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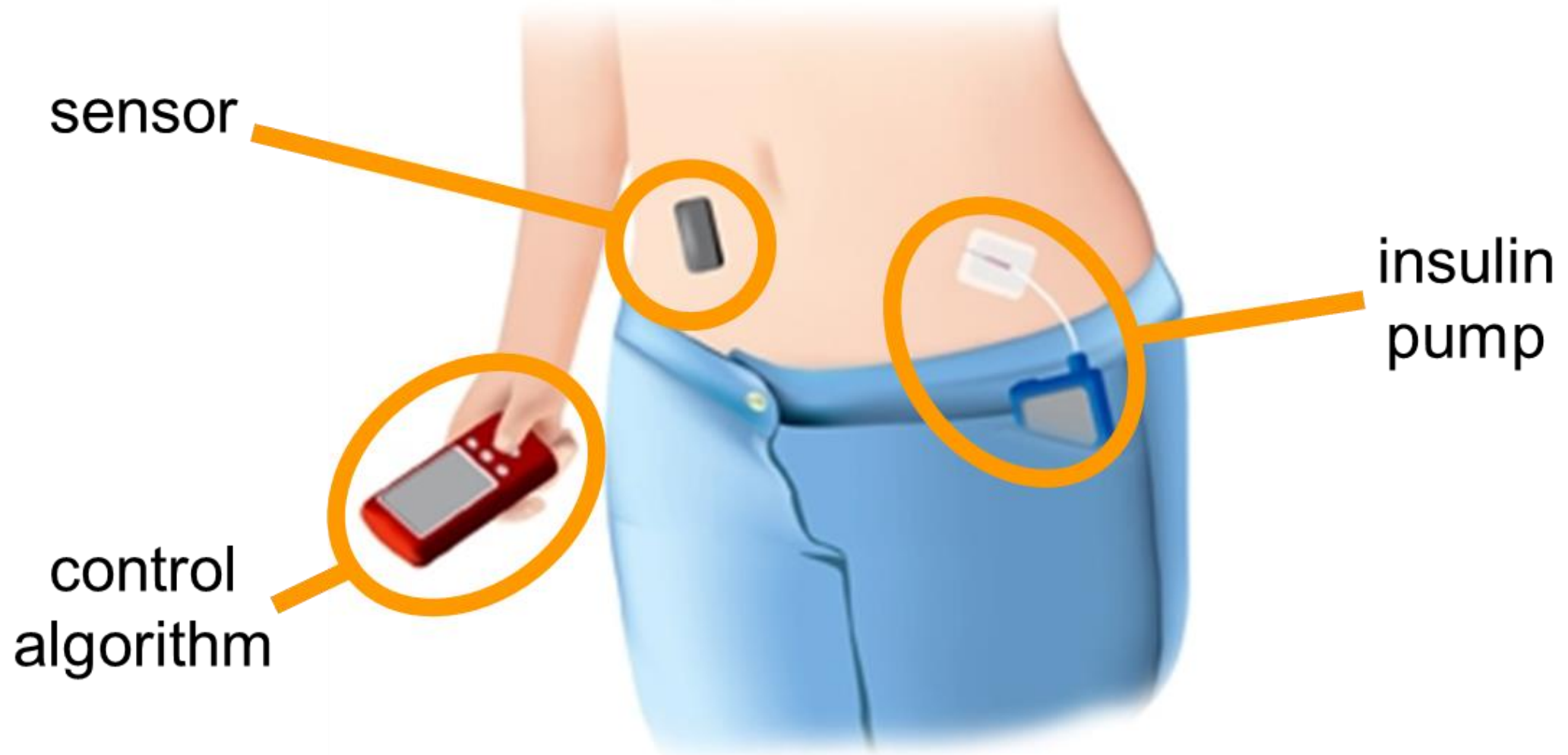
Closed-loop across the ages: the Cambridge experience

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Disclosures

CB reports Consultancy fees from CamDiab and Speaker honoraria from Ypsomed

Closed-loop / automated insulin delivery



The road to closed-loop insulin delivery



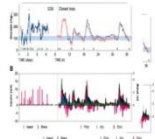
1960s

IV AP
Kadish



1970s

Insulin
& Glucagon
IV pump



2006

First clinical
study



JDRF AP
consortium



2010

Overnight
Control



Bi-Hormonal
Glucagon



2011

DiAs – 1st
wearable AID



2016

1st Commercial HCL
Minimed 670G



2022

Commercial HCL
1st Tubeless



1970s

Biostator
Albisser/Pfeiffer



1980s

1st
Commercial
Pump



1999

1st introduced
CGM: Minimed



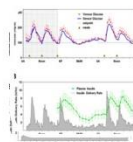
2008

1st ATTD



2009

Hybrid
AP



2010

IP AP



2011

1st outpatient
camp study



2019

Control IQ



Commercial HCL
Minimed 780G



2020

CamAPS FX



Regulatory approved HCL systems: 2024



CamAPS FX



**Diabeloop
DBLG1**



**Medtronic
670G & 780G**



Omnipod 5



**Tandem
Control IQ**

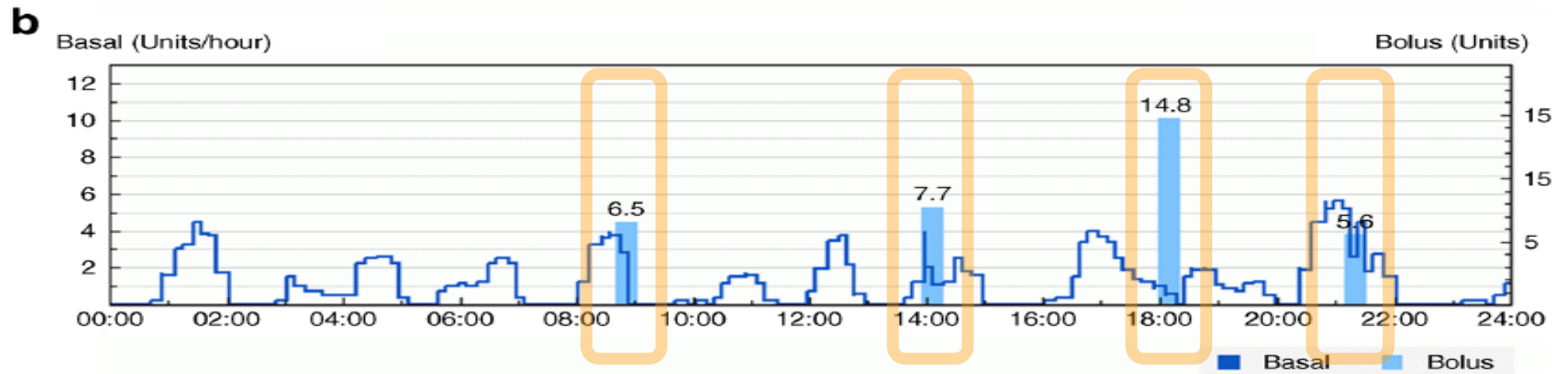
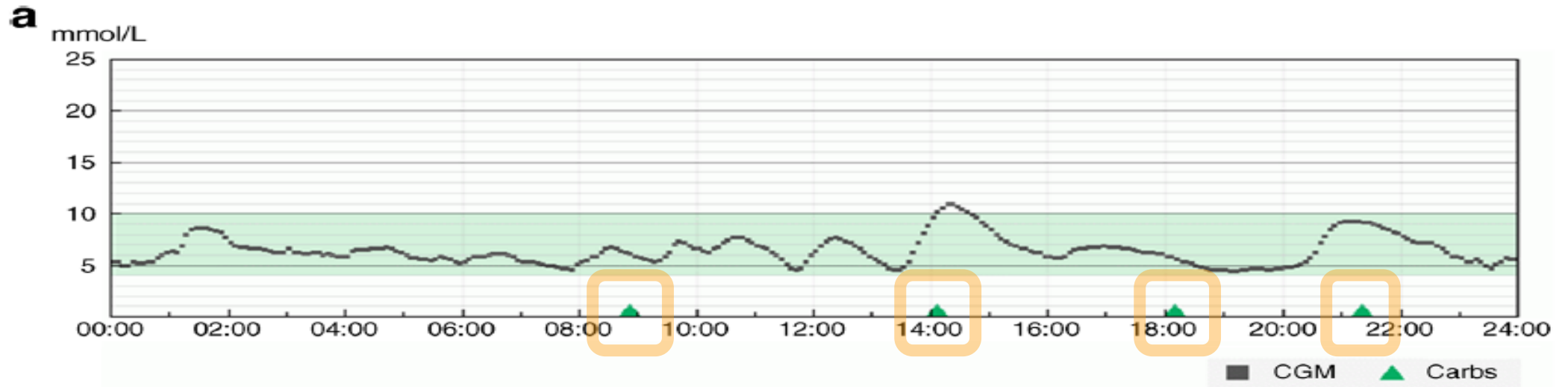


**Beta Bionics
iLet**

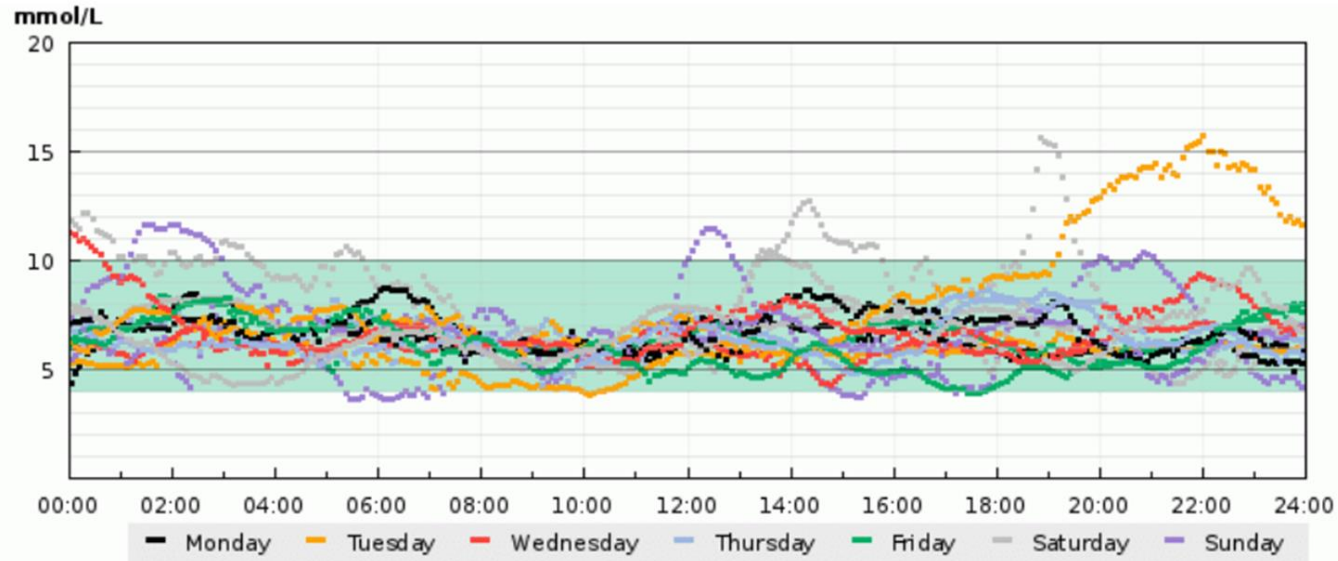


Tidepool Loop

“Hybrid” closed-loop



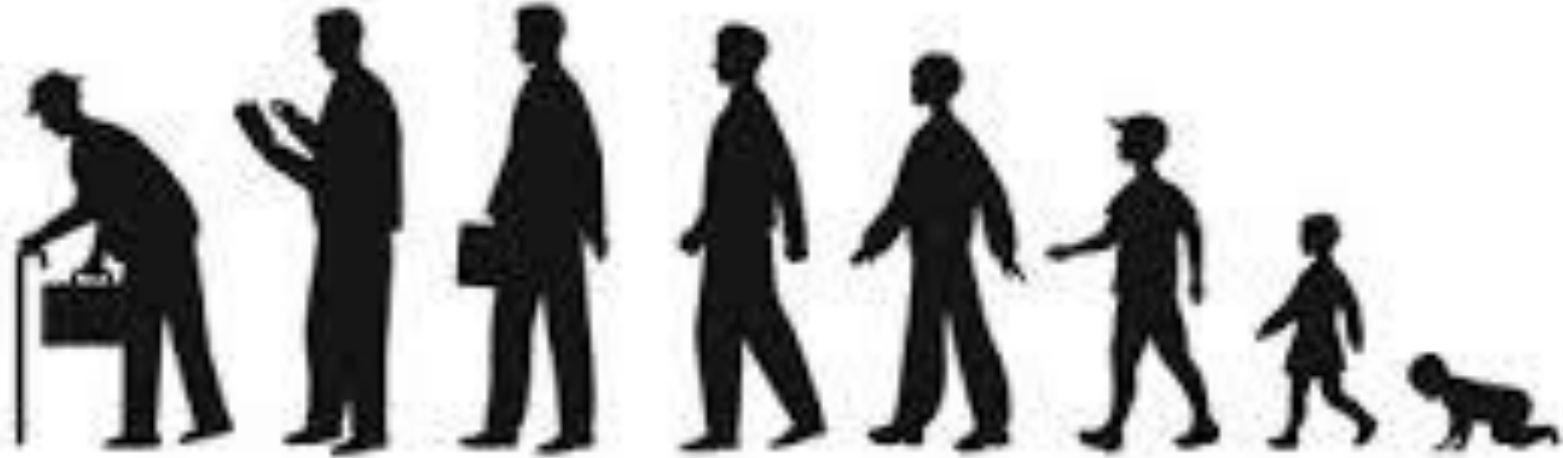
What makes a “good closed-loop”



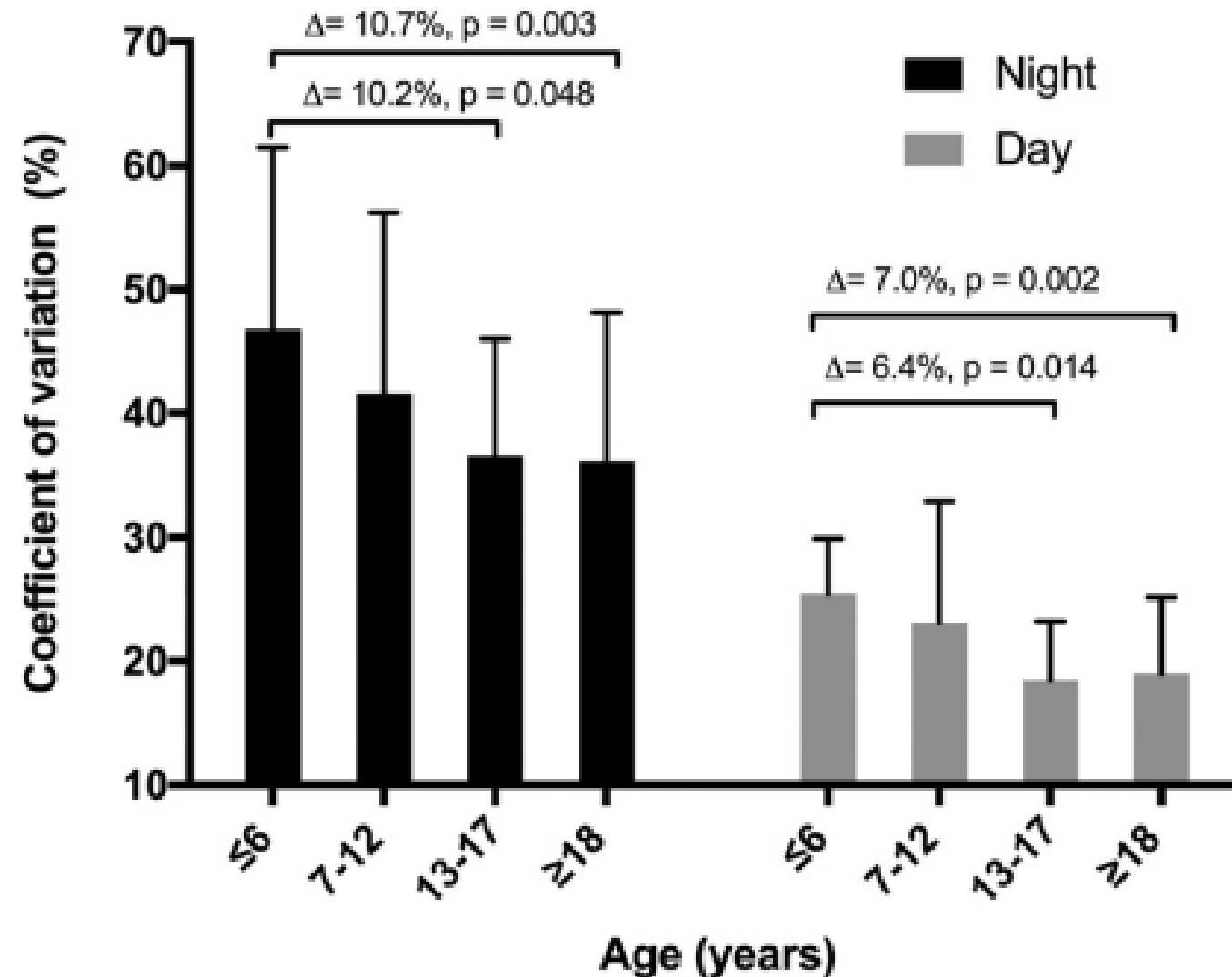
What makes a “good closed-loop”

- Glucose outcomes
 - $\geq 70\%$ Time in Range between 3.9 to 10 mmol/l
 - Low hypoglycaemia exposure
 - $\leq 4\%$ below 3.9 mmol/l
- Low diabetes burden
 - User interaction 10 to 20 min a day
 - Low alarm burden
 - Low device burden
 - Low rate of technical issues

Who needs closed-loop?



Closed-loop for very young children?



CamAPS FX: very young children

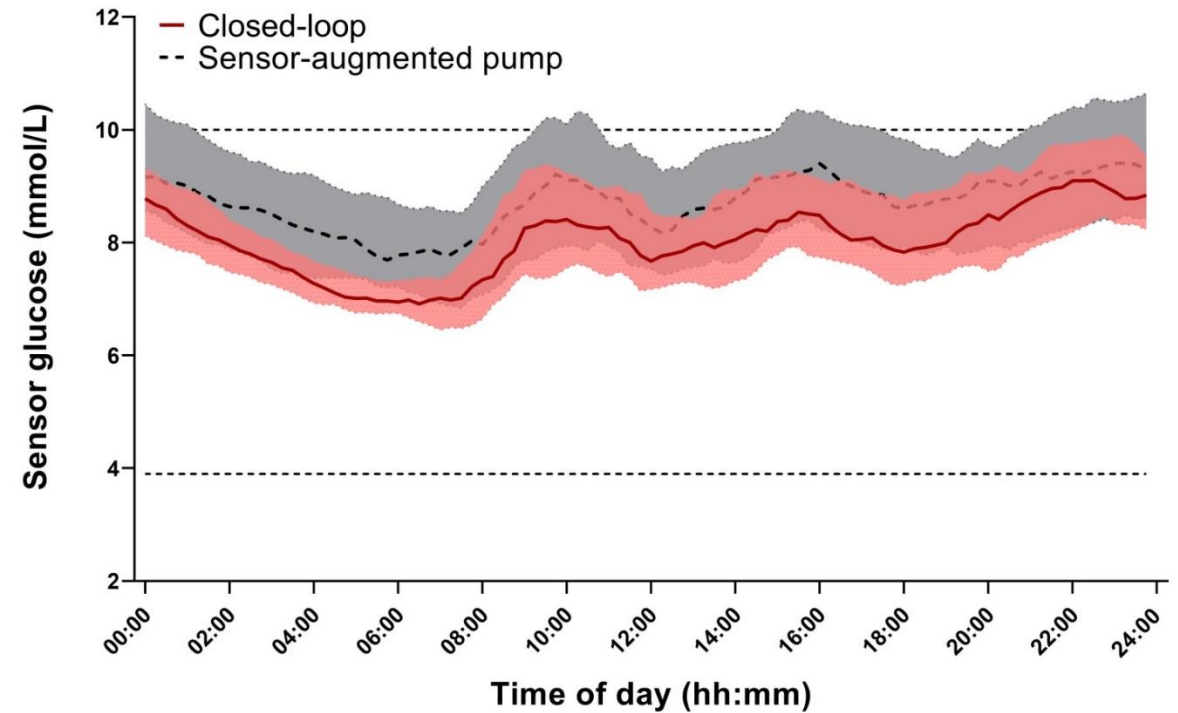


16 week crossover RCT:

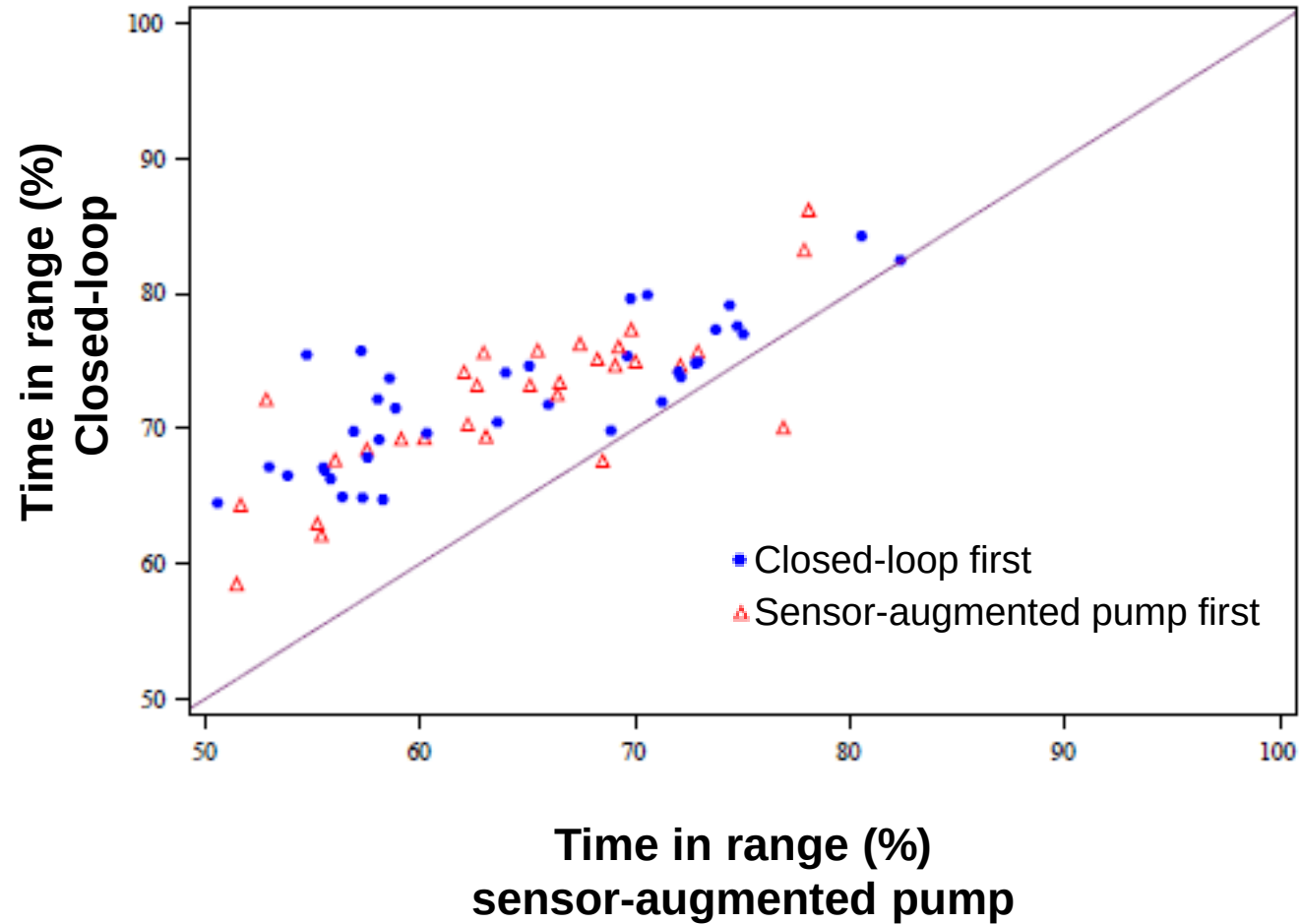
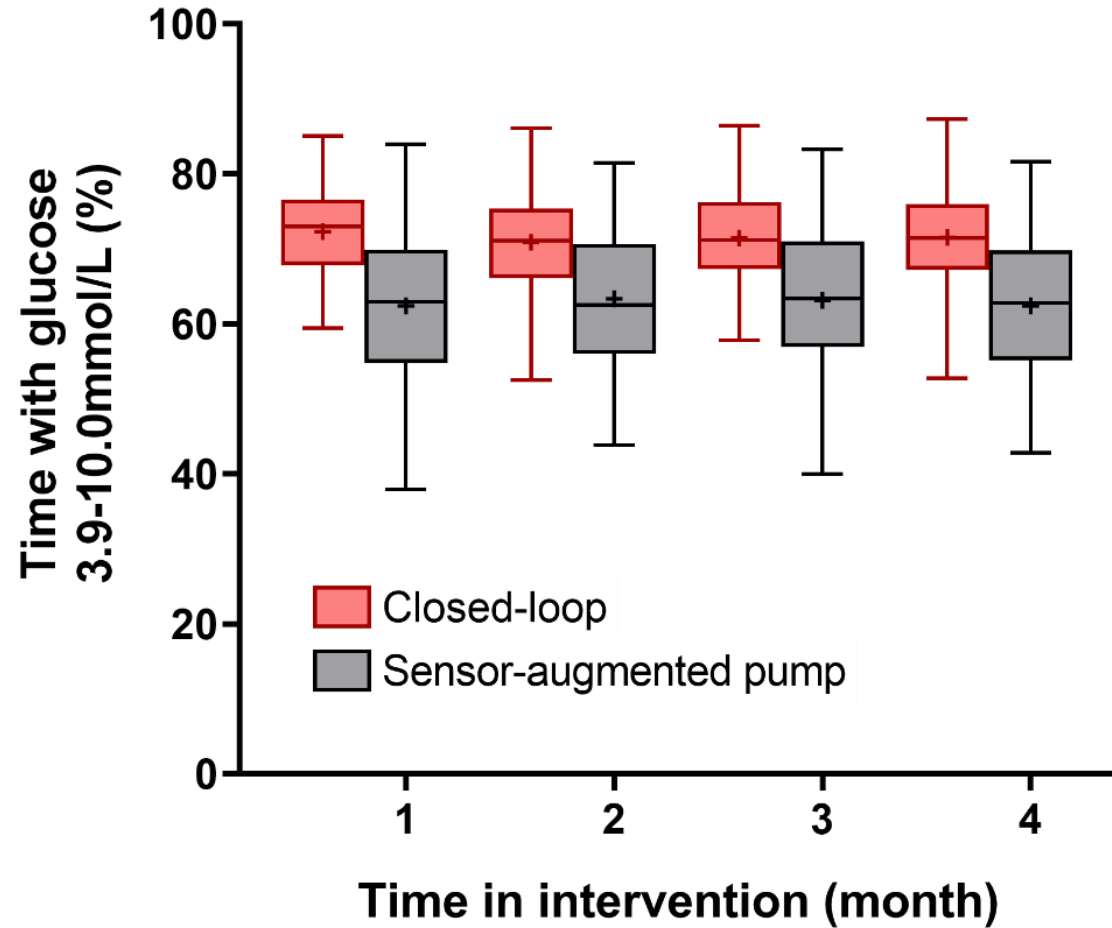
- Children 1 to 7 years (n=75)
- UK and Europe (7 centres)
- Baseline HbA1c: 7.3% (57mmol/mol)

Results

- Time in target range: ↑9 percentage points
- Mean glucose: ↓0.7 mmol/L
- Time <3.9 mmol/l: no change
- HbA1c: ↓0.4 percentage points



CamAPS FX: very young children



Boxplot shows median as horizontal line, mean as + symbol, IQR as box and range as whiskers.

Psychosocial impact for carers of very young children

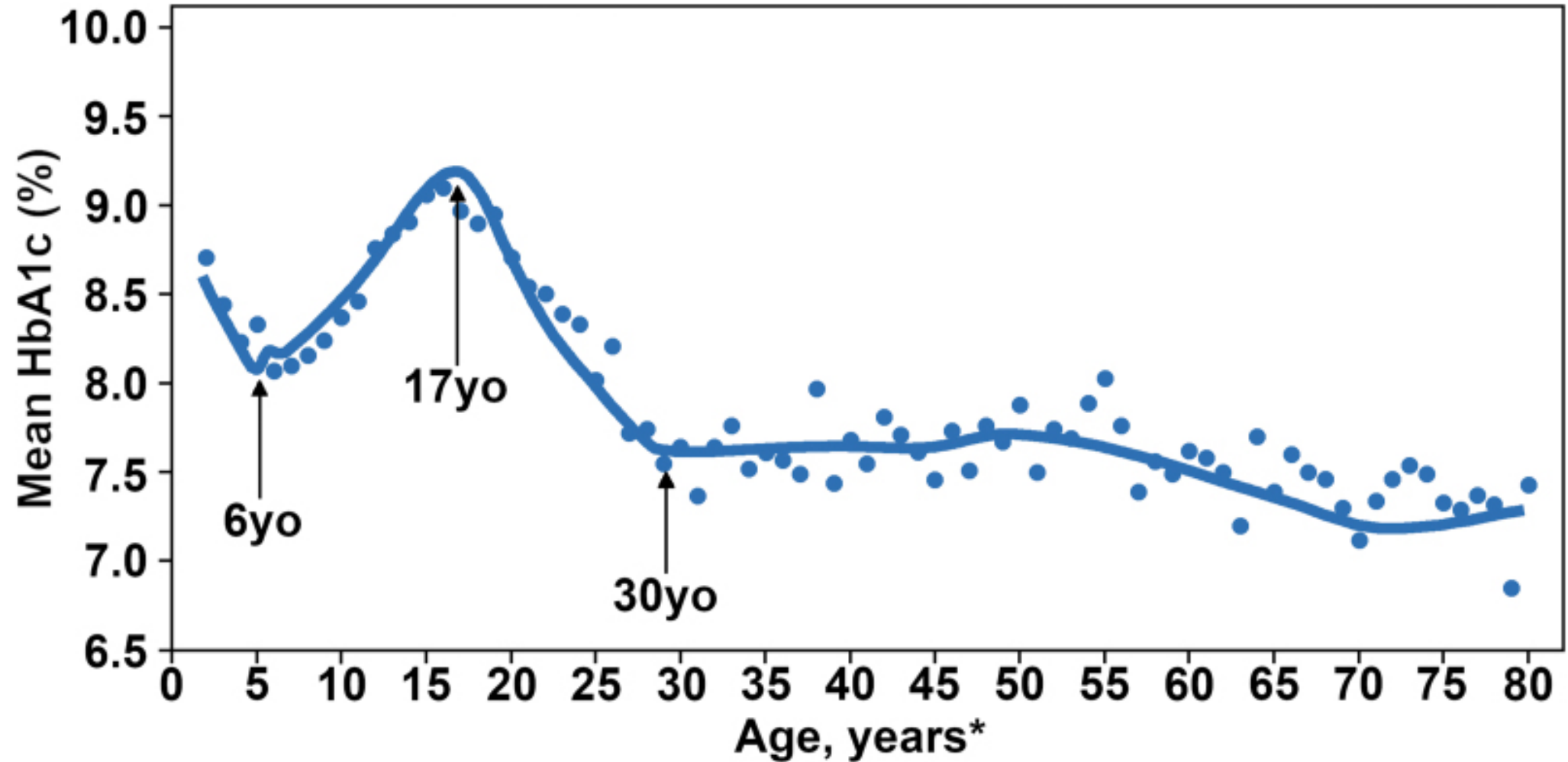
- Having to do **less diabetes-related work** and needing less clinical input over time.
- Facilitated **more normality**, including sleeping better, worrying less about their child, and feeling more confident and **able to outsource care**.
- More normality for the child (alongside **better sleep, mood and concentration**, and lessened distress) and siblings.
- Parents liked being able to **administer insulin using a smartphone**.

“We had to talk numbers a lot around her. And then she’s hearing this conversation. Now we just have normal discussions, so it must feel so nice for her. We’ve had more time just to be her parents and do play and fun things.”

“It’s like her temperament has changed. She’s been so much calmer in herself. She’s just generally much more able to get along with her peers when she’s playing, she’s able to compromise better, problem-solve better.

“the closed-loop system has given us part of our lives back because we are not constantly that worried if school can cope or whoever can cope”

Closed-loop for older children



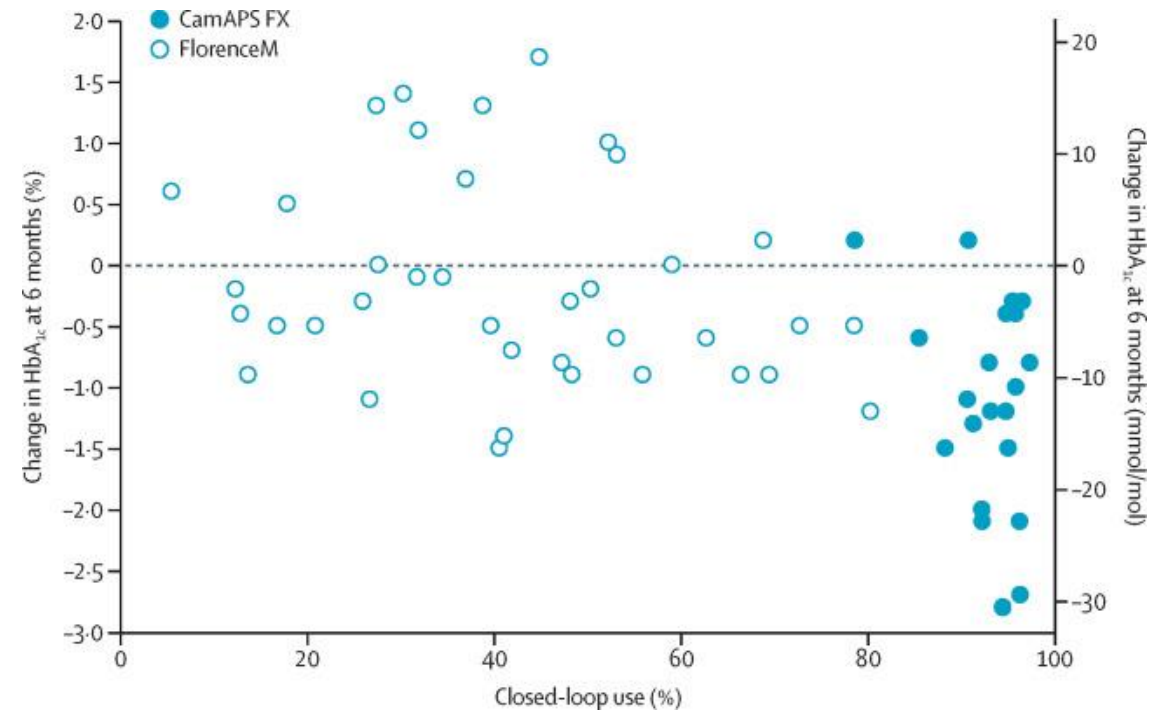
CamAPS FX: older children

6 month parallel RCT:

- Closed-loop vs pump $\pm$ sensor
- 6 to 18 years (n=133)
- UK and USA (12 centres)
- Baseline HbA1c: 8.2-8.3% (63-64 mmol/mol)

Results (FX cohort only)

- Time in target: 63% v 49%
- Mean glucose: 7.8 v 9.8 mmol/L
- Time <3.9 mmol/l: no change
- HbA1c: 6.8% v 7.9% (51 v 63 mmol/mol)



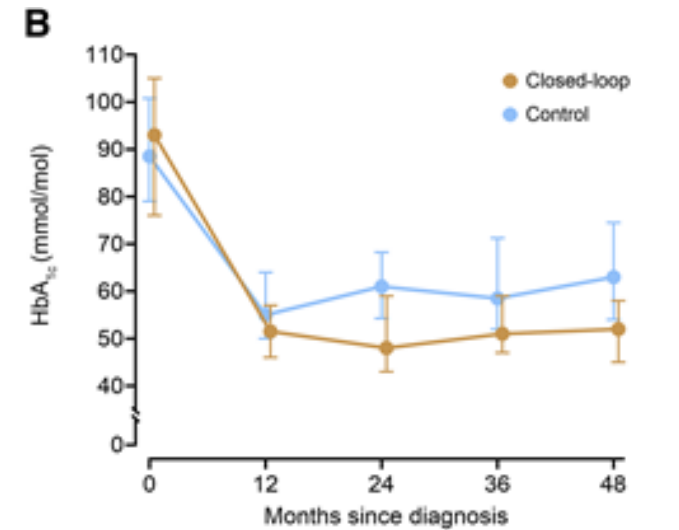
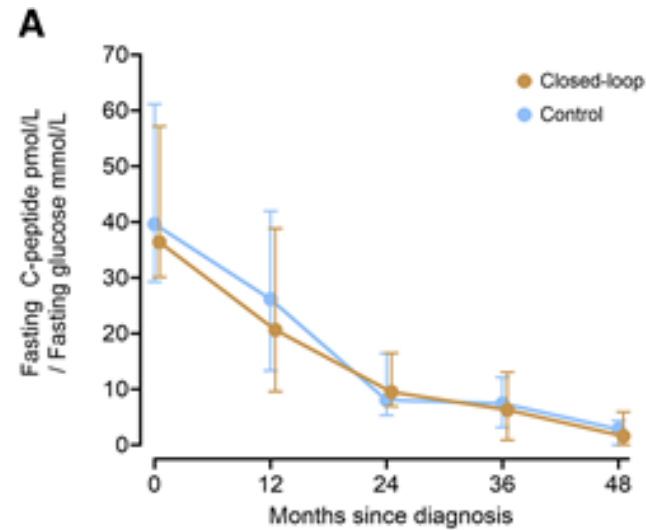
Closed-loop from onset of diabetes

48 months parallel RCT:

- Hybrid closed-loop vs usual care
- 10 to 16 years (n=97)
- UK (7 centres)
- **Recruited within 21 days of diagnosis**

Results (at 4 years)

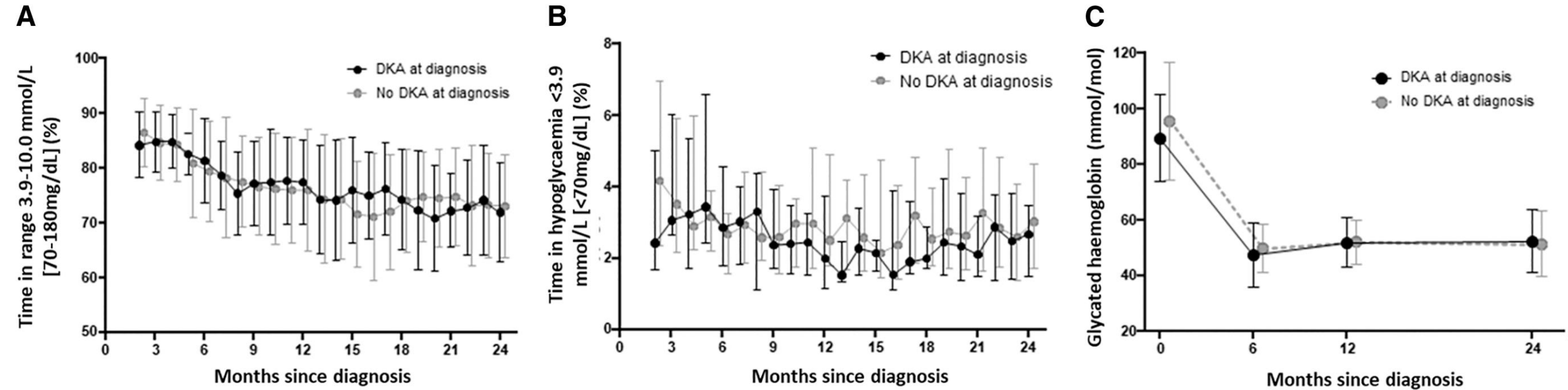
- C-peptide AUC: no change
- Time in target: ↑12 percentage points
- Mean glucose: ↓1.4 mmol/l
- Time <3.9 mmol/l: no change
- HbA1c: ↓0.9 percentage points



Control group, No (%) using

Insulin pump	4 (10)	16 (43)	15 (44)	13 (39)
Sensor	21 (57)	25 (68)	31 (91)	31 (94)
Hybrid CL	0 (0)	0 (0)	4 (12)	5 (15)

Closed-loop from onset of diabetes – impact of DKA at diagnosis



Psychosocial impact for adolescents newly diagnosed with T1D

- Participants reported **very few disruptions to their lives** when using closed-loop.
- Reports of **family conflict were minimal** as the closed-loop enabled dietary flexibility and glucose levels to be checked effortlessly.
- Adolescents described **doing 'normal' activities** without worrying about high/low glucose, and parents reported allowing them to do so **unsupervised** because the closed-loop would regulate their glucose and keep them safe.

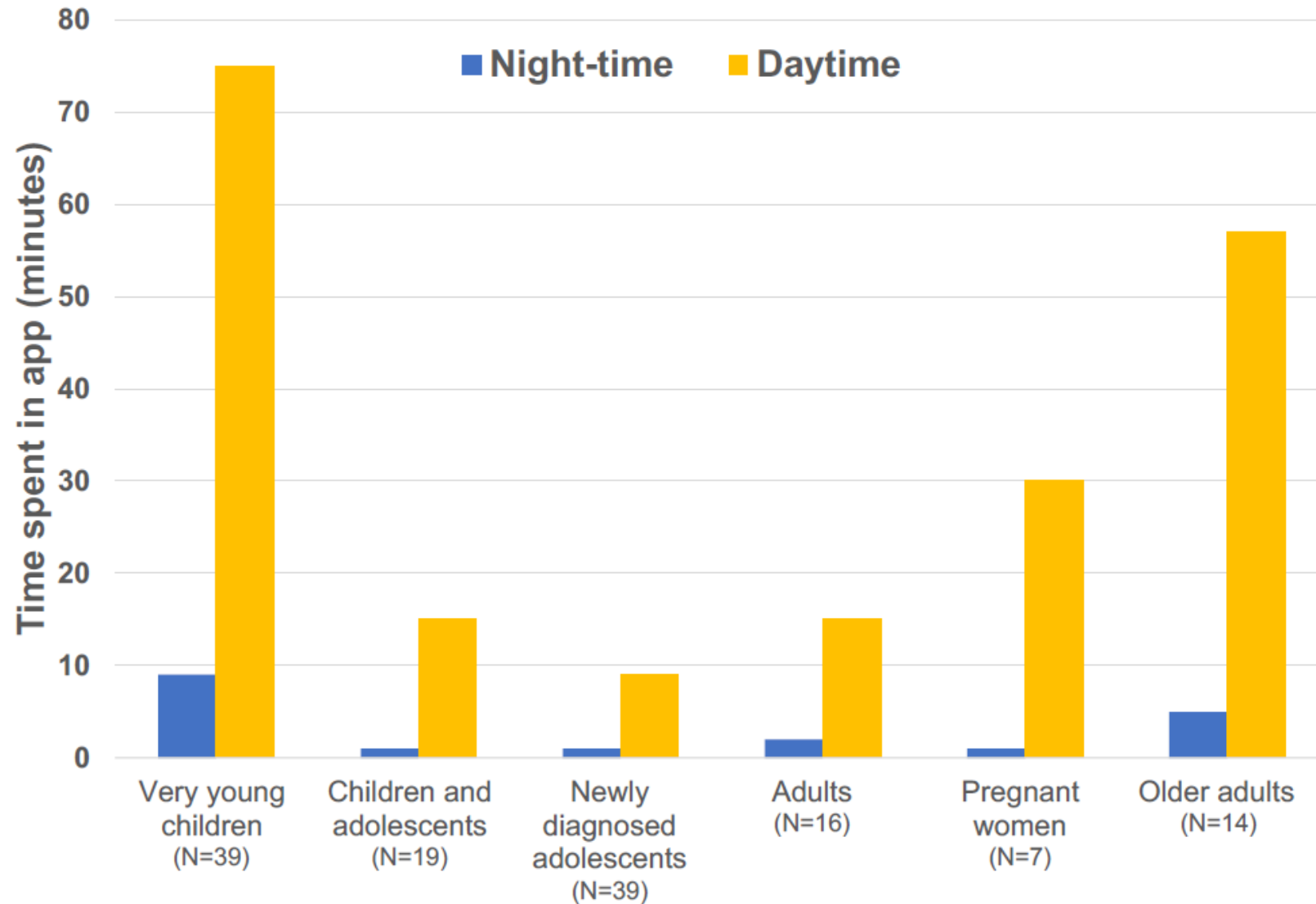
Closed-loop helped to reduce the biographical disruption of type 1 diabetes in this age group.

He's quite independent and I try to let him do everything and not restrict it because of anything. So just hanging around with his mates, having fun.

I can still do things with this closed-loop. I was out at this youth club that I go to and we went to Laser Tag, and I was asking myself, can I do this with diabetes? And it's fine. I feel like it's making sure that my bloods are level, and like they don't shoot up or shoot down.

I just try to like forget about it [diabetes], and that makes me feel better ... and it [closed loop] makes me feel that I don't have to check [glucose levels] as much, cause it gives me insulin when I'm high and it stops giving me it when I'm low which makes me able to forget about it [diabetes] more.

Burden of diabetes management



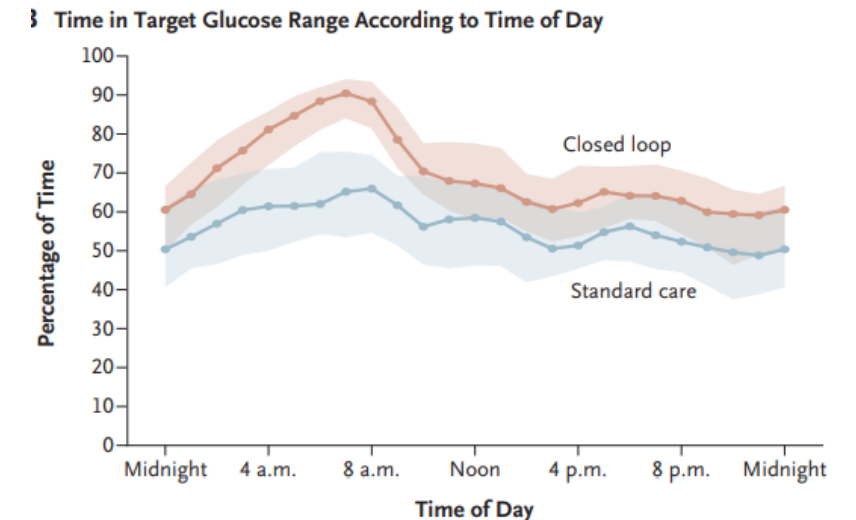
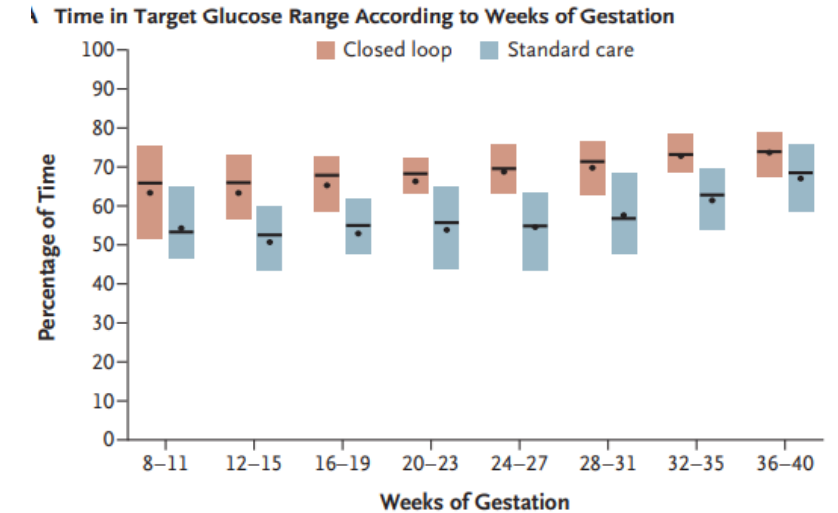
CamAPS FX in pregnancy

Parallel RCT:

- Hybrid closed-loop vs standard insulin therapy
- Pregnant women with T1D (n=124)
- UK (9 centres)
- Baseline HbA1c: 7.7% (61 mmol/mol)

Results

- Time in target (3.5-7.8 mmol/L): 68% v 56%
- Mean glucose: 6.9 v 7.6 mmol/L
- Time <3.5mmol/l: no change
- HbA1c: 6.0% v 6.4% (42 v 46 mmol/mol)



Psychosocial impact for pregnant women with T1D

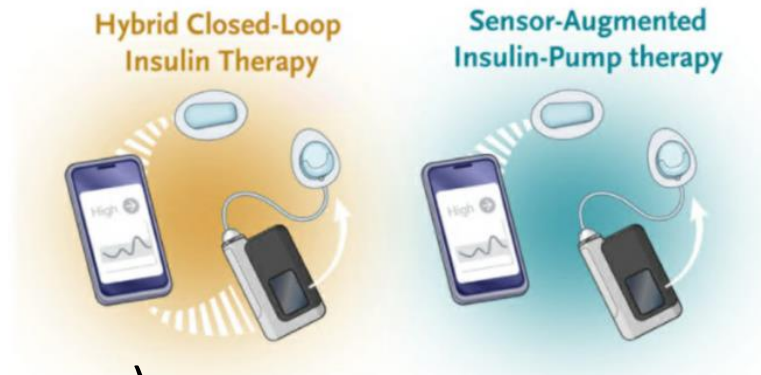
- Closed-loop **lessened the physical and mental demands** of diabetes management, enabling them to feel more normal and sleep better.
- By virtue of spending increased time-in-range, women also **worried less** about risks to their baby and being judged negatively by health care professionals.
- Women emphasized that attaining pregnancy glucose targets **still required ongoing effort** from themselves and the health care team.
- All women reported **more enjoyable pregnancy experiences** as a result of using closed-loop; some also noted being able to remain longer in paid employment.

“It's definitely took the worry away for me, 'cause I'm quite active in the day with my kids, so if I'm dipping low and I'm busy with the kids, I'm then alerted before anything goes wrong”

“[Without the closed-loop] I wouldn't have done as much as what I done. I would have stopped work a lot more sooner than what I did especially when you're self-employed, it does make a helluva lot of difference.”

“It's nice that somebody else can look at this data... they can see the graph of what's going on, how it's happening, how much insulin I've had. So because they've got all that data, they can then tell me the exact thing that I need to do, which then sorts it out straightaway.”

Closed-loop in older adults

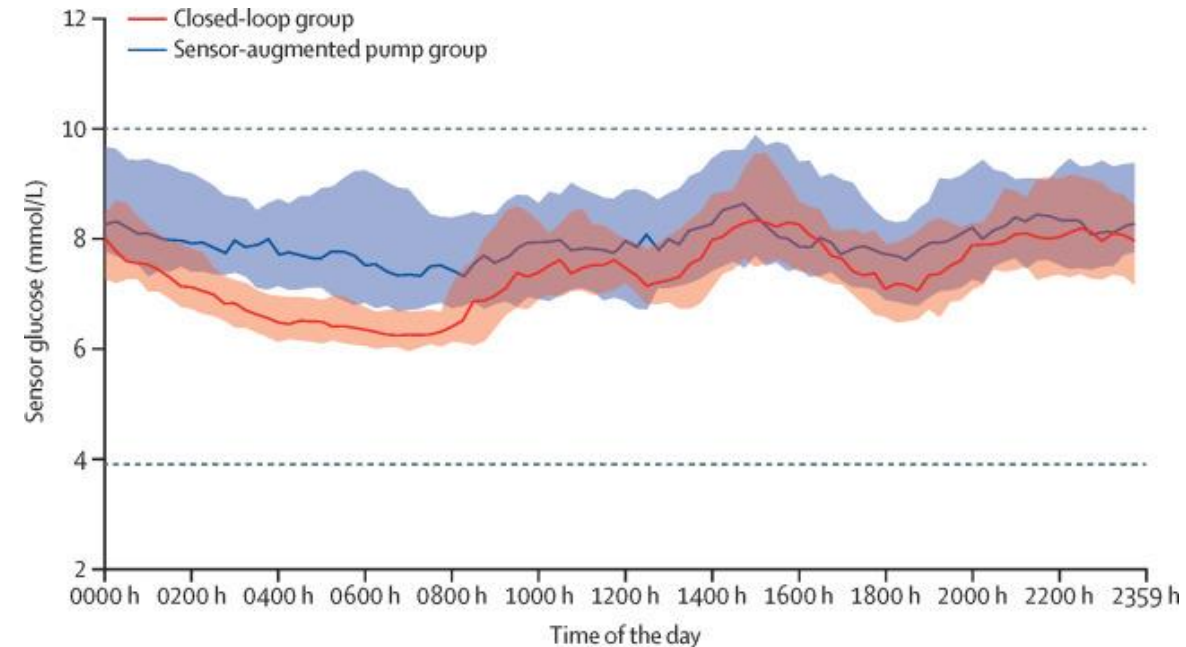


16 week crossover RCT:

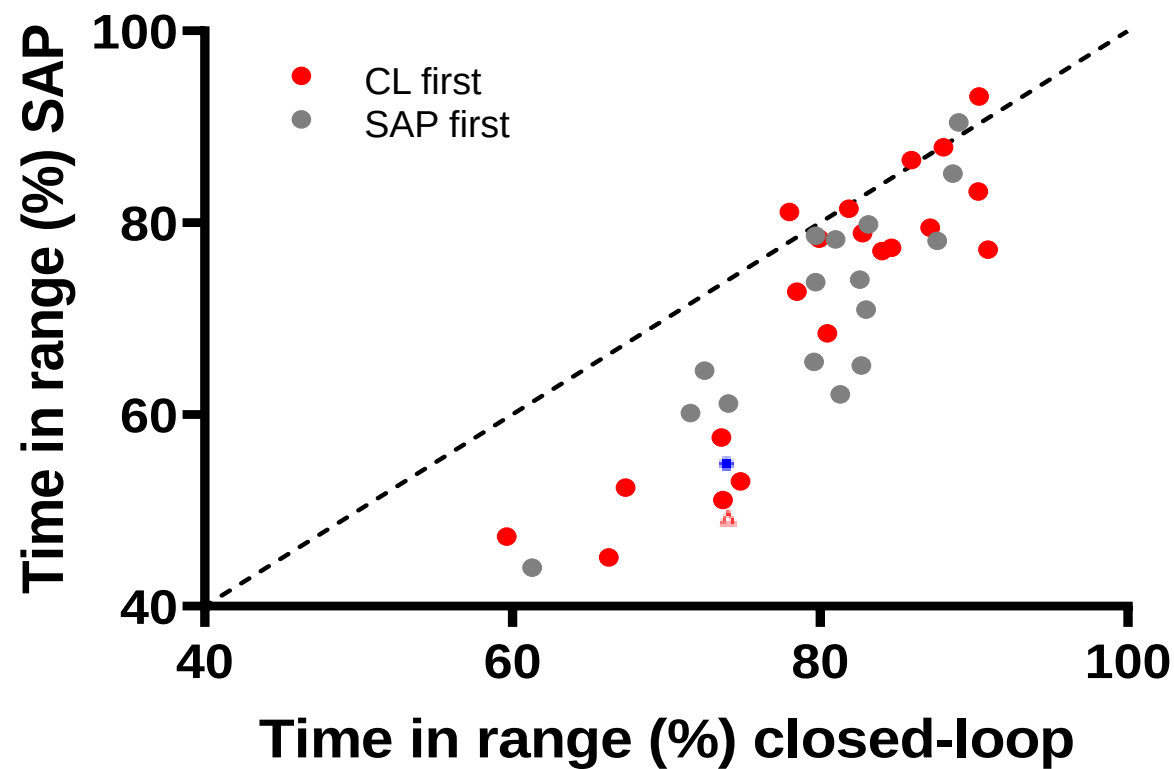
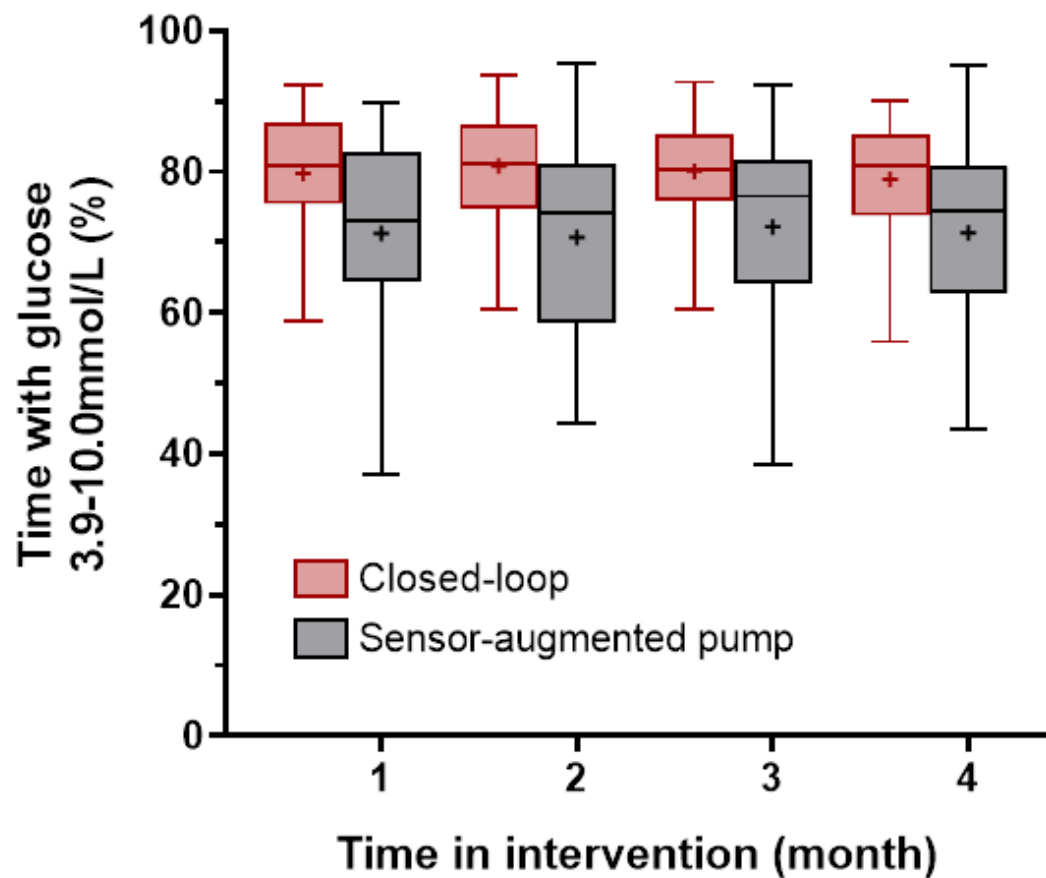
- Adults aged ≥ 60 y (n=37)
- Multinational (4 sites in UK and Europe)
- Baseline HbA1c: 7.4% (57mmol/mol)

Results

- $\uparrow$ time in range - 80% v 71%
- $\downarrow$ time in hyperglycaemia - 17% v 21%
- $\downarrow$ HbA1c - 6.7% v 6.9%
- **No increase in time in hypoglycaemia**



CamAPS FX: older adults 60 years and above



CamAPS FX: Real world analysis

	Overall	≤ 6 years	7 – 14 years	15 – 21 years	22 – 64 years	≥ 65 years
Users (n)	1805	214	203	95	820	43
Observation period (days)	84.0 (54.0, 118.0)	95.0 (61.0, 122.0)	84.0 (55.5, 117.0)	77.0 (47.5, 116.0)	88.0 (58.0, 124.0)	81.0 (59.5, 127.0)
Age (years)	30.2±19.3	3.8±1.5	10.3±2.2	17.3±2.0	41.4±10.9	69.2±3.4
Total daily insulin (U/day)	37.3 (20.8, 5.2)	11.2 (7.6, 16.0)	30.8 (21.7, 43.3)	55.9 (43.4, 76.6)	42.8 (29.9, 62.3)	42.3 (30.4, 54.4)
Time using closed-loop (%)	94.7 (90.0, 96.9)	95.6 (92.6, 97.1)	93.9 (89.0, 96.4)	93.2 (84.5, 95.0)	94.9 (90.4, 96.9)	96.1 (93.7, 97.4)
Mean glucose (mmol/L)	8.4±1.1	8.8±1.1	8.5±1.1	8.7±1.2	8.2±1.1	7.7±0.8
Glucose SD (mmol/L)	3.1±0.7	3.4±0.7	3.3±0.8	3.5±0.9	2.9±0.7	2.4±0.5
Glucose CV (%)	36.2±5.5	38.7±4.5	38.9±5.5	39.5±5.9	35.1±5.1	30.9±4.1
GMI (%)	6.9	7.1	7	7.1	6.9	6.6
Percentage of time with glucose						
3.9-10.0 mmol/L	72.6±11.5	66.9±11.7	70.5±10.4	68.9±11.2	74.2±11.3	81.8±8.7
>10.0 mmol/L	24.7±11.8	29.7±12.0	26.3±10.7	28.5±11.5	23.3±11.8	16.4±9.1
>13.9 mmol/L	5.2 (2.5, 9.4)	7.9 (4.2, 13.4)	7.1 (3.9, 10.5)	8.6 (4.6, 13.7)	4.3 (1.9, 7.8)	1.8 (0.8, 3.2)
<3.9 mmol/L	2.3 (1.3, 3.6)	3.0 (1.8, 4.5)	2.9 (1.8, 4.3)	2.2 (1.3, 3.5)	2.1 (1.1, 3.3)	1.3 (0.7, 2.6)
<3.0 mmol/L	0.4 (0.2, 0.7)	0.5 (0.3, 0.9)	0.5 (0.3, 0.9)	0.4 (0.2, 0.7)	0.3 (0.1, 0.6)	0.1 (0.1, 0.4)
Data are mean±SD or median (IQR). SD=standard deviation. CV=coefficient of variation. GMI=glucose management indicator.						

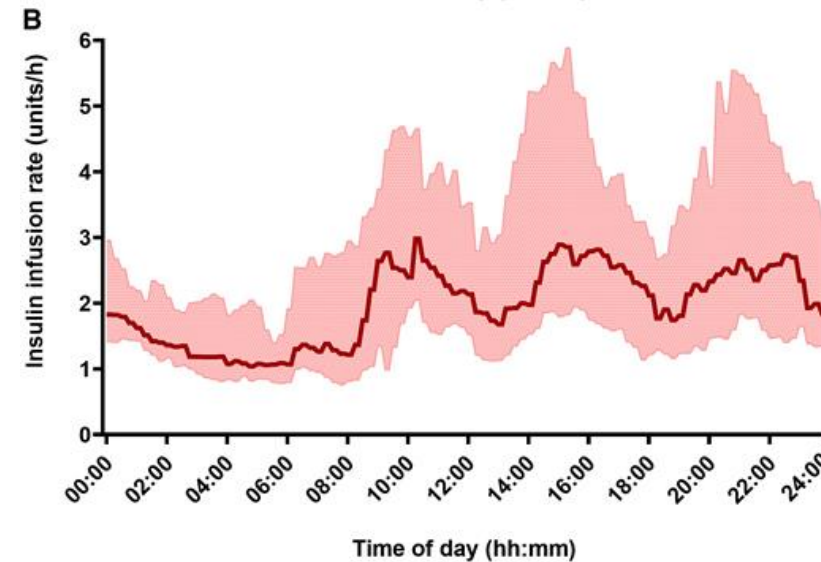
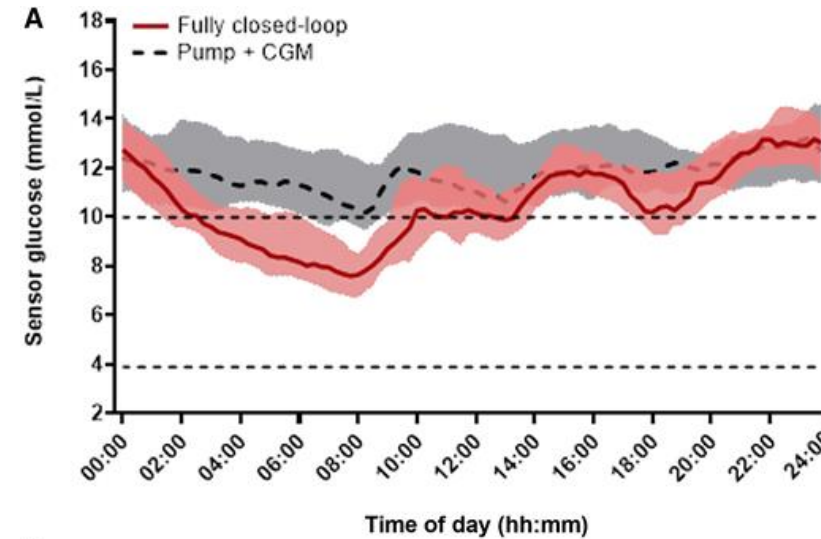
Fully closed-loop for T1D

8 week crossover RCT:

- Adults with HbA1c $\geq 8.0\%$ (n=36)
- Fully closed-loop v pump + sensor
- Single centre (Cambridge)
- Baseline HbA1c: 9.2% (77mmol/mol)

Results

- Time in target: $\uparrow 12$ percentage points
- Mean glucose: $\downarrow 1.4$ mmol/l
- Time < 3.9 mmol/l: no change
- HbA1c: $\downarrow 0.5$ percentage points



Android smartphone
hosting CamAPS HX

Psychosocial impact of FULLY closed-loop for T1D

- Interviewees reported enjoying a **reduction in diabetes burden, freed-up mental capacity and improved mood**.
- All were happy with **overnight glycaemic control**, with the majority reporting benefits on sleep.
- While experiences of post-prandial glucose control varied, all found **mealtimes easier** and less stressful, particularly when eating out.

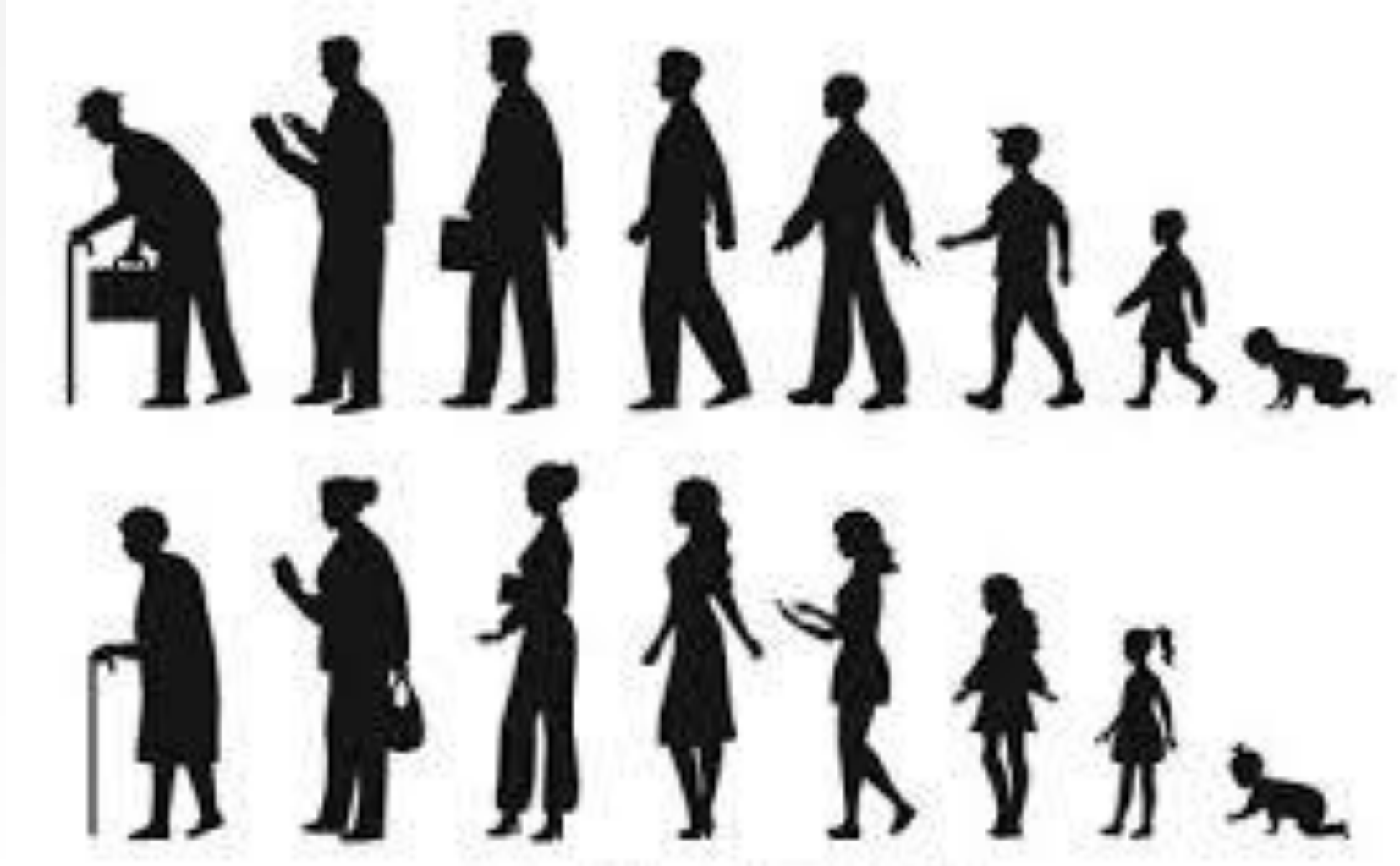
In adults with type 1 diabetes, use of a fully closed-loop insulin delivery system had significant quality-of-life benefits and provided a welcome break from the day-to-day demands of living with diabetes.

Freedom to eat without stressing over carb counting particularly in social situations

The amazing difference it had on my mood and quality of life. Diabetes worked around my life rather than my life around diabetes. It made me feel 'normal' – very clever system

Not having to carb count or feel guilty about miscalculating / forgetting a bolus

Who needs closed-loop?



What next for closed-loop in T1D?

- **Ensuring equitable access**
 - HCP training
- Fully closed-loop systems:
 - Ultra-rapid insulins
 - Adjuncts
 - Dual hormone approaches
 - Additional wearables
- Increased interoperability

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

Technology appraisal guidance | TA943 | Published: 19 December 2023



Breakthrough T1D requests letters of intent for:
Development of devices and drugs for fully automated insulin delivery at meals



Funders and supporters



- Our study participants and families
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Cambridge Artificial Pancreas research group

