THE LANCET Diabetes & Endocrinology

Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplementary material

Tables S1 to S6 show additional information obtained during exploratory analyses and not pre-specified in the data analysis plan.

Figure S1 and S2 show details of the two severe hypoglycaemia episodes. As noted in both figures and analyses, closed loop suspended insulin delivery approximately an hour before both severe hypoglycaemia episodes occurred. Thus, no insulin was instructed to be given by the control algorithm. When communication with the pump was lost, the pump automatically reverted to its usual basal delivery rate as pre-programmed by the participant.

Table S1. Outcomes during morning period (06:00 – 11:00).

	Closed loop (n=24)	Control (n=24)	p value
Mean glucose (mmol/l)	7·9±0·7	9·0±1·0	<0·001
Time spent at glucose level (%)			
3·9 to 8·0mmol/l	55·6±8·9	35·7±8·8	<0·001
< 3·9mmol/l*	0·8 (0·31, 2·1)	1·7 (0·49, 3·1)	0·23
AUC below 3·5mmol/l* (mmol/l × minutes)	0·57 (0·03, 4·3)	2·3 (0·02, 9·9)	0·11

Data are presented as mean±SD or *median (IQR)

Table S2. Analysis of glucose control during the day-time period (07:00-23:00).

	Closed loop (n=24)	Control (n=24)	p value
Mean glucose (mmol/l)	8·9±0·9	9·4±1·1	0·003
SD of glucose (mmol/l)	2·9±0·4	2·9±0·4	0·9
Time spent at glucose level (%)			
3·9 to 10·0mmol/l	62·8±7·9	59·1±11·0	0·04
> 10·0mmol/l	33·4±10·2	38·2±12·2	0·009
< 3·9mmol/l*	1·4 (0·8, 3·0)	1·9 (1·0, 3·0)	0·28

Data are presented as mean ± SD, or *median (interquartile range)

Table S3. Insulin bolus doses during meal periods.

	Closed loop (n=24)	Control (n=24)	p value
Breakfast period (06:00-11:00)	3·0 (1·9, 3·8)	3·8 (2·4, 5·2)	<0·001
Lunch period (11:00-16:00)	4·7 (3·5, 6·8)	4·7 (4·0, 7·3)	0·097
Dinner period (16:00-00:00)	7·7 (5·5, 9·2)	8·3 (6·4, 10·0)	0·009

Data are presented as median(IQR)

Table S4. Comparison between run-in and Week 4 of control period. Data are from midnight to 07:00.

	Run-in	Control Week 4	p value
Mean glucose (mmol/l)	8·4±1·8	8·8±1·5	0·26
Time spent at glucose level (%)			
3·9 to 8·0 mmol/l	34·8±11·5	40·6±16·0	0·11
> 8·0mmol/l	51·3±19·1	55·3±18·8	0·38
< 3·9mmol/l*	7·8 (4·0, 17·0)	1·2 (0, 3·2)	0·002

Data are presented as mean ± SD, or *median (interquartile range)

Table S5. Comparison between run-in and Week 4 of control period. Data are from midnight to midnight.

	Run-in	Control Week 4	p value
Mean glucose (mmol/l)	9·0±1·3	9·1±1·2	0·9
Time spent at glucose level (%)			
3·9 to 10·0mmol/l	56·9±9·8	61·1±12·0	0·10
> 10·0mmol/l	36·1±11·7	35·4±13·6	0·78
< 3·9mmol/l*	4·6 (2·4, 7·1)	1·5 (0·9, 3·0)	0·004

Data are presented as mean ± SD, or *median (interquartile range)

Table S6. Analysis of glucose control during Week 1 and Week 4 of control period. Data are from midnight to 07:00.

|	Control Week 1	Control Week 4
Mean glucose (mmol/l)	8·9±1·6	8·8±1·5
Time spent at glucose level (%)		
3·9 to 8·0mmol/l	39·4±18·6	41·8±15·7
> 8·0mmol/l	55·5±20·5	54·5±18·1
< 3·9mmol/l*	1·7 (0·0, 7·6)	1·2 (0·0, 3·2)

Data are presented as mean ± SD, or *median (interquartile range)

Figure S1. Additional information related to the first of the two severe hypoglycaemia episodes.

Sensor glucose is denoted by red circles (recorded every 10 minutes during open loop and every minute during closed loop), capillary glucose measurements by red squares, delivered insulin by thick blue line, planned (pre-programmed but not delivered) insulin by thin blue line, carbohydrate intake by orange down-facing arrows (top of the picture), and insulin boluses by blue line at the top of the figure. Closed loop cycle is denoted by series of vertical letters (occurring every 12 minutes) representing internal diagnostic of the control algorithm.

Closed loop had stopped giving insulin from 01:39 as it predicted decreasing glucose. At 02:42, closed loop automatically reverted to open loop due to pump communication failure. Pump reverted to usual basal. Closed loop was not operational from here onwards.

Thin blue line - usual basal rate settings.
Shown for illustration.
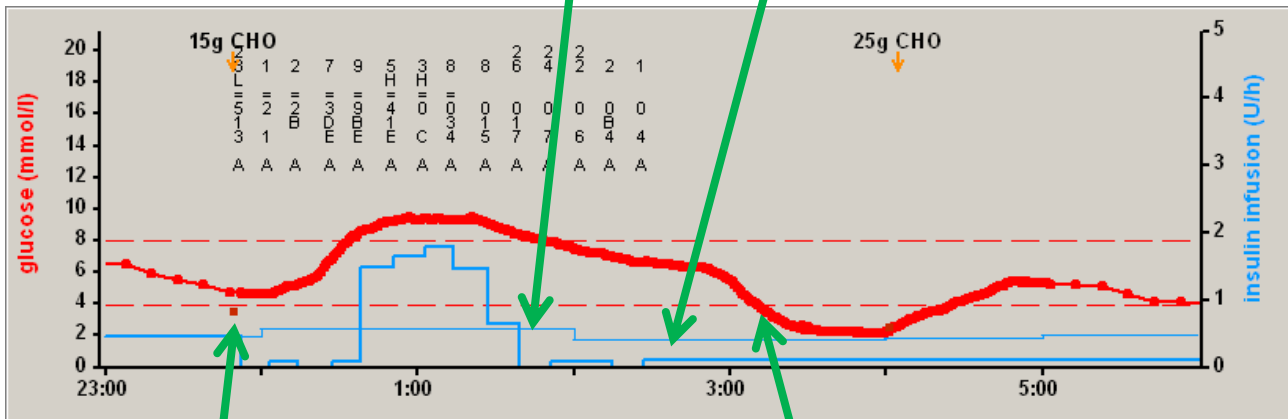
At 23:49, capillary glucose = 3.6 mmol/l. Took 15g CHO. Started closed loop at 23:52 which gave little insulin initially (thick blue line).

Patient stated that he was woken up by pump alarm stating "occlusion". At 3.10 am, patient refilled new reservoir and changed set. Primed set with 19.7 units. Hypo occurred around 4am.

Figure S2. Additional information related to the second of the two severe hypoglycaemia episodes. Algorithm/pump was only delivering little or no insulin from the start of closed loop (at all times less than the pre-programmed rate). Closed loop terminated as it lost communication with pump at 02:10. Message that closed loop terminating was acknowledged by subject immediately at 02:10. Pump reverted to participant's usual basal rate. Subject immediately tried to re-start closed loop, but failed control algorithm device was unable to communicate with pump.

Sensor glucose is denoted by red circles (recorded every 10 minutes during open loop and every minute during closed loop), capillary glucose measurements by red squares, delivered insulin by thick blue line, planned (pre-programmed but not delivered) insulin by thin blue line, carbohydrate intake by orange down-facing arrows (top of the picture), and insulin boluses by blue line at the top of the figure. Closed loop cycle is denoted by series of vertical letters (occurring every 12 minutes) representing internal diagnostic of the control algorithm.