Institute of Metabolic Science

NHS
Cambridge University Hospitals
NHS Foundation Trust

Hybrid Closed Loop
What Dietitians need to know

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Disclosures

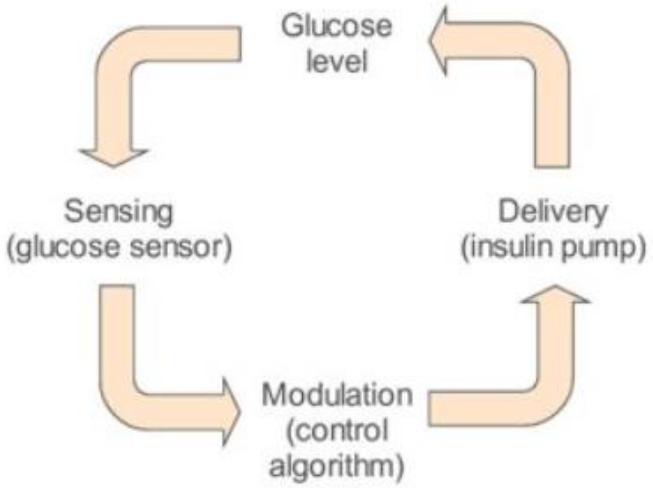
- Member of Medtronic advisory board
- Director of Ask Diabetes Ltd - providing training and research support in health care settings
- Received training honoraria from Medtronic, Sanofi and Dexcom & consulting fees for CamDiab.

Learning Objectives

By the end of this session the aim is that you will:

- Have increase awareness of the different types of closed loop systems commercially available along with the evidence base
- Understand the adjustable's of each system
- Have an appreciation of the training components and differences between management compared to usual pump therapy
- Appreciate the importance of carb counting and bolus timing with HCL
- Have an awareness of strategies to manage very young children considering dilute insulin use, breast feeding, weaning and reluctant eating.

Components of a hybrid closed-loop insulin delivery



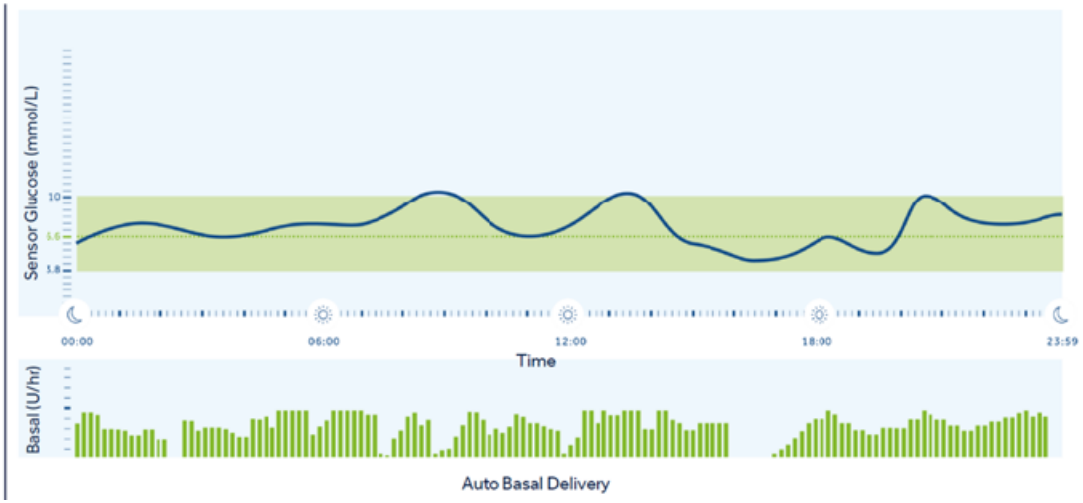
All systems have:

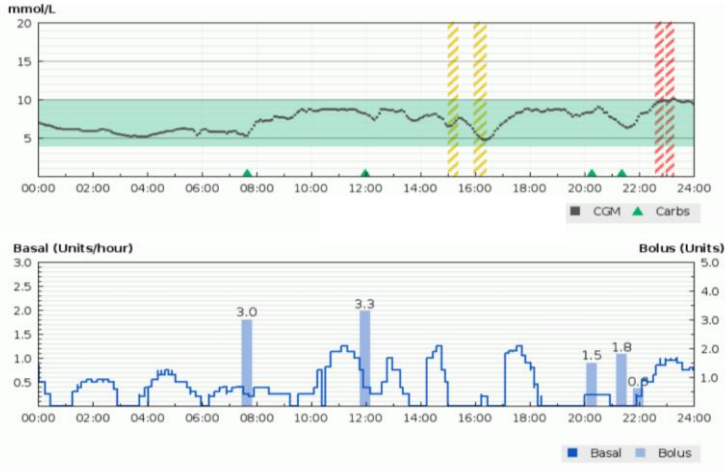
- an insulin pump
- a continuous glucose sensor
- a control algorithm either embedded in the insulin pump itself or housed in an app downloaded on to a smartphone
- A platform for uploading and viewing data

How does Hybrid closed-loop work?

Closed loop automates insulin delivery by

- Switching off normal basal insulin
- uses small bolses of insulin delivered every few minutes
- Responding according to sensor glucose levels
- Systems for type 1 diabetes are currently hybrid meaning meal boluses are still needed.





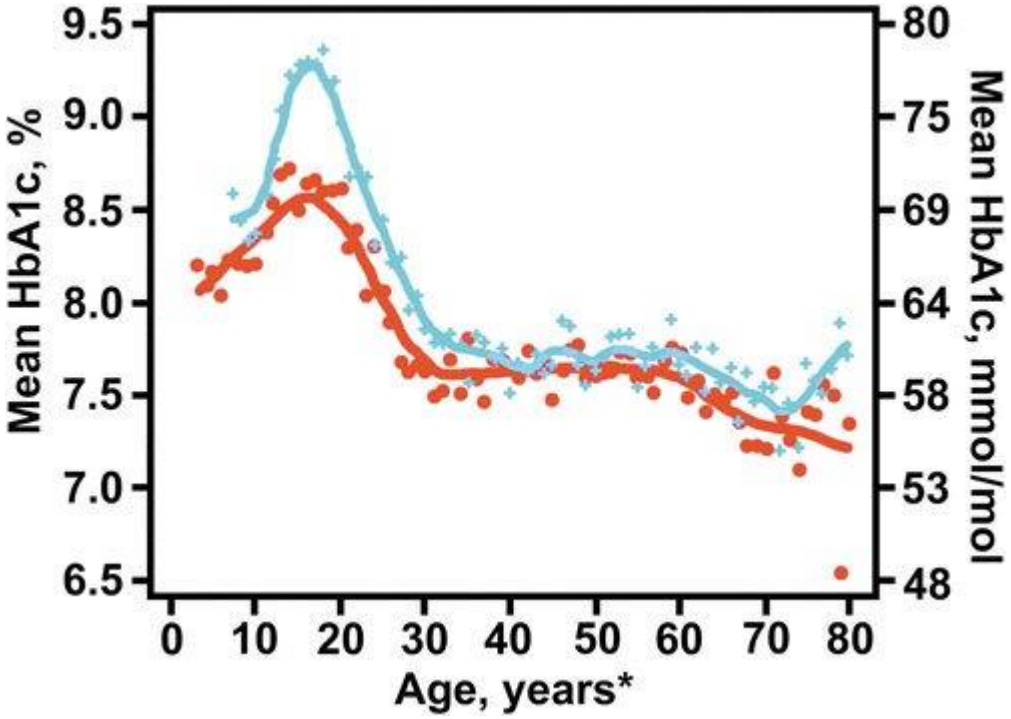
Why do we need Closed-loop ?

- Data from the National Paediatric Diabetes Audit (2018/2019)*showing mean HbA_{1c} of 64mmol/mol in children with type 1 diabetes versus the NICE recommended target of 48mmol/mol.

- Data from the National Diabetes Audit in England and Wales** shows that less than 31% of adults with type 1 diabetes achieve the recommended target HbA_{1c} of less than 58mmol/mol

*Royal College of Paediatrics and Child Health. National Paediatric Diabetes Audit. 2018-2019 https://www.rcpch.ac.uk/work-we-do/quality-improvement-patient-safety/national-paediatric-diabetes-audit.
**NHS Digital. National Diabetes Audit. 2021. https://digital.nhs.uk/data-and-information/publications/statistical/national-diabetes-audit

Why do we need Closed-loop ?



2010–2012 cohort

2016–2018 cohort

✓**Other priorities: work, school, college**

✓ **Busy lifestyles**

✓ Discretion

✓ Exercise / stress

✓ Engagement

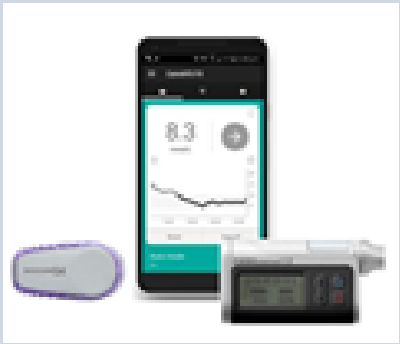
Nicole C. Foster, Roy W. Beck, et al for the T1D Exchange Clinic Network.Diabetes Technology & Therapeutics.Feb 2019.66-72

Why do we need Closed-loop ?

- Hybrid Closed-loop insulin delivery has been shown to be safe & effective in:
  - Improving time in range
  - Reducing the risk of hypoglycaemia
  - Reducing the burden of diabetes

In people with Type 1 diabetes

Commercially available Hybrid closed-loop systems (Sept 2021)

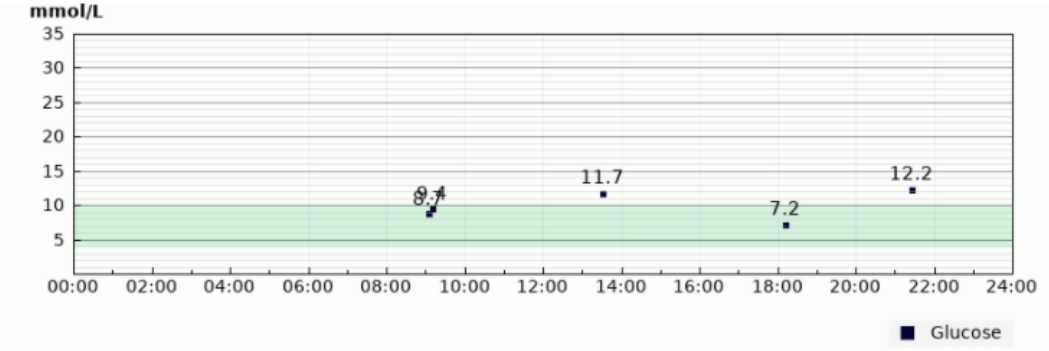
Medtronic 670G	Medtronic 780G	Control-IQ	CamAPS FX
			
Licenced from age 7		Licenced age 6	Licenced age 1

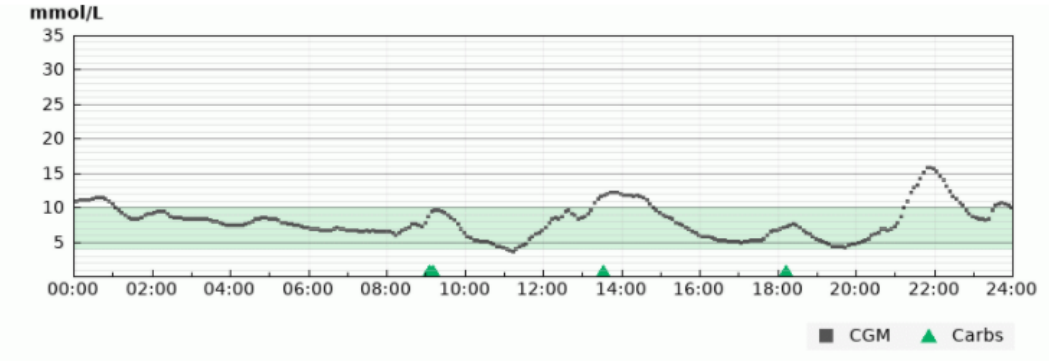
https://www.bdcpantherdiabetes.org/

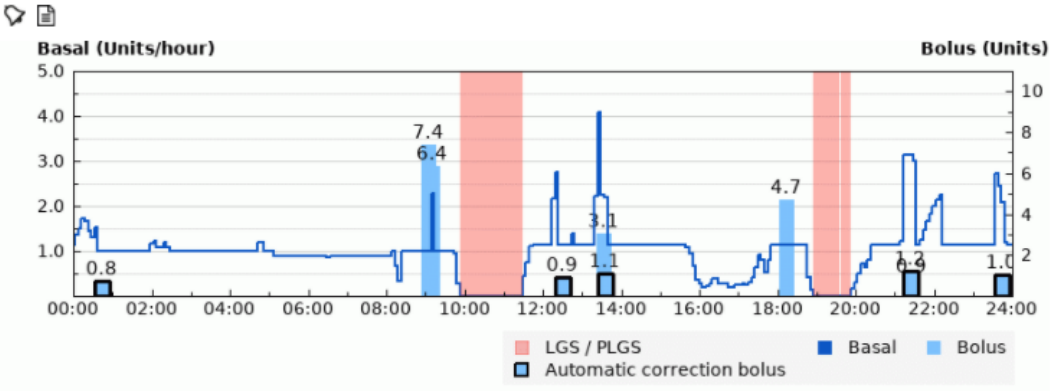
Medtronic 780G

Tandem T-Slim with control IQ

Tuesday 5/25







Bolus 54%
27.5 U

Basal 46%
23.1 U

Basal

Time	U/h
00:02	1.364
00:07	1.499
00:12	1.724
00:17	1.654
00:22	1.449
00:27	1.319
00:32	1.525
00:37	1.000
01:57	1.171
02:02	1.230

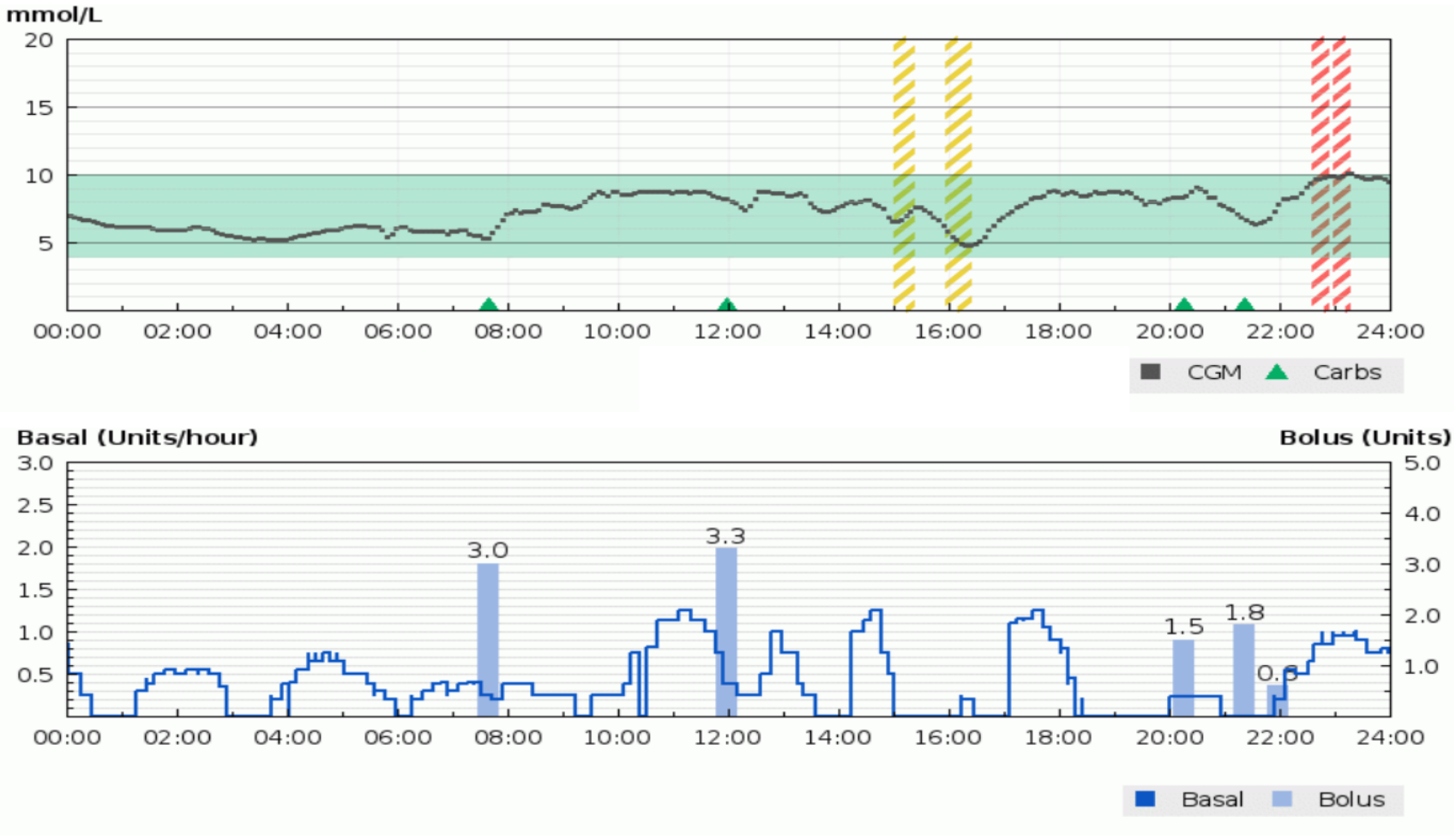
Bolus Expand

Time	U
00:32	0.75
(Corr:	0.75)
(IOB:	1.11)
09:05	7.40
(Corr:	1.04)
(Meal:	6.36)
09:11	6.36
(Meal:	6.36)
(IOB:	7.43)
12:19	0.90

Carbohydrates

Time	
09:05	35g
09:10	35g
13:32	20g
18:13	30g

CamAPS FX

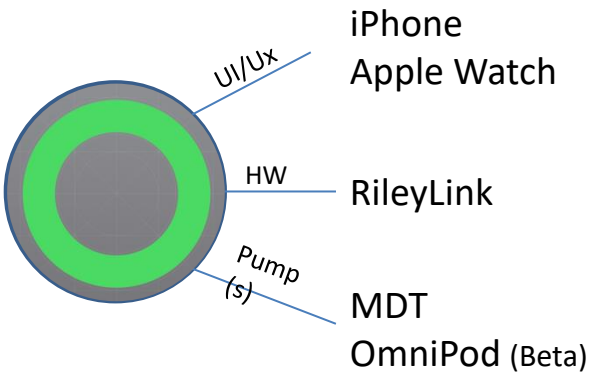

mmol/L
20
15
10
5
00:00
02:00
04:00
06:00
08:00
10:00
12:00
14:00
16:00
18:00
20:00
22:00
24:00
CGM
Carbs
Basal (Units/hour)
Bolus (Units)
3.0
2.5
2.0
1.5
1.0
0.5
5.0
4.0
3.0
2.0
1.0
3.0
3.3
1.5
1.8
0.6
Basal
Bolus

System comparisson

Comparison

	CamAPS FX	Tandem Control IQ	Medtronic 670G / 780G
Manufacturer	UK	USA	USA
Age	1 year up (incl pregnancy)	6 years up	7 years up
Factory calibration	✓	✓	
Always in automode	✓	✓	
System setup	TDD, weight	TDD, weight, ICR, CF, basal rate	TDD, weight, ICR, CF, basal rate
Adaptive learning	Overall, diurnal, meals	Based on basal	Overall
Bolusing from phone	✓		
Personal glucose target	4.4 – 11 mmol/L	Night 6.1 - 6.7 mmol/L	780G: 5.5, 6.1, 6.7 mmol/L
Ease-Off / Activity mode	Now and planned	Now	Now
Boost mode	Now and planned	Sleep	
Remote monitoring	SMS (Follow 2021)	Follow	780G: ✓
Automated cloud upload	Diasend (Clarity 2021)		780G: ✓
Insulin	Rapid and Ultra-rapid	Rapid	Rapid

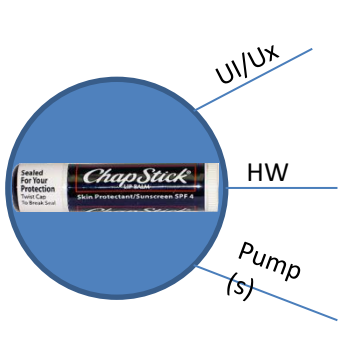
DIY Systems



iPhone
Apple Watch

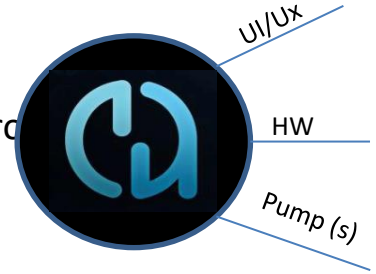
RileyLink

MDT
OmniPod (Beta)



Pump
Pebble
Watch
Linux micro
computer

MDT



Android Phone
SmartWatch

None

Dana R
Dana RS
Combo
omnipod
Insight
Virtual Pump

DIY Loop OpenAPS AndroidAPS

- not approved by regulatory bodies
- some concern from diabetes healthcare providers over the lack of safety data & use of off licence and out of warranty pump and CGM devices
- Retrospective data which demonstrates improved mean glucose, reduction in HbA_{1c} and increased time in range

Kesavadev J, Srinivasan S, Saboo B, et al. The Do-It-Yourself artificial pancreas: a comprehensive review. Diabetes Therapy. 2020;11(6):1217-35.
Lum JW, Bailey RJ, Barnes-Lomen V, Naranjo D, Hood KK, Lal RA, et al. A real-world prospective study of the safety and effectiveness of the loop open source automated insulin delivery system. Diabetes Technol Ther. 2021 May;23(5):367-375.

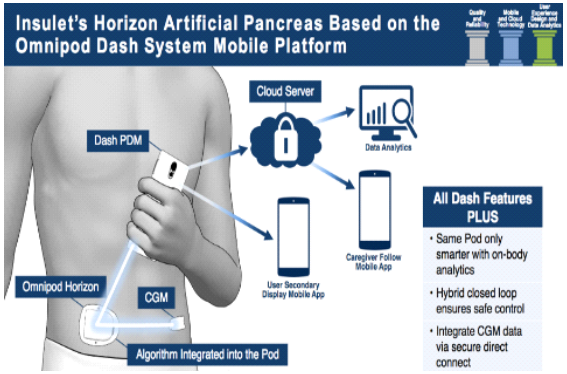
Future developments

Diabeloop

Recently launched in Germany with Roche pump

Adjuncts: Basal insulin / SGLT2

Dual hormone systems: glucagon / Pramlintide



Insulet

Tidepool

Beta Bionics

Education & Training

- Translating benefits observed in clinical trials in to clinical benefit will require a structured approach to training of both HCP's and system users
- Important to understand settings that can be adjusted in each system
- important to be able to interpret the data on the relevant platform (users & HCP's)
- Appreciation of differences between HCL systems and standard pump therapy

Understanding what can be adjusted

	Medtronic 780G	Control-IQ	CamAPS FX
Initialisation	Basal infusion rates	Total daily insulin dose and weight	Total daily insulin dose and weight
Run-in required	Yes. Minimum 48 hours	No	No
Adjustable settings influencing glucose control	• Insulin to carb ratio • Active insulin time • Glucose target	• Basal infusion rates • Insulin to carb ratio • Correction factor	• Insulin to carb ratio • Glucose target
Settings which do not impact closed-loop insulin delivery	• Basal infusion rates • Correction factor	• Active insulin time	• Basal infusion rates • Correction factor • Active insulin time
Corrective insulin	Automated correction boluses delivered hourly if glucose predicted to rise > 10.0mmol/L aiming for glucose of 6.7 mmol/L.	Automated correction boluses delivered hourly providing up to 60% of calculated correction factor to a target of 6.1 mmol/L Optional manual correction boluses	Automated correction boluses delivered as modulation of basal rate. Optional manual correction boluses
Calibration requirements	Yes (4-6 per day)	No	No

Messer LH, Berget C, Forlenza GP. A clinical guide to advanced diabetes devices and closed-loop systems using the CARES paradigm. Diabetes Technol Ther. 2019;21(8):462-9.

Training – the basics are important

- **Accurate Carbohydrate counting** and **consideration of portion size and type of carbohydrate**

- Appropriate pump set up.
  - The safety default for closed loop systems is to revert back to the usual pump basal rate if there is a problem with the system
  - Systems use the insulin pumps bolus calculator to establish bolus dose

- Calibration technique and timing
  - If using a system which has glucose sensors which require calibration it is important to calibrate well.

- Changing set regularly – 2-3 days due to algorithm learning

- Follow- up. It is not Plug & Play!

Carbohydrate counting

- Accurate carbohydrate counting remains as important as ever
- Consider portion size
- Consider the type of carbohydrate
- Pre meal bolus

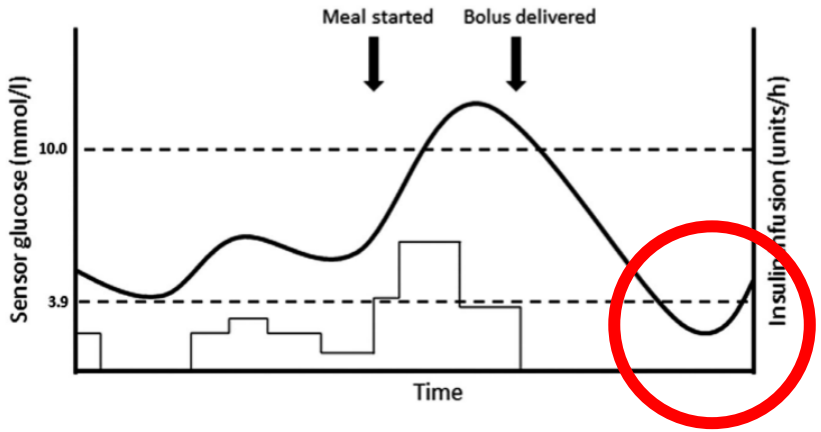
Faster insulins could reduce the importance in the future

Key differences to standard pump therapy

- Timing of meal bolus
- Managing hypoglycaemia
- Managing Exercise
- Managing Alcohol
- Managing illness
- Suspending the pump if not attached for more than 15 minutes

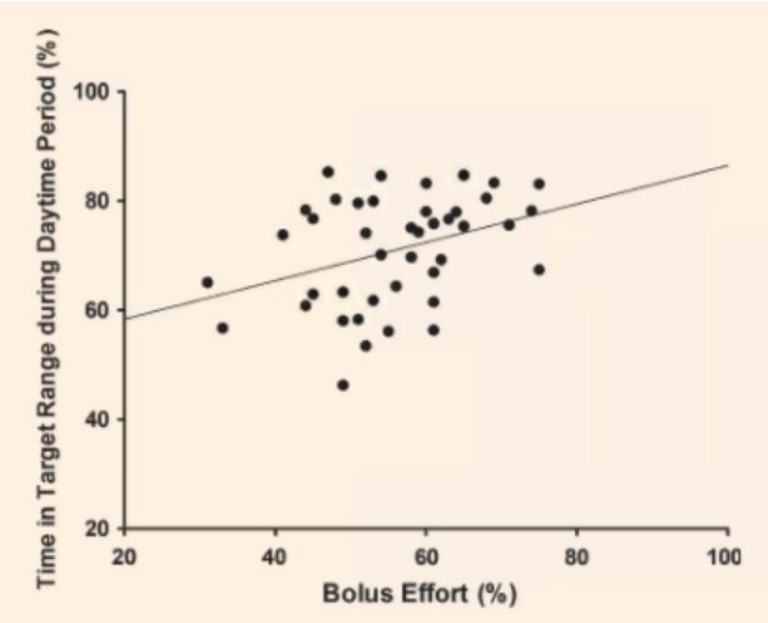
Bolus Behaviour

- Aim to bolus 10 – 15 minutes prior to eating
- Late bolus's can lead to post meal hypoglycaemia



Bolus Behaviour

More (accurate) bolusing = better glucose control



DIABETICMedicine

DOI: 10.1111/dme.13436

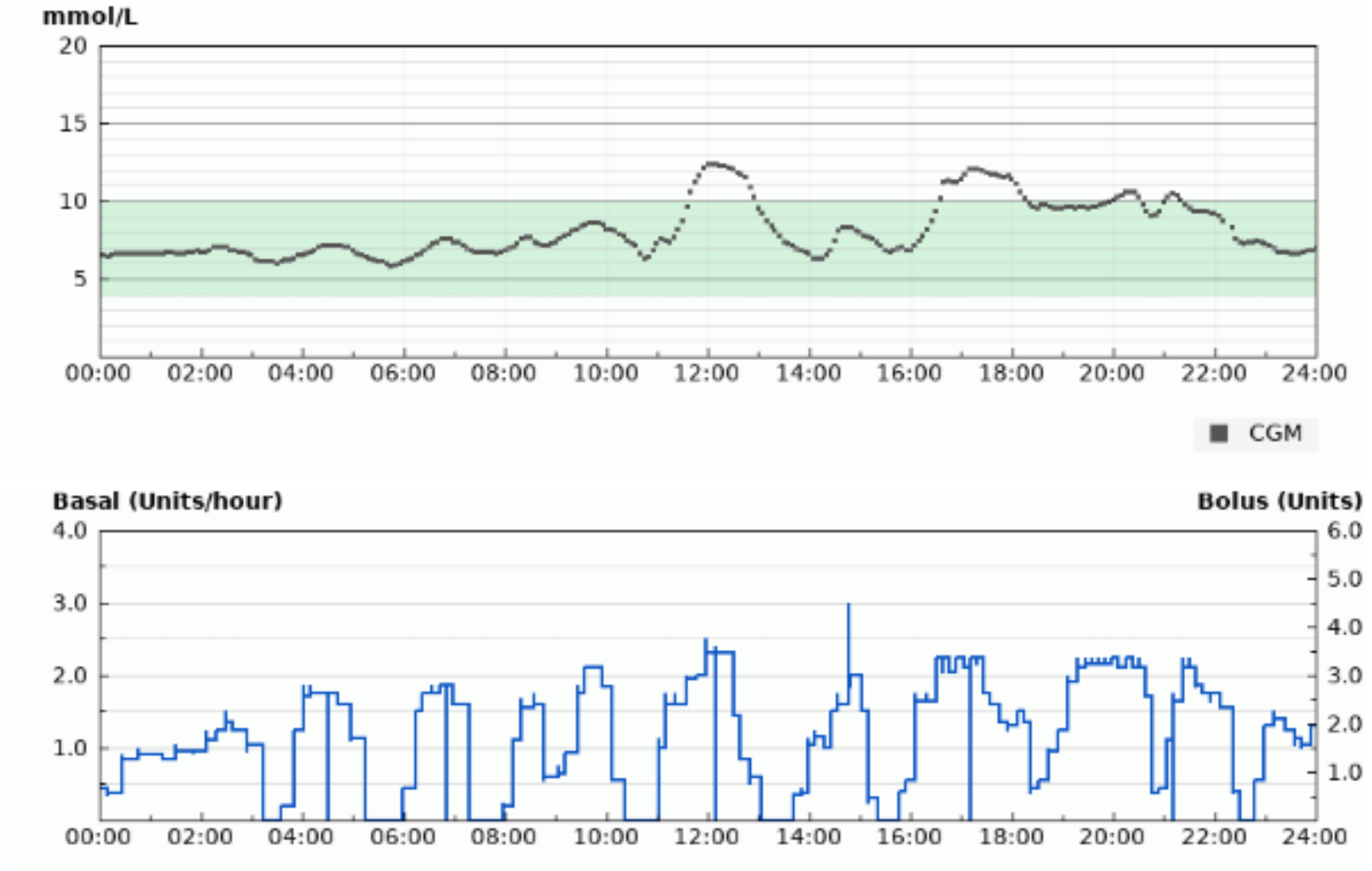
Short Report: Treatment

Bolusing frequency and amount impacts glucose control during hybrid closed-loop

L. Bally[1,2,3,*], H. Thabit[1,2,*], Y. Ruan [1,4], J. K. Mader[5], H. Kojzar[5], S. Dellweg[6], C. Benesch[6], S. Hartnell[2], L. Leelarathna[7], M. E. Wilinska[1,4], M. L. Evans[1,2], S. Arnolds[6], T. R. Pieber[5] and R. Hovorka[1,4]

Conclusion: More frequent bolusing and higher proportion of insulin delivered as bolus during hybrid closed-loop use correlated positively with time glucose was in target range. **This emphasises the need for user input and educational support to benefit from this novel therapeutic modality.**

Bolus Behaviour



Extended / dual wave bolus's

what to do for meals that would previously have required a dual or extended bolus?

- T-Slim allows extended boluses
- Other systems suggest splitting bolus as previously eg 70% up front then leaving CL to deal with the rest

- CamAPS FX has a "slowly absorbed meal" function

Less Hypo treatment is usually required

- Less hypo treatment may be required due to low insulin delivery before a hypo.

- Take into account insulin delivered in the previous 90 minutes

- Use the direction of fall arrows as a guide
  - 4 gms of carbohydrate if ↘ Eg 1 jelly baby
  - 8 gms of carbohydrate if ↓ Eg 2 jelly babies

Managing Exercise

- Temporary increased targets or reduction functions to reduce the aggressiveness of the system should be used.
  - Ideally starting 90 minutes prior to the activity.
  - Pre-programable in some systems.

- Avoid Pre-exercise Carbohydrate loading
  - can cause rise in closed-loop driven insulin delivery
  - Often better to “drizzle” in carbs as required

- Suspending insulin delivery for a defined period of time may be required for long duration cardiovascular exercise

- Individualised planning is important

Managing Alcohol

- Consuming a bed time snack as a strategy to avoid overnight hypoglycaemia is unlikely to be helpful.
- Closed-loop insulin delivery will rise with rising glucose level from the snack
- Consider using a temporary increased target or use functionality to reduce aggressiveness

Managing illness

- Allow closed-loop algorithm to manage non-significant hyperglycaemic glucose excursions
  - Some systems have a boost function to make the algorithm more aggressive for a defined period of time.

DO NOT used closed loop if

- unwell with ketones - follow usual sick day rules

A word on Fat and Protein Counting

- Evidence of benefit is lacking generally and no evidence in HCL

- Methods of counting often complex

- The nature of CL systems mean that they mop up additional glucose hours after meal bolus

- Understanding which meals can be higher in fat & protein may help identify meals which may benefit from reduced up front bolus or slowly absorbed meal setting.

Low carb diets not recommended for children with Diabetes

Diabetes UK position Statement 2017

Reluctant eaters / weaning

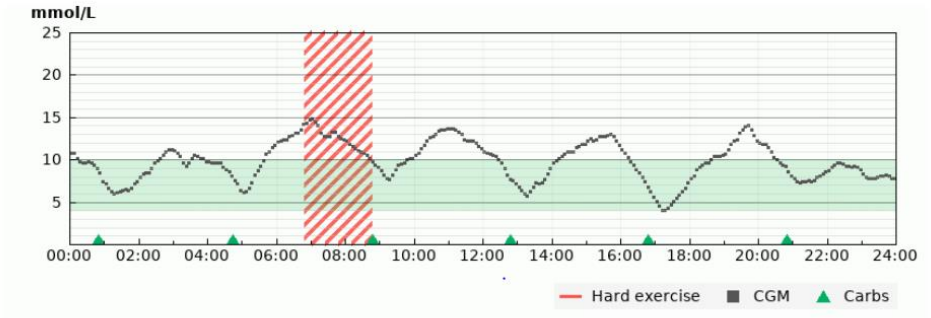
- Bolus for the amount you can guarantee 10-15 mins pre meal
- Top-up' as soon as the child has finished the meal
- Do not 'top up' too late – can cause system to compensate with basal and lead to a hypo
- Utilise trend arrows and see if carb replacement is needed for a meal that was unfinished – CL can back off to nothing but can't suck the insulin back out!

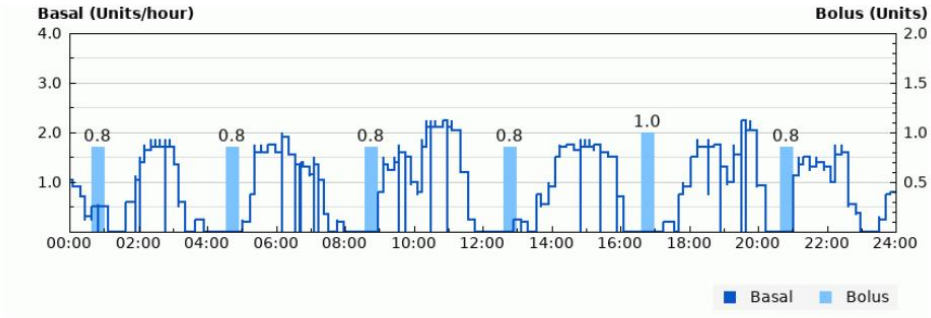
- Keep to a routine – 3 meals and 1-2 snacks/day (snacks at set times)
- Limit mealtimes to 30 minutes

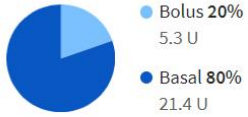
HCL in the very young

- Experience of using CamAPs FX in children as young as 5 weeks old
- Total Daily doses of less than 7.5 units per day require dilute insulin (usually 10% but also used 5%)

Monday 13/9







Basal

Time	U/h
00:06	0.900
00:06	1.000
00:18	0.700
00:18	0.750
00:26	0.300
00:26	0.250
00:38	0.500
00:38	0.250
00:50	0.000
00:50	0.500

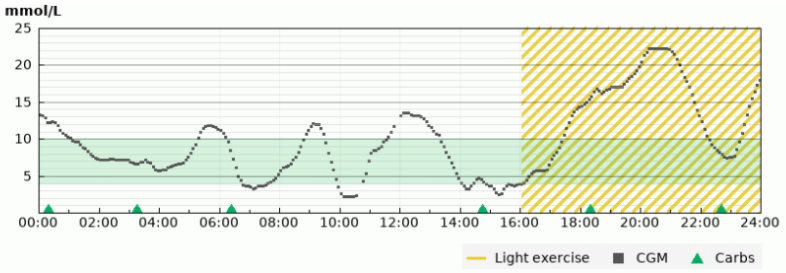
Bolus

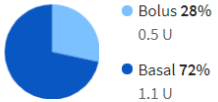
Time	U
00:49	0.85
(Meal:	0.85)
04:44	0.85
(Meal:	0.85)
08:47	0.85
(Meal:	0.85)
12:48	0.85
(Meal:	0.85)
16:48	1.00
(Meal:	1.00)

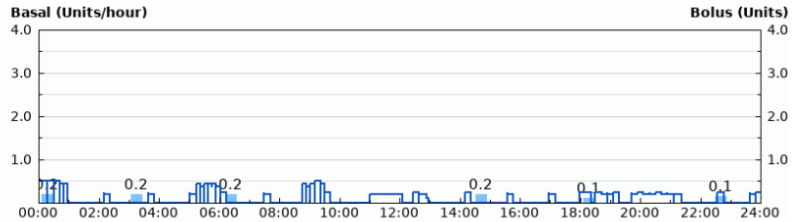
Carbohydrates

Time	
00:49	6g
04:43	6g
08:47	6g
12:48	6g

Dilute Insulin

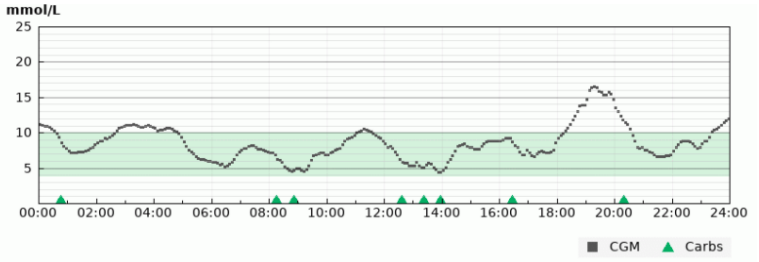


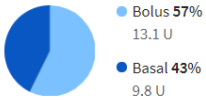


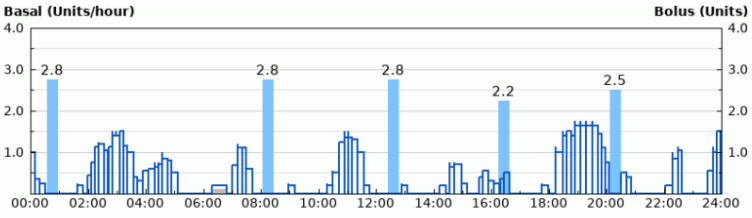


Basal	
Time	U/h
00:06	0.500
00:18	0.000
00:18	0.500
00:30	0.000
00:30	0.500
00:42	0.000
00:42	0.380
00:42	0.450
00:50	0.000

Bolus
Time
00:18
(Mea
03:15
(Mea
06:24
(Mea
14:44
(Mea
18:19







Basal	
Time	U/h
00:10	0.000
00:10	0.350
00:10	0.380
00:18	0.000
00:18	0.250
00:30	0.000
01:38	0.200
01:38	0.250
01:50	0.000
01:58	0.380

Bolus
Time
00:46
(Meal:
06:18
(Ext.
08:16
(Meal:
12:36
(Meal:
16:27
(Meal:

Breast Feeding

- Successful use of CamAps FX in Breast fed babies
- 7g carbs/100ml (approx.)
- Challenge to know how much they have/will take in a feed
- Suggest conservative bolus at start of feeding

- Rough guide: 0-6 month old = 150ml/kg (then divide by the rough number of feeds in a day)
- Closed loop will manage better than the alternatives

Summary & Key Messages

- Hybrid closed-loop has been shown to be safe and effective in improving glycaemic control in children with type 1 diabetes.
- Diabetes burden has been shown to be positively impacted using hybrid closed-loop systems.
- A range of devices are commercially available and understanding their features and key differences are important.
- Translating the benefits seen in research studies into real-world settings will require a structured approach to training of both healthcare professionals and system users.

Learning Outcomes

- We have covered:
  - The different types of closed loop systems commercially available along with the evidence base
  - The features and adjustable's of the different systems
  - Training needs and specifically differences between management of HCL compared to usual pump therapy
  - The importance of carb counting and bolus timing with HCL
  - Strategies to manage very young children including dilute insulin use, breast feeding, weaning and reluctant eating.

Any Questions?