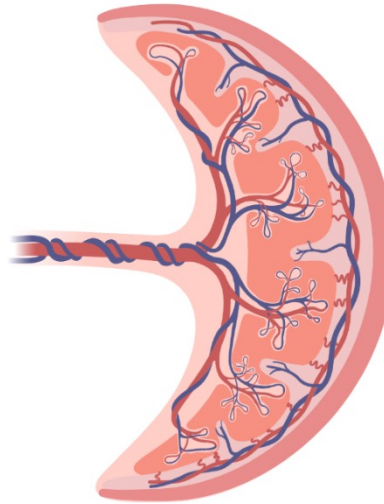


Time in range

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



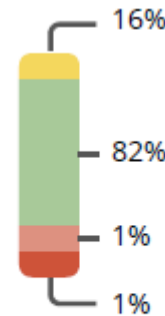
Mum's glucose



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

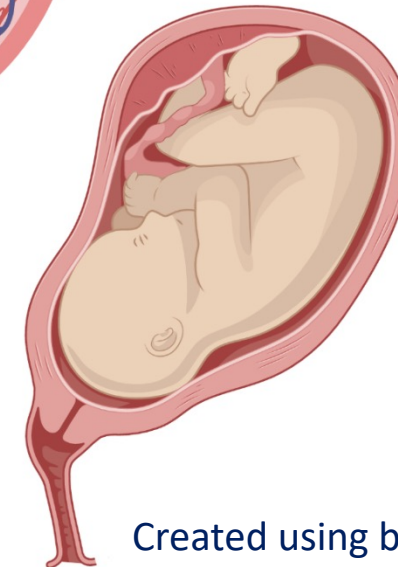


N= 108



Time in range

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



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

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]



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



95%

Real-world CGM use – N=2055



Wearing continuous **glucose monitors** improved:

 **glucose levels** for mothers

 **outcomes** for women and babies



Improved pregnancy glucose levels with:

✓ Fewer LGA babies

LGA >90th 54 vs 49%

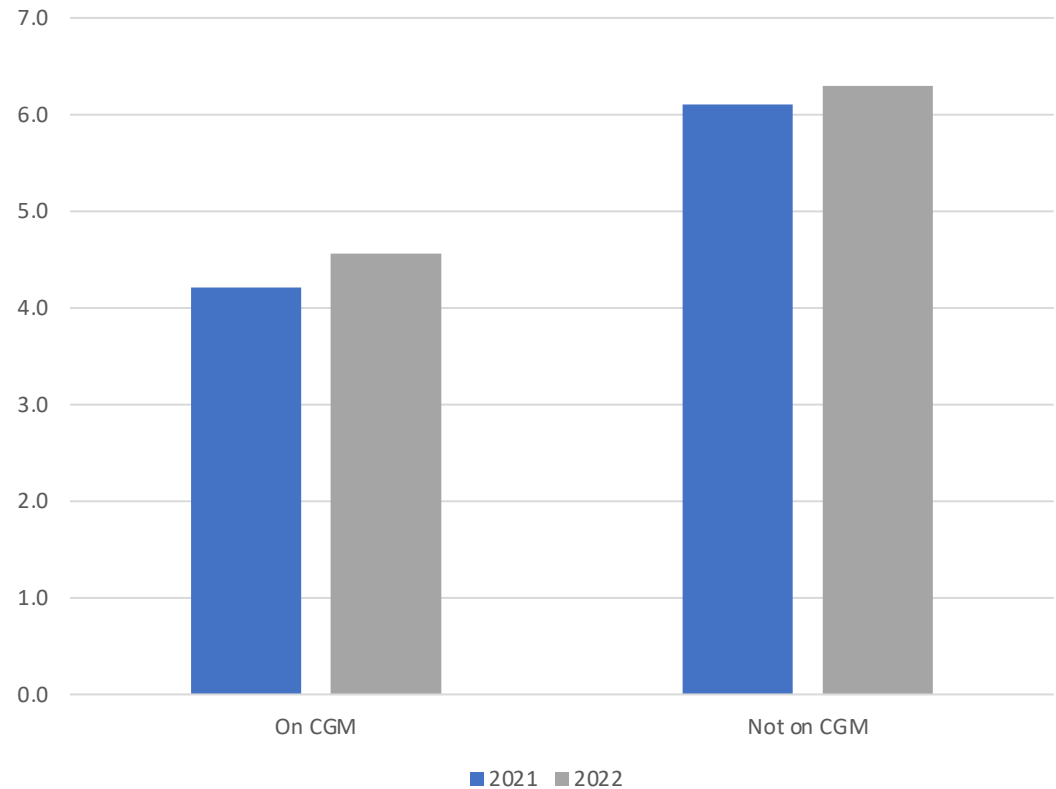
✓ Fewer preterm births

49 vs 42%

✓ Fewer neonatal care admissions

46 vs 40%

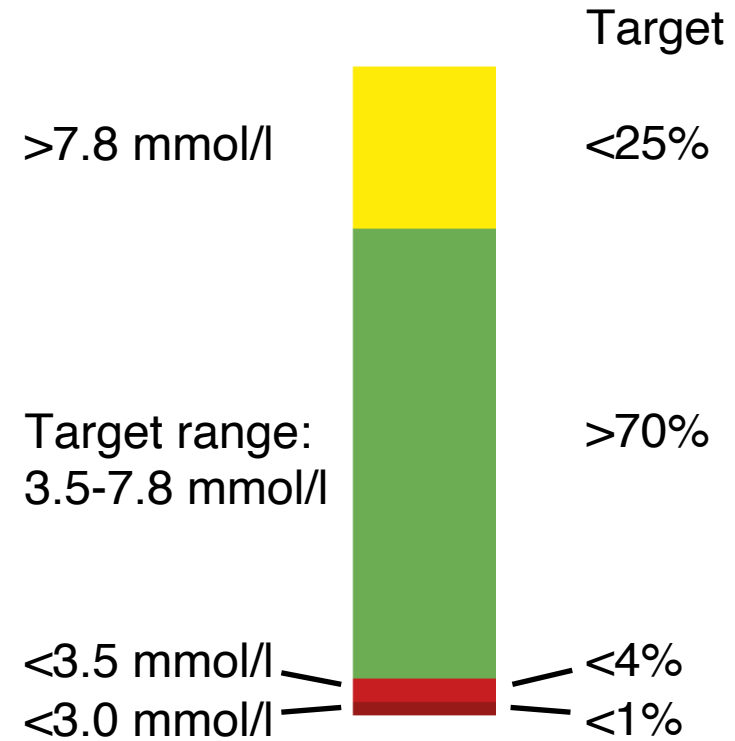
Serious adverse pregnancy outcomes (Birth defects, stillbirth, baby death)



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 Time in T1D Pregnancy Range (TIRp)



Challenges to managing diabetes in pregnancy

Tighter pregnancy targets

Aiming HbA1c <43 by 3rd trimester

Changing insulin resistance and sensitivity

Increased day to day variability

Fear of hyperglycaemia and effect on baby

Huge mental burden of self-management

Gestation	What to expect?
4-8 weeks	Very labile glucose levels
8-16 weeks	Increased hypos and insulin sensitivity
16 weeks +	Increasing insulin resistance – often every few days
Late 3 rd trimester	Slight increase in insulin sensitivity
Straight after delivery	Rapid decrease in insulin requirements Transient 'insulin holiday'

Dahlberg & Berg,
Int J Qual Stud Health Well-being 2020
The lived experiences of healthcare during pregnancy, birth, and three months after in women with type 1 diabetes mellitus

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)

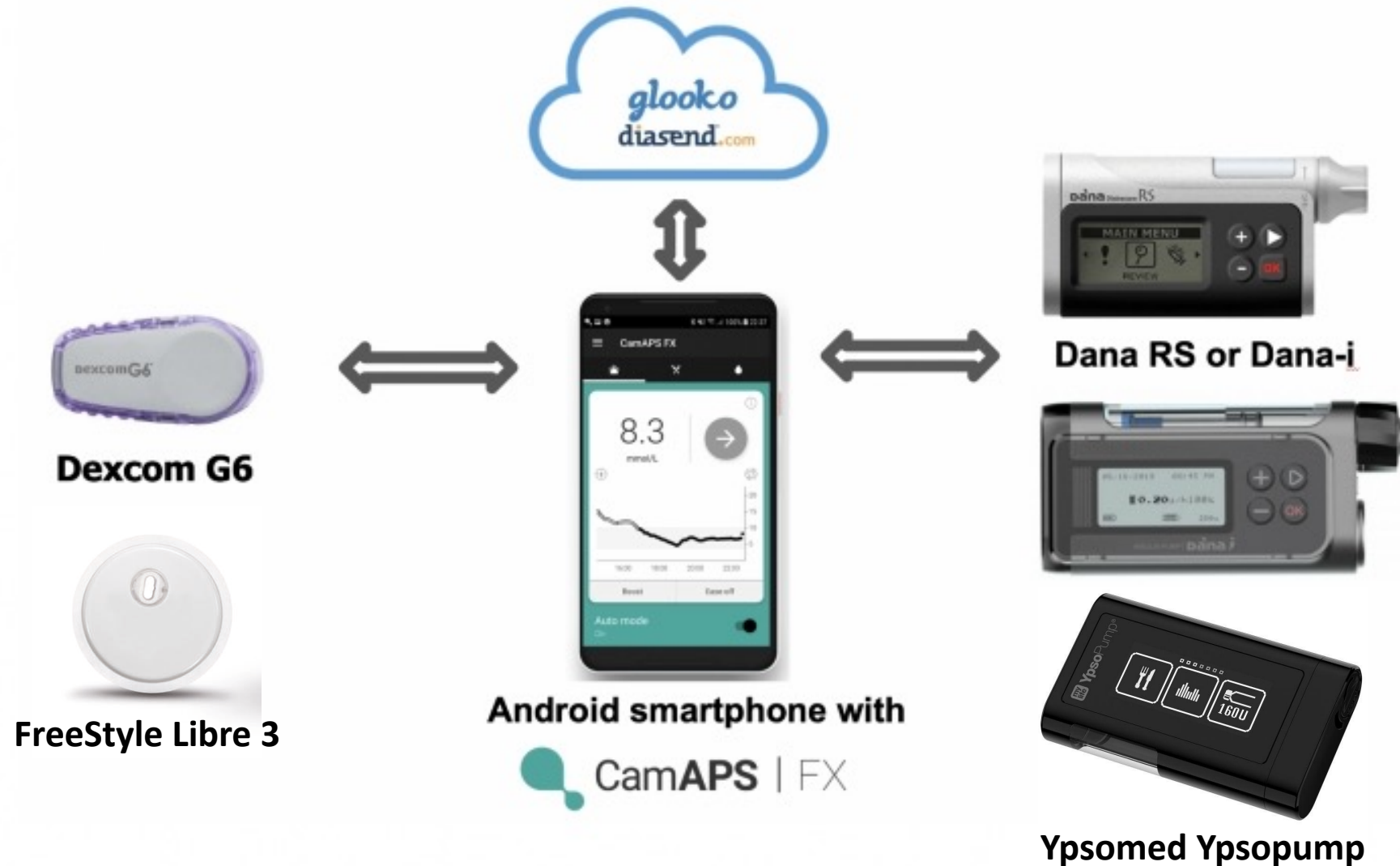
Crossover RCT
n = 16
4 weeks overnight
HCL vs. SAP
Home setting
Optional continuation

**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

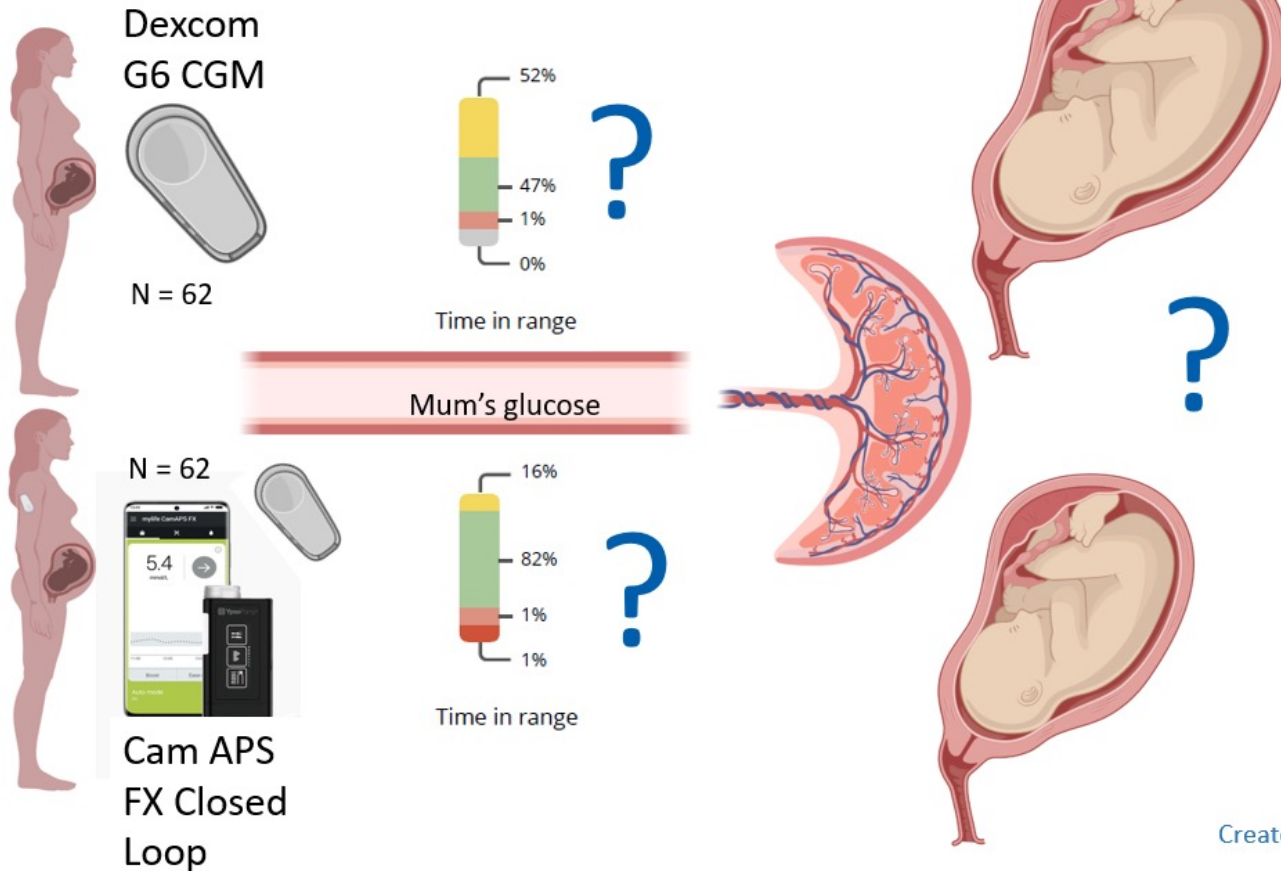


CamAPS FX (CamDiab)





Automated Insulin Delivery Amongst Pregnant women with Type 1 diabetes



Maternal glucose (TiRp)

Qualitative data

Neonatal outcomes (NICU, LGA)

Health economic data

Created with biorender.com

% Time in the Pregnancy range (3.5 – 7.8mmol/L)

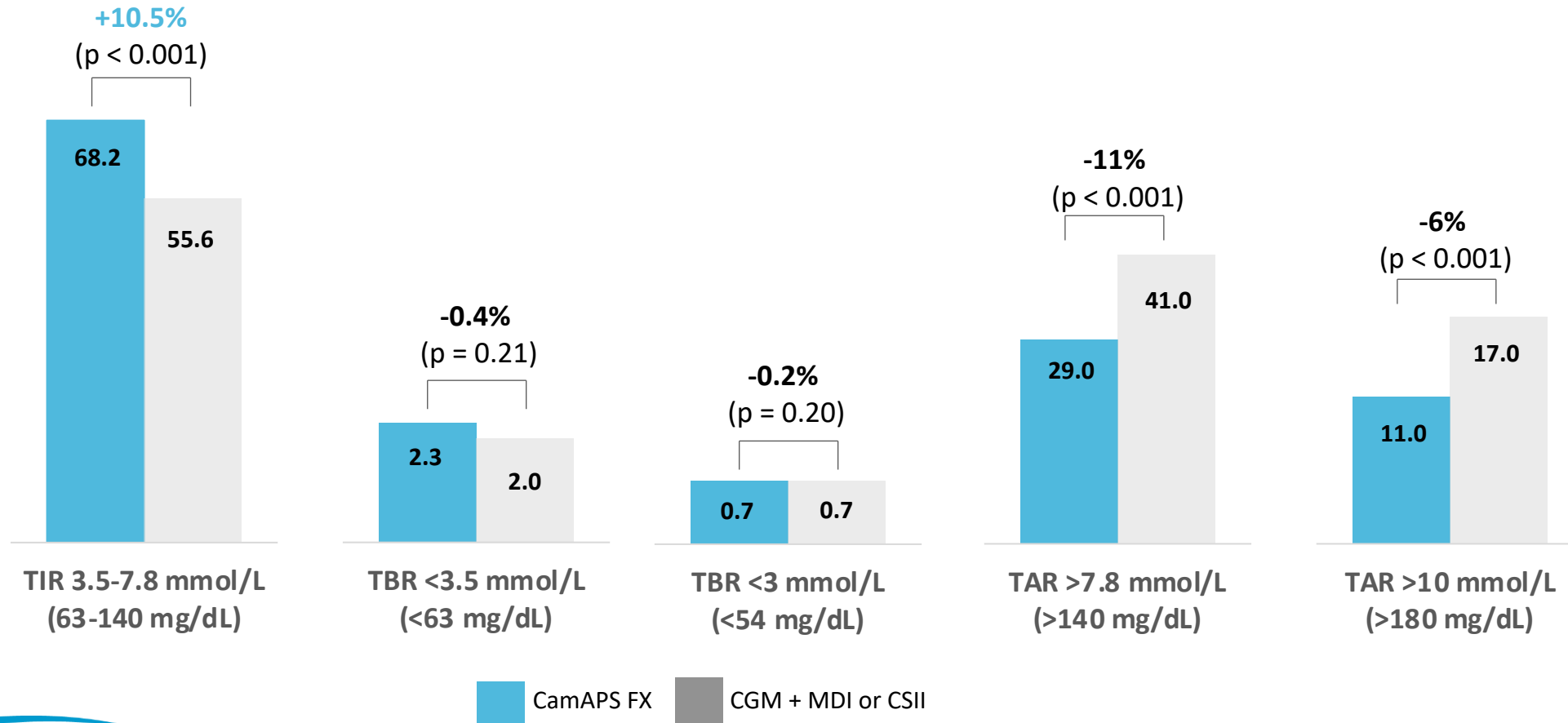
End Points	Baseline		16 weeks' gestation until delivery		P-value ^a
	Closed loop (N=59)	Standard care (N=59)	Closed loop (N=59)	Standard care (N=61)	
% TIR 3.5-7.8 mmol/l	47.8% ± 16.4%	44.5% ± 14.4%	68.2% ± 10.5%	55.6% ± 12.5%	NA
Change from baseline	NA	NA	20.4% ± 13.8%	11.0% ± 11.6%	NA
Adjusted difference ^a mean (95% CI)			10.5% (7.0%, 14.0%)		<0.001

Data are mean ± SD or median (IQR)

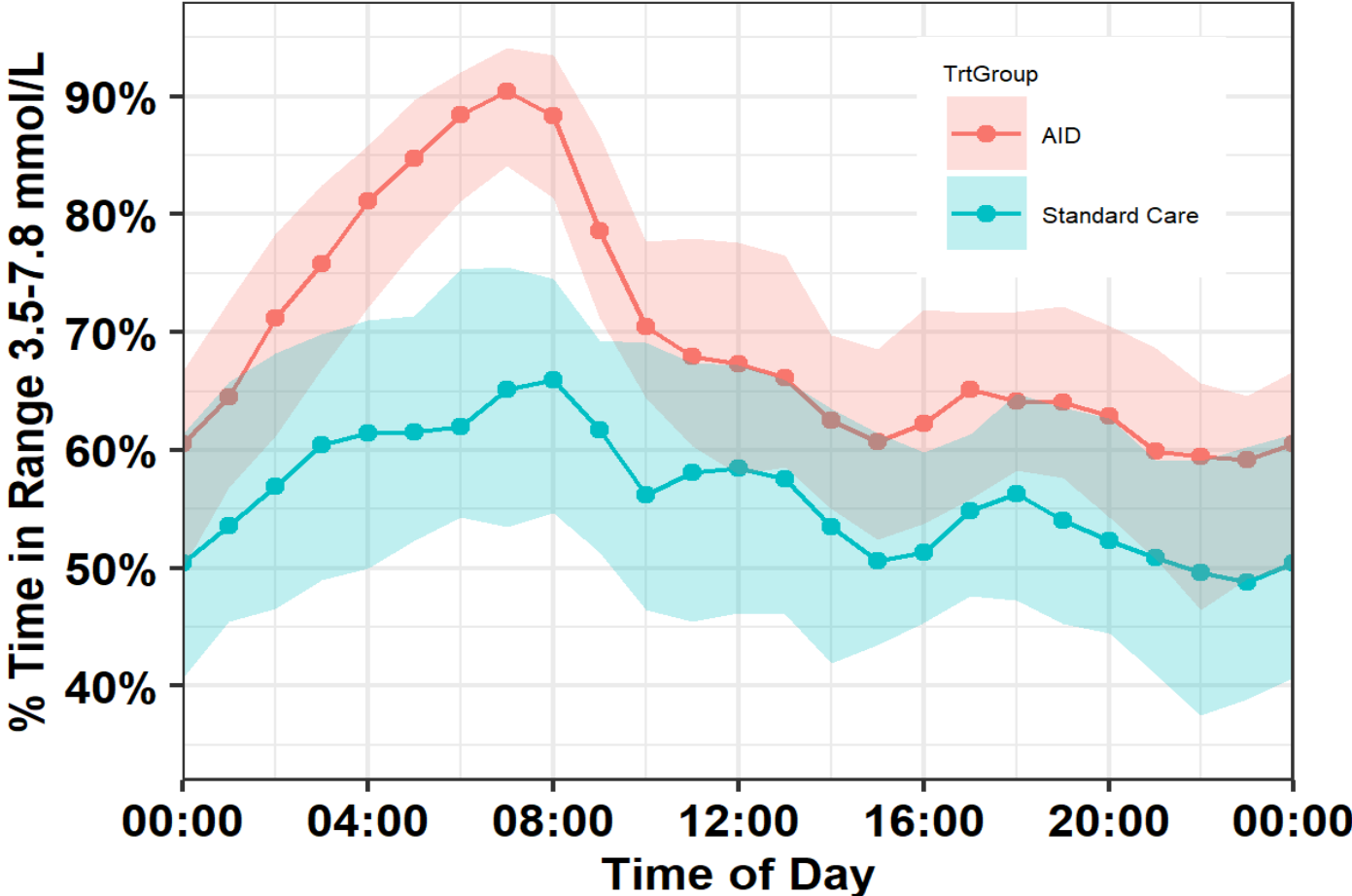
^a Model adjusted for baseline % TIR, insulin delivery, and site as a random effect



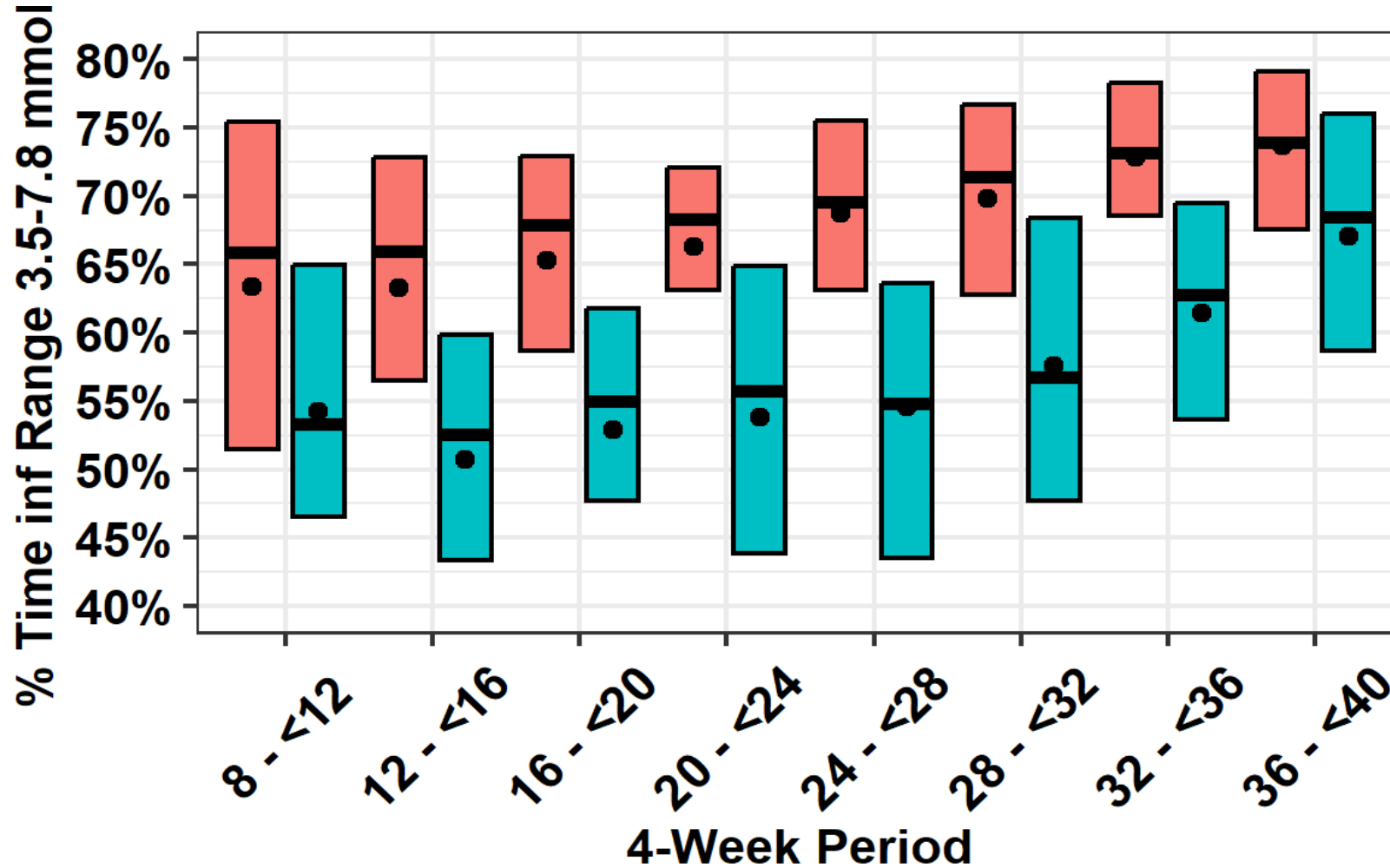
CamAPS FX improved TiRp by reducing hyperglycaemia



CamAPS FX improved TiRp across 24-hr day



CamAPS FX improved TiRp from ~12 weeks



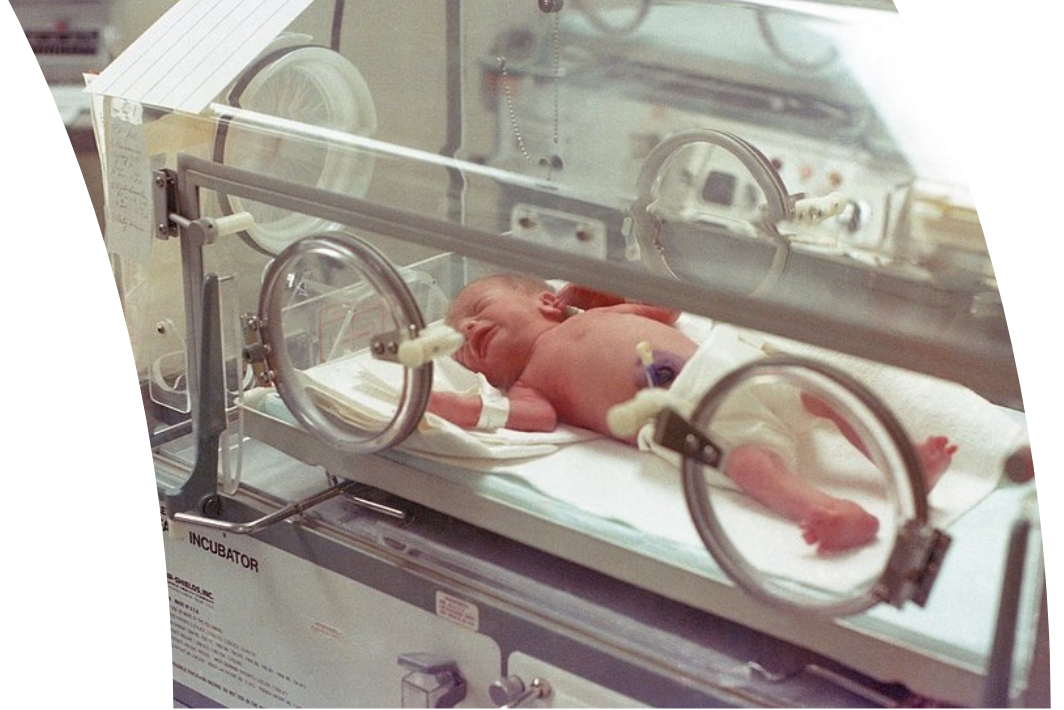
TrtGroup AID Standard Care

Additional Benefits.....

- ✓ Less worry, less work, more enjoyable pregnancy
- ✓ 3.7kg less gestational weight gain
- ✓ Less gestational hypertension
- ✓ Low rates of LGA/NICU



Lawton et al, Diabetes Technol Ther. 2023
Listening to Women



Time in Range by Patient Characteristics

	Closed loop		Standard Care		P-value for interaction ^a
	N	Change from baseline (mean ± SD)	N	Change from baseline (mean ± SD)	
Overall	59	20% ± 14%	59	11% ± 12%	
Maternal Age					0.91
18-24	9	20% ± 15%	15	14% ± 13%	
25-35	41	19% ± 13%	35	10% ± 12%	
>35	9	25% ± 16%	9	9% ± 8%	
Baseline HbA1c					0.91
≥42 – 53mmol/mol	22	17% ± 11%	11	10% ± 10%	
≥53 – 64mmol/mol	20	26% ± 16%	23	12% ± 12%	
≥64mmol/mol	17	18% ± 13%	25	10% ± 12%	
Insulin pre-enrolment					0.91
Pump	30	19% ± 13%	22	8% ± 10%	
MDI	27	22% ± 14%	36	13% ± 12%	
AID	2	20% ± 18%	1	9% ± 0	



Data are mean ± SD.

^a FDR-adjusted p-value for interactions between treatment group.

Time in Range by Baseline HbA1c

Baseline HbA1c	Closed-loop	Control
≥42 – 53mmol/mol	17% ± 11%	10% ± 10%
≥53 – 64mmol/mol	26% ± 16%	12% ± 12%
≥64mmol/mol	18% ± 13%	10% ± 12%

Interaction p-value=0.91

Data are mean ± SD

FDR-adjusted p-value for interactions between treatment group



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

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

NICE National Institute for Health and Care Excellence

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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](#)

CamAPS FX



n=59

- ✓ 50% achieved TIRp 70%
- ✓ 3.7kg less weight gain
- ✓ LGA 39%

Off-label Commercial HCL

Medtronic 780G (80%)

Tandem Control IQ (10%)



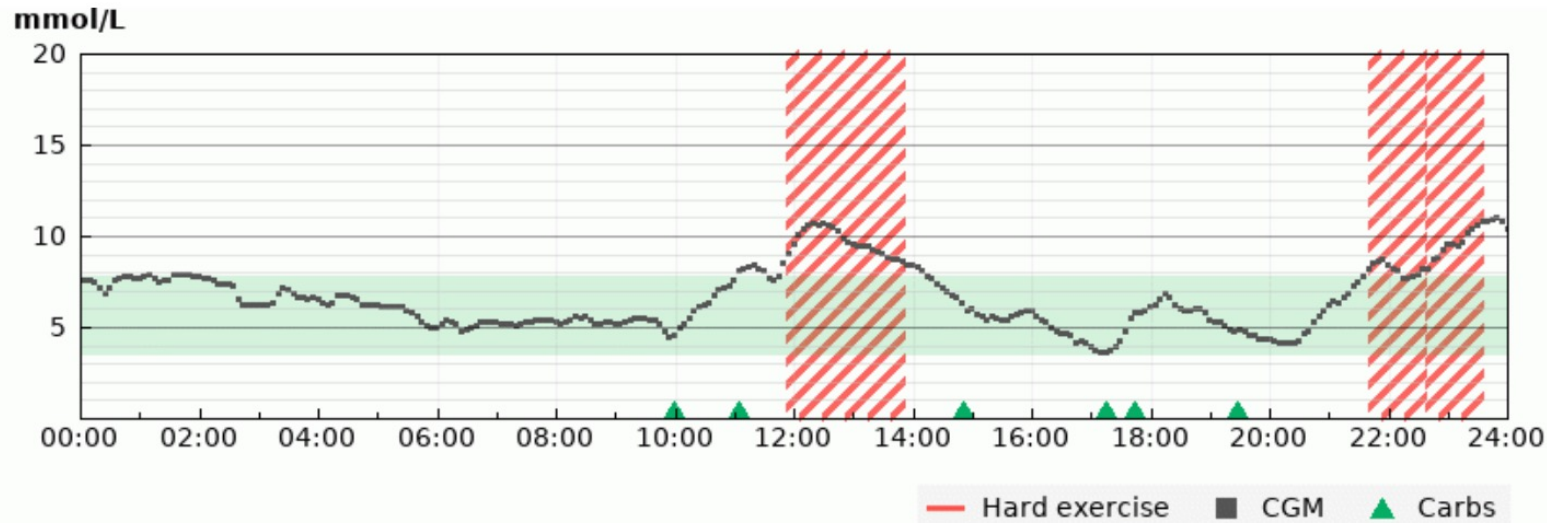
n=59

- ✗ 5% achieved TIRp 70%
- ✗ 3.3-5.4 kg more weight gain
- ✗ LGA on HCL 69%

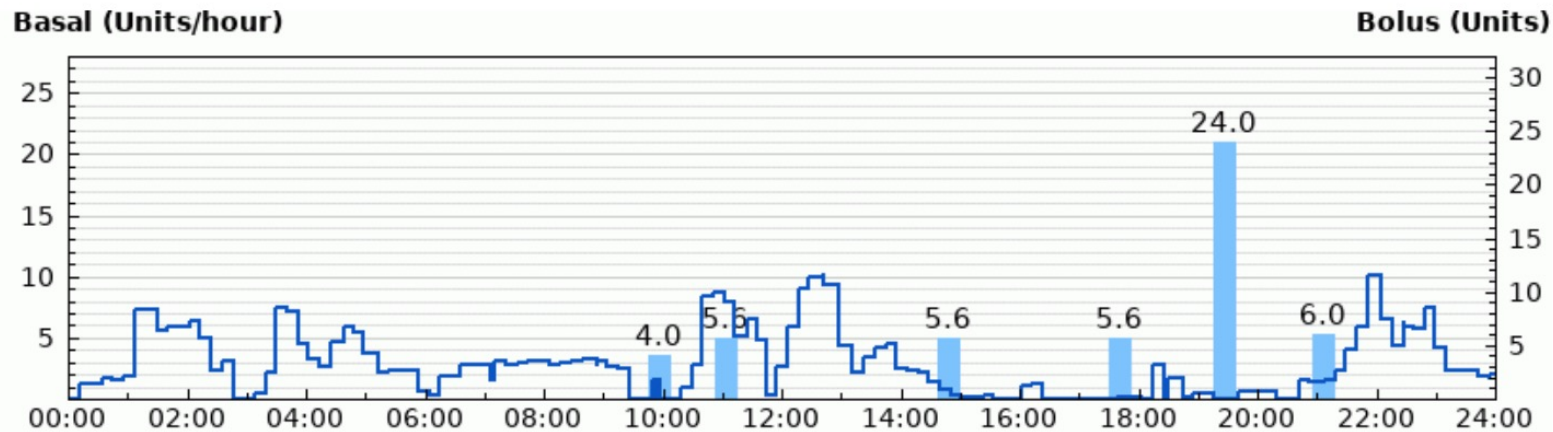


Diabeloop (10%)

How does CamAPS Fx work?



- Modulates basal insulin delivered by adjusting insulin every 8-12 minutes
- Hybrid closed-loop
Still requires insulin boluses for carbohydrate

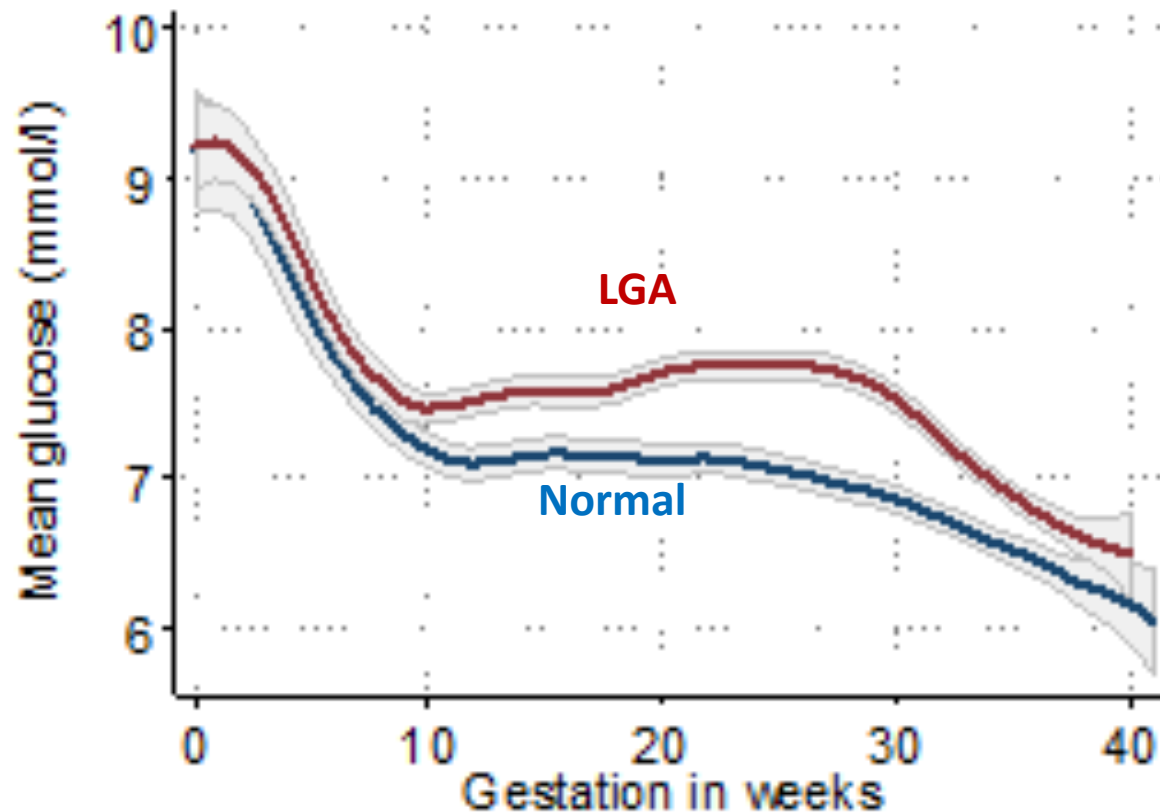


What can we do and when?



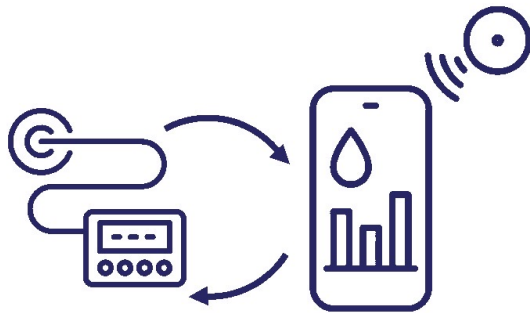
When do we start Hybrid Closed Loop (HCL)?

A) Mean glucose (mmol/l)



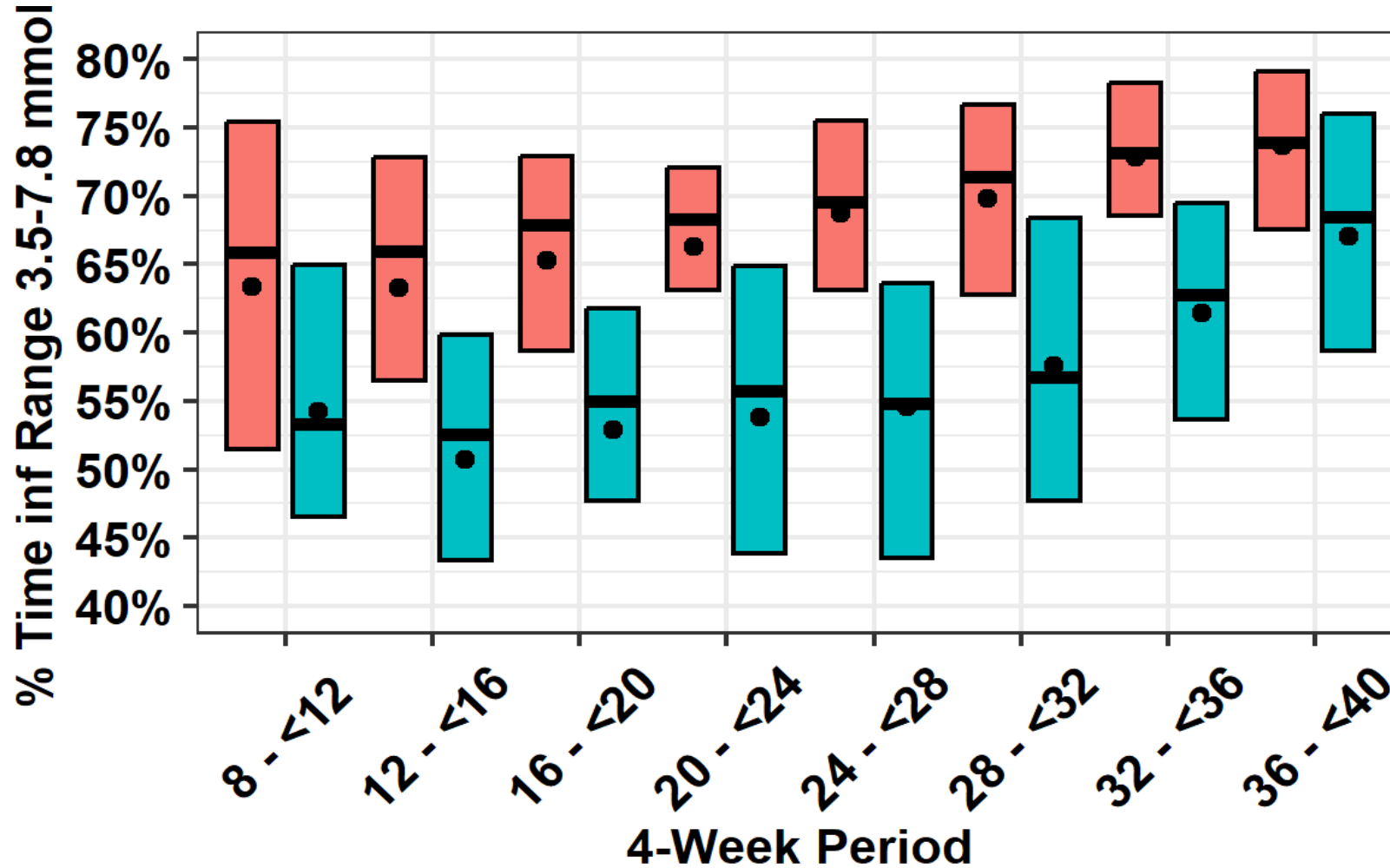
- Maternal glucose trajectory by ~10 weeks gestation determines the relationship to birthweight for the rest of pregnancy
- Demonstrates central role of maternal glucose to the pathogenesis of LGA from early gestation
- Normal growth associated with mean glucose of <7 mmol/l (<126 mg/dL) (from ~10 weeks)

What can we do and when?



- Start pre-pregnancy or as soon as possible once pregnancy confirmed
- Remember if 1st trimester to watch for hypos / labile levels
- Improvement in glycaemia seen in days

CamAPS FX improved TiRp from ~12 weeks



TrtGroup AID Standard Care

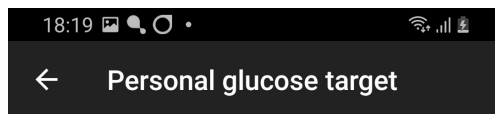
Supporting optimal HCL use?



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

Personal glucose target

Algorithm target adjustable at different times of day & night



Personal glucose target

From	To	Target (mmol/L)
00:00	06:00	4.5
06:00	22:00	5.0
22:00	24:00	4.5

Suggested algorithm targets in pregnancy:

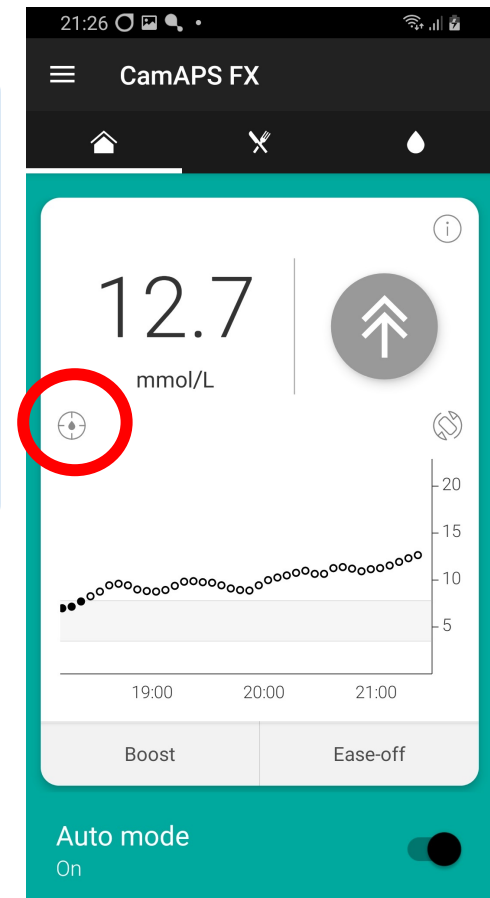
- 1st trimester: 5.5 mmol/L
- 2nd trimester (or earlier if hypo risk low): 4.5-5.0 mmol/L
- Postpartum 6.0mmol/L

Treat to target:

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

When to adjust target

- Lower target if glucose variability low
- Raise target if period of frequent hypoglycaemia



Other Hybrid Closed-Loop Systems

	Medtronic MiniMed 670/770G	Medtronic MiniMed 780G	Tandem Control IQ	Omnipod 5
Algorithm	Automode - Uses TDD from last 2-6 days	SmartGuard Mode - Uses TDD from last 2-6 days - Automated corrections (max. every 5 mins)	Control-IQ - Adjusts programmed basal rates in response to glucose - Automated corrections (max 1/hr) to target 6.1mmol/L	Omnipod 5 - Automated basal based on programmed basal rates (after 1 st pod change, based on actual TDD)
Glucose target (mmol/L)	6.7 Temp target 8.3	5.6, 6.1 or 6.7 Temp target 8.3	Regular 6.3 – 8.9 Sleep 6.3 – 6.7 Exercise 7.8 – 8.9	6.1, 6.7, 7.2, 7.8 or 8.3
Modifiable settings in automated mode	I:C ratio Active insulin time	I:C ratio Active insulin time	I:C ratios Basal rates Correction factor	I:C ratio Correction factor Active insulin time Target glucose
Data upload destination	Carelink	Carelink	Diasend (Manual upload)	Diasend

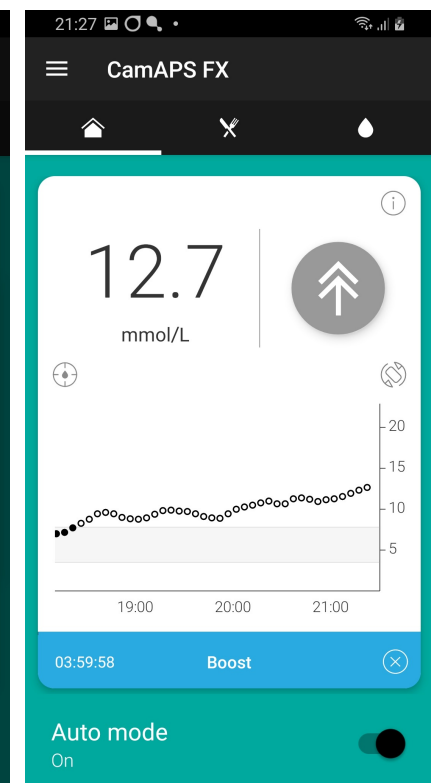
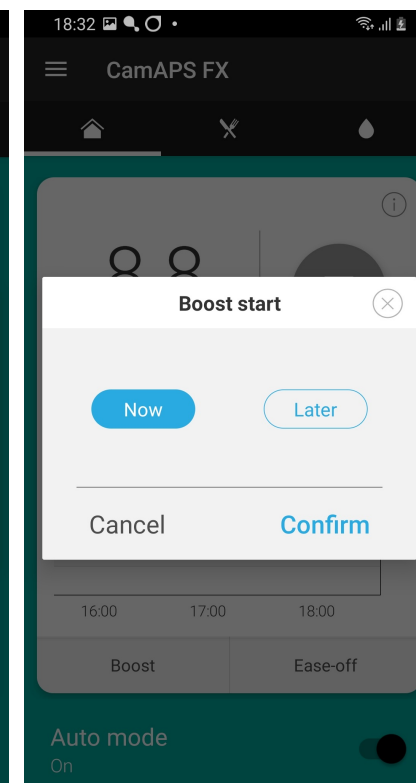
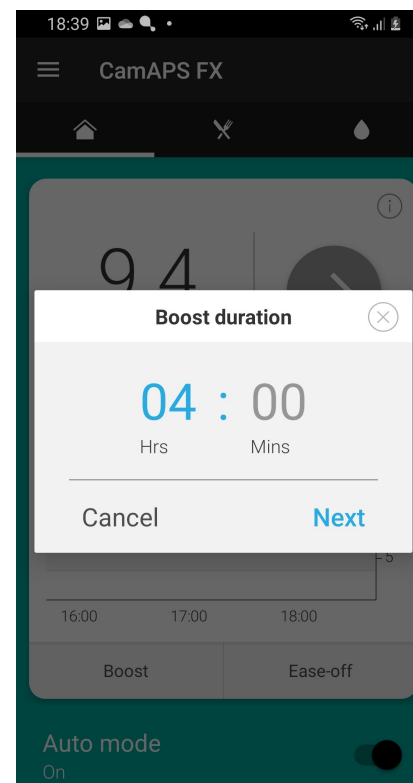
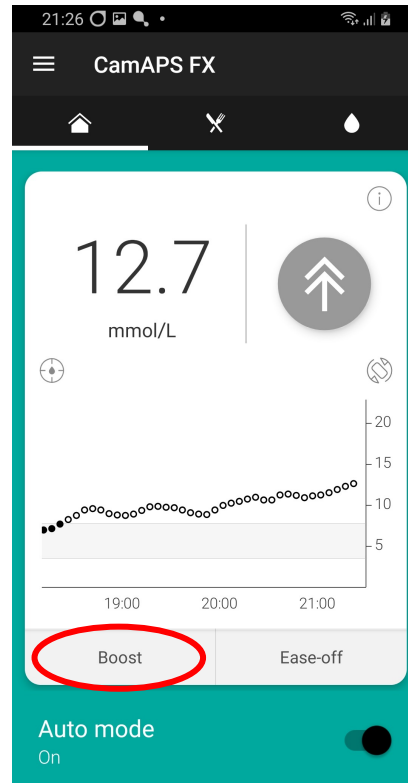


Boost

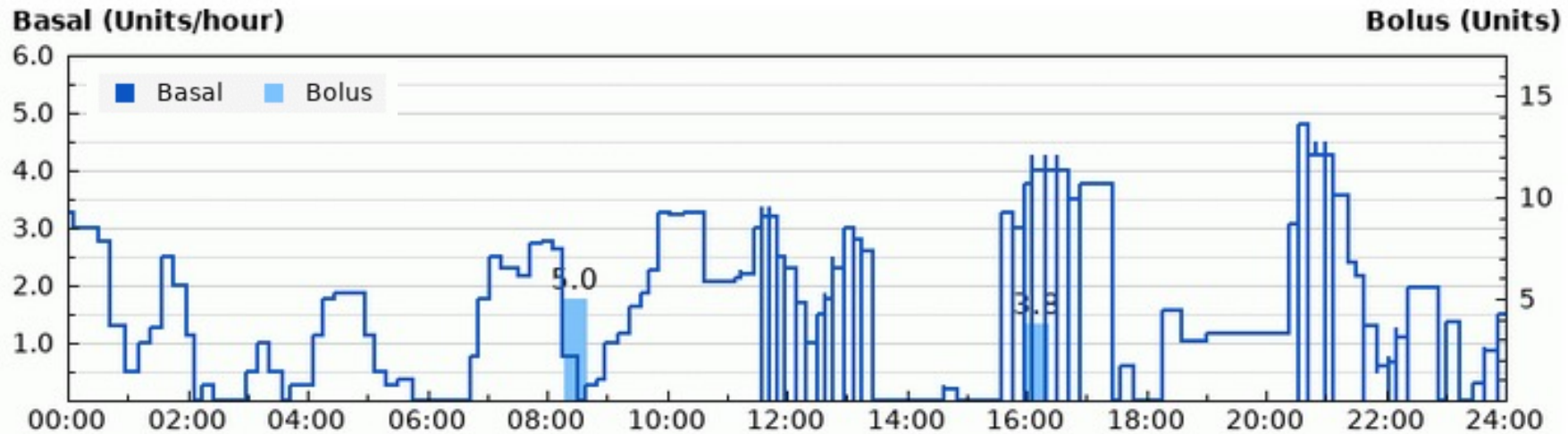
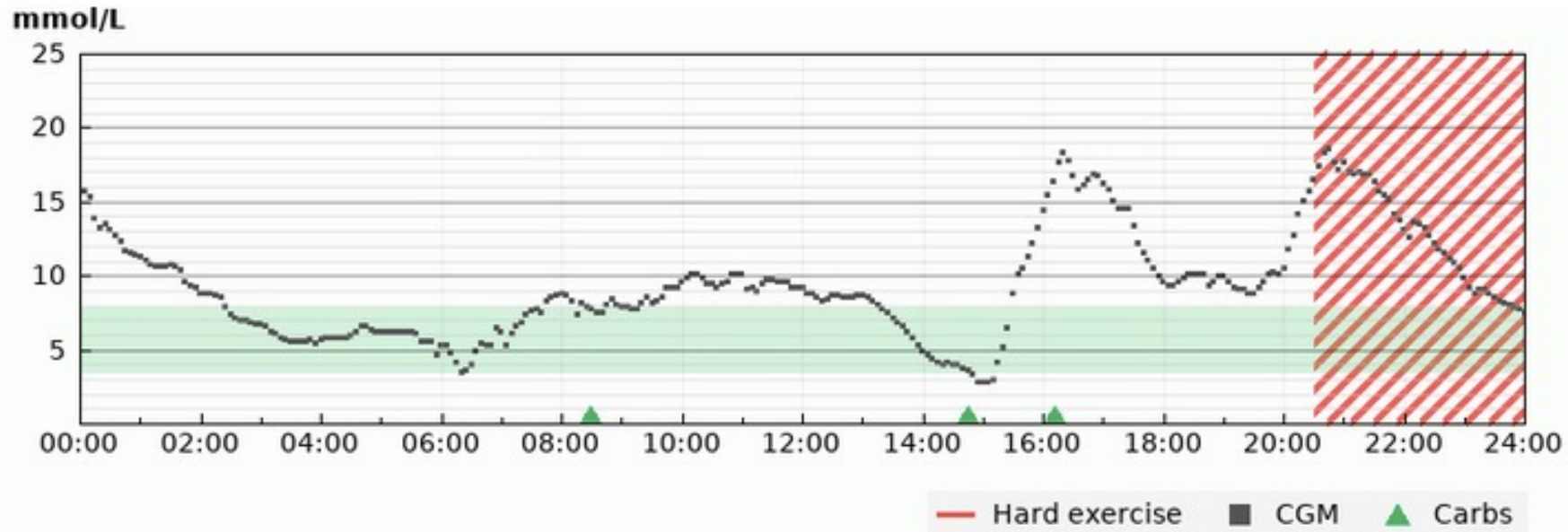
- Increases basal insulin delivery by ~35%
- Once glucose reaches target, boost **will not** continue to increase insulin delivery

When to use Boost?

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

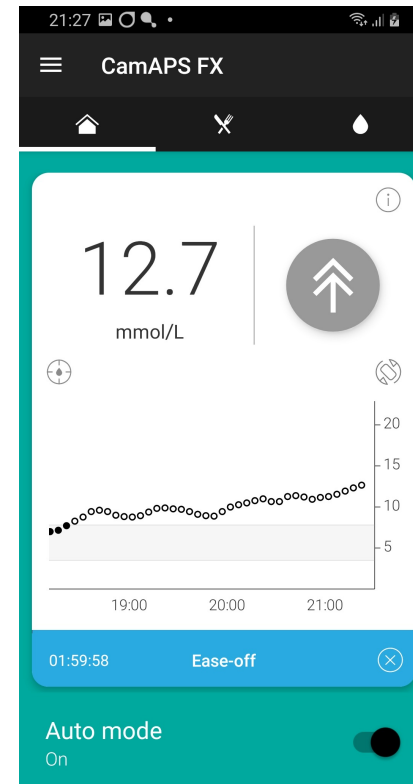
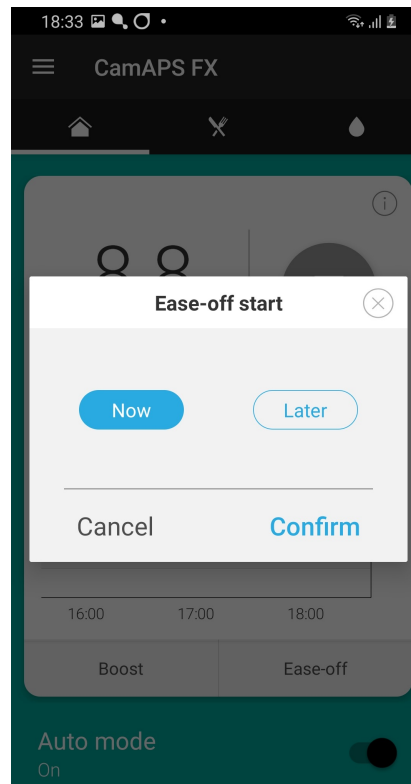
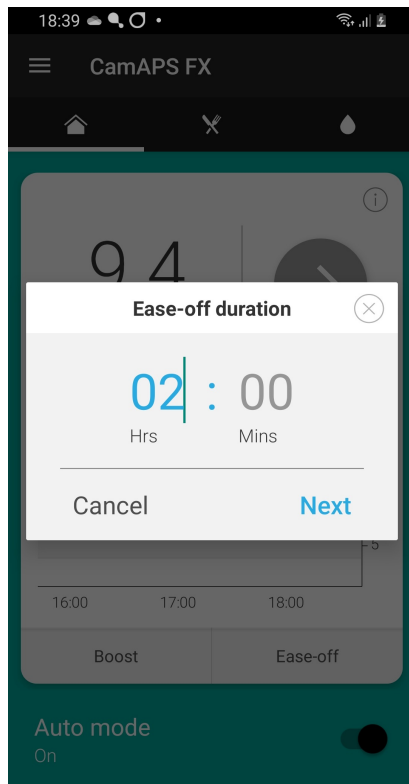


Boost



Ease off

- Substantially reduces basal insulin delivery
- Raises glucose target temporarily
- Insulin delivery will suspend at a higher level



When to use Ease Off?

- Before, during and/or after exercise/activity
- Following hypoglycaemia
- Hot weather

Meals and Pre-bolusing

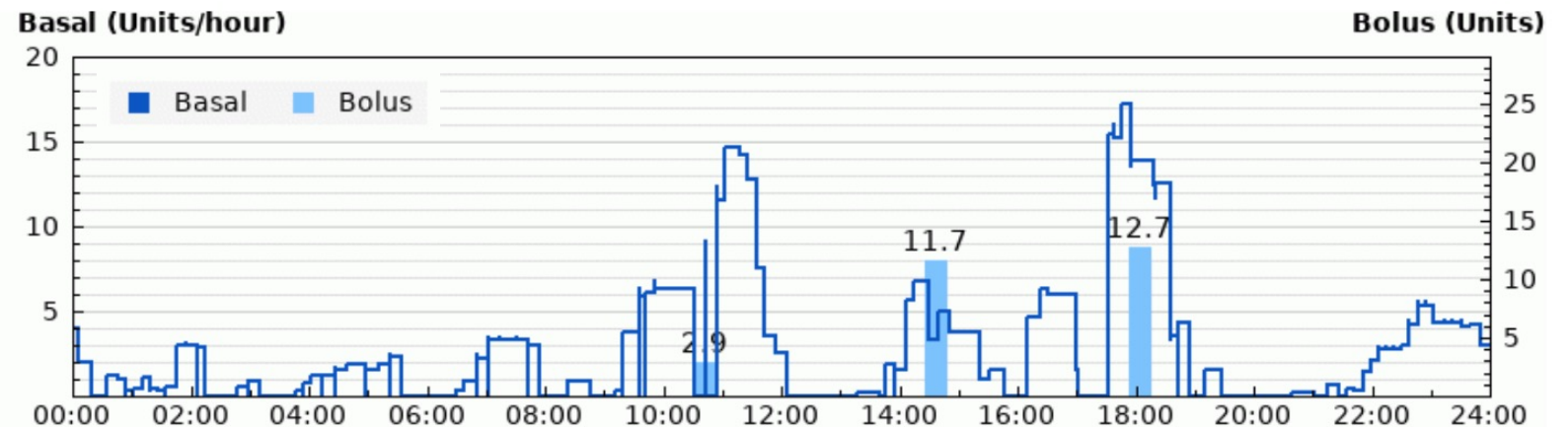
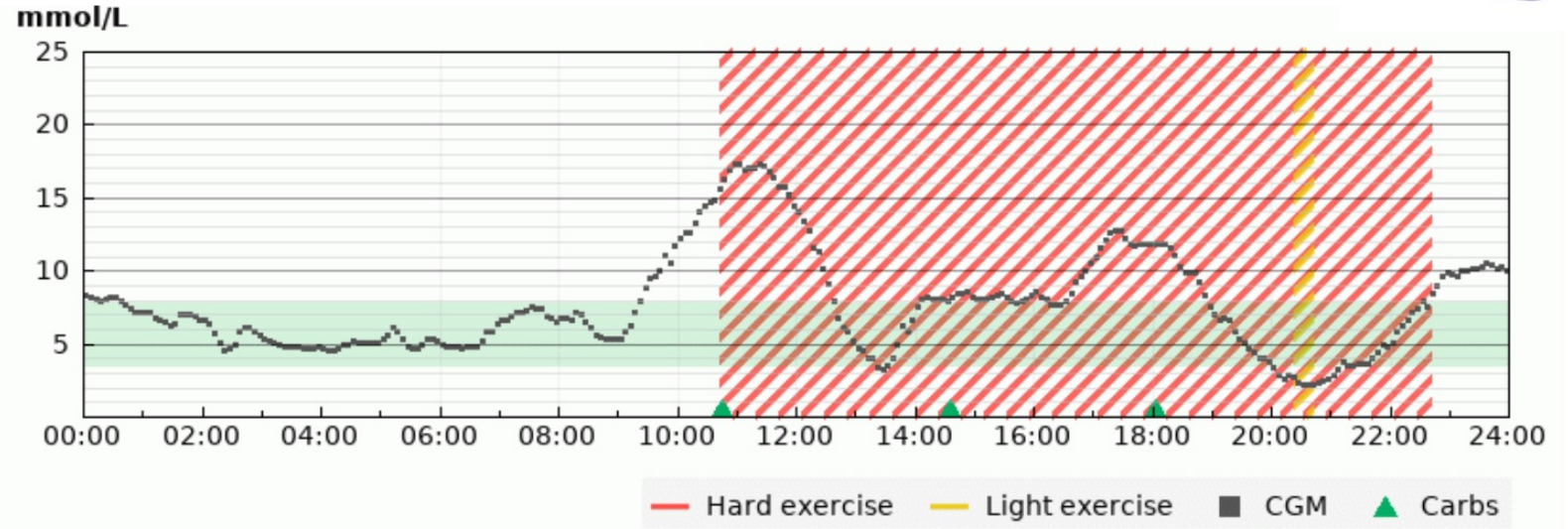


Strengthen insulin-carbohydrate ratios

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

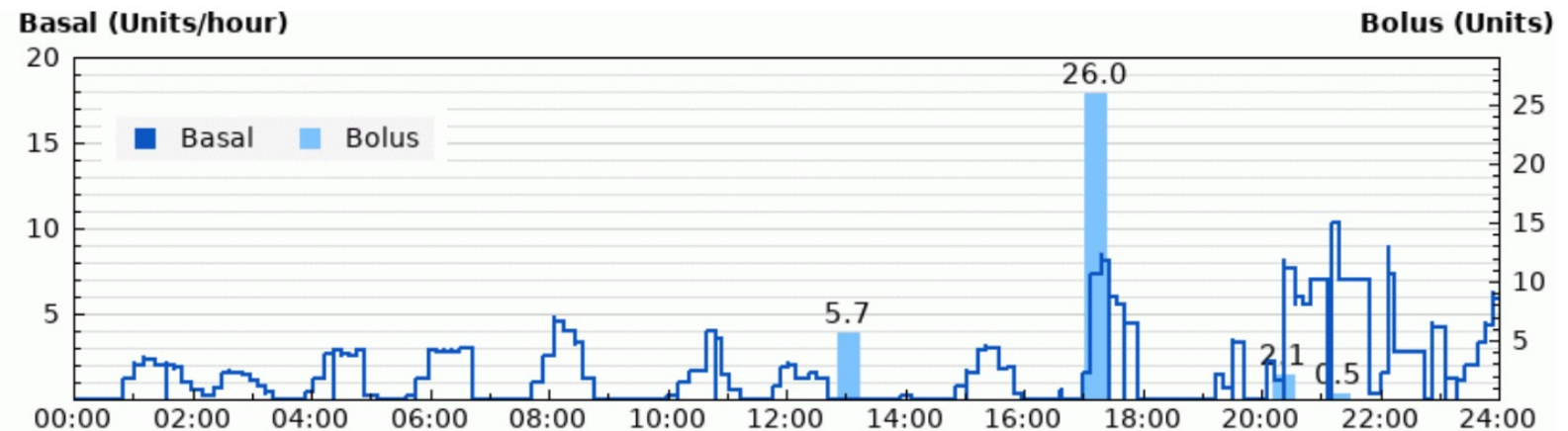
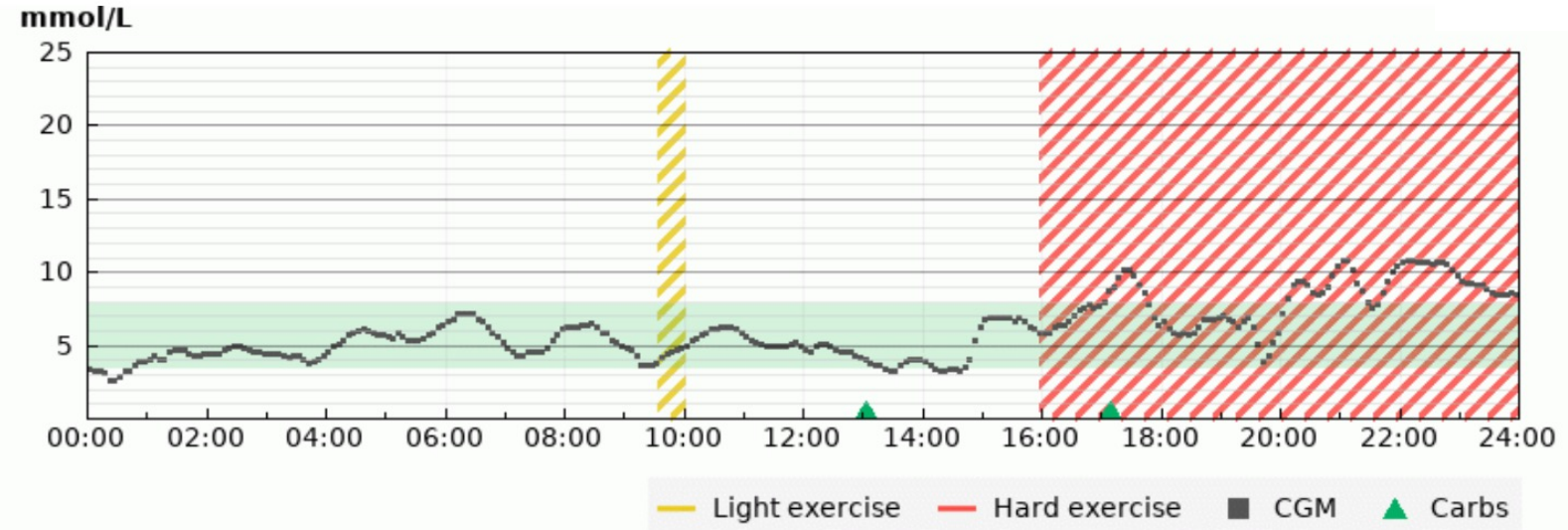


Suggested bolus interval

First trimester:
10-15mins

Second trimester:
20-30mins

Third trimester:
45-60mins



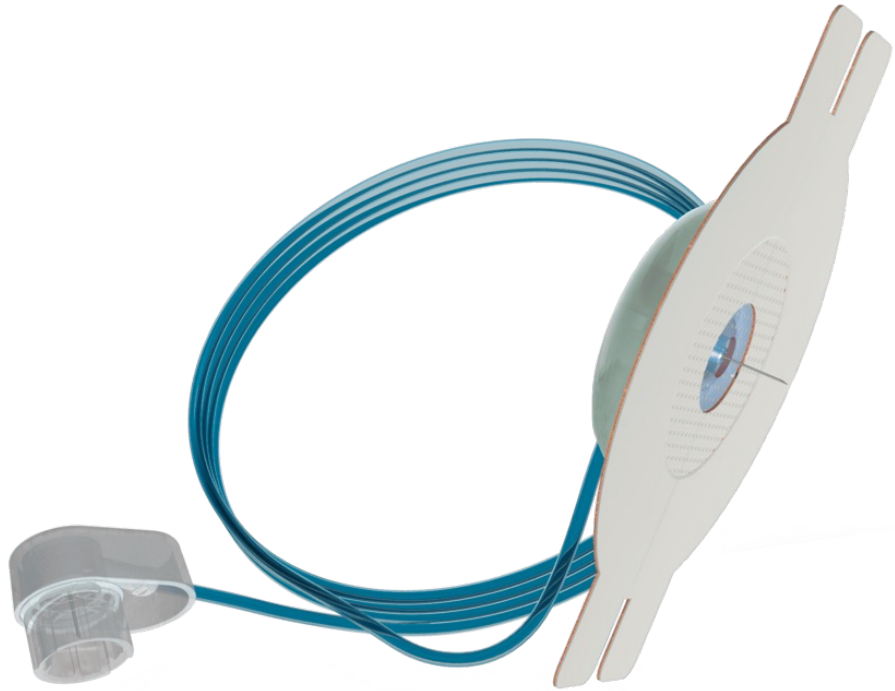


**My super
expensive
sensor**

**My state
of the art
closed
loop pump**

**Me
forgetting
to bolus
for a meal**

Set changes



Suggested set change frequency

Pre-pregnancy - first trimester:
At most every 3 days

Second-third trimester:
May need to increase to
alternate days / daily



What can we do and when?



- Labour
- Theatre and caesarean sections
- Steroid administration for fetal lung maturation

When is it safe to continue?

Mother is well enough and happy to self-manage

If unwell or not able to confident self-manage -> IV insulin

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

What can we do and when?



- Rapid drop in insulin requirements as soon as placenta is delivered
- Watch for hypoglycaemia
- Breastfeeding

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 basal rates
 - Pre-pregnancy rates

Further guidance for breastfeeding



Guidance

- Ease off
- ICR 1:15g
(can always be strengthened after a few days)
- Have pre-packaged hypo treatments / snacks
- Can raise PGT if still struggling with hypos

Take home messages

- ✓ CGM has revolutionized T1D care
- ✓ CGM alone (and/or with CSII) inadequate for optimal glycaemia
- ✓ Not all HCL algorithms are the same
 - Only CamAPS Fx has targets adjustable for pregnancy
 - has evidence of improved maternal glycaemia
 - is licensed in pregnancy
- ✓ For those on HCL not licensed in pregnancy
 - We await data in pregnancy
 - Consider switching to CamAPS Fx
 - Consider coming out of hybrid closed loop (auto-mode) during pregnancy
- ✓ Aim for 70% TIRp but every 5% matters
- ✓ Start early with rapid optimisation of PGT and CIR

