

SUPPLEMENTARY DATA

Supplementary Table 1. Participants' baseline characteristics. Values are mean (SD) or median (interquartile range).

Characteristic	Study participants (n=12)
Gender (male/female)	5/7
Age (yrs)	15.0 (1.4)
Body Mass Index (kg/m ²)	21.4 (2.6)
HbA _{1c} (%)	7.9 (0.7)
Duration of diabetes (yrs)	5.7 (3.4, 9.4)
Duration of insulin pump use (yrs)	1.3 (0.5, 3.5)
Total daily insulin dose (U/kg)	0.9 (0.8, 1.2)
Basal insulin delivery (% of total dose)	40 (34, 53)

SUPPLEMENTARY DATA

Supplementary Table 2. Study outcomes evaluated during different time periods based on plasma glucose levels. Values are median (interquartile range).

Study Period	Time in target 71 – 180mg/dl (%)		Time less than or equal to 70 mg/dl (%)	
	Insulin pump therapy (n=12)	Closed-loop delivery (n=12)	Insulin pump therapy (n=12)	Closed-loop delivery (n=12)
Morning (08:00 to 13:00)	40 (30, 71)	77 (60, 86)	16.3 (0.0, 26.4)	15.4 (4.3, 21.4)
Afternoon (13:00 to 19:00)	57 (35, 83)	61 (50, 78)	1.9 (0.0, 12.3)	0.6 (0.0, 11.1)
Evening (19:00 to 24:00) at Day 1	82 (67, 99)	79 (40, 100)	0.0 (0.0, 2.3)	0.0 (0.0, 8.6)
Evening (19:00 to 24:00) at Day 2	79 (34, 100)	94 (52, 100)	0.0 (0.0, 0.0)	0.2 (0.0, 4.7)
Morning exercise (10:40 to 13:00)	56 (24, 70)	79 (54, 99)	22.3 (0.0, 47.2)	20.9 (0.0, 40.4)
Afternoon exercise (17:30 to 19:00)	71 (18, 95)	60 (54, 88)	0.0 (0.0, 0.0)	0.0 (0.0, 40.1)

SUPPLEMENTARY DATA

Supplementary Table 3. Study outcomes over 32 hours (from midnight on Day 1 until 8:00am on Day 3) based on continuous glucose monitor glucose levels. Data are mean (SD) or median (interquartile range).

Outcome	Insulin pump therapy (n=12)	Closed-loop delivery (n=12)	p value
Primary outcome			
Time in target 71 – 180mg/dl (%)	47 (25, 54)	74 (69, 79)	0.01
Secondary outcomes			
Mean glucose (mg/dl)	181 (59)	142 (16)	0.06
SD of glucose (mg/dl)	58 (46, 66)	50 (47, 54)	0.18
Time in target 71 – 145mg/dl (%)	24 (18, 45)	54 (46, 59)	0.02
<i>Hypoglycemia:</i>			
Less or equal 70mg/dl (%)	4.2 (0.2, 11.4)	5.2 (3.0, 7.8)	0.81
Less or equal 63mg/dl (%)	2.0 (0.0, 10.0)	3.3 (1.6, 4.8)	0.77
Low blood glucose index (unitless)	0.9 (0.1, 2.6)	1.4 (0.9, 2.1)	0.69
<i>Hyperglycemia:</i>			
Greater than 180mg/dl (%)	52.8 (16.0, 70.5)	20.4 (16.2, 21.9)	0.07
Greater than 300mg/dl (%)	1.9 (0.0, 23.1)	0.0 (0.0, 1.0)	0.08

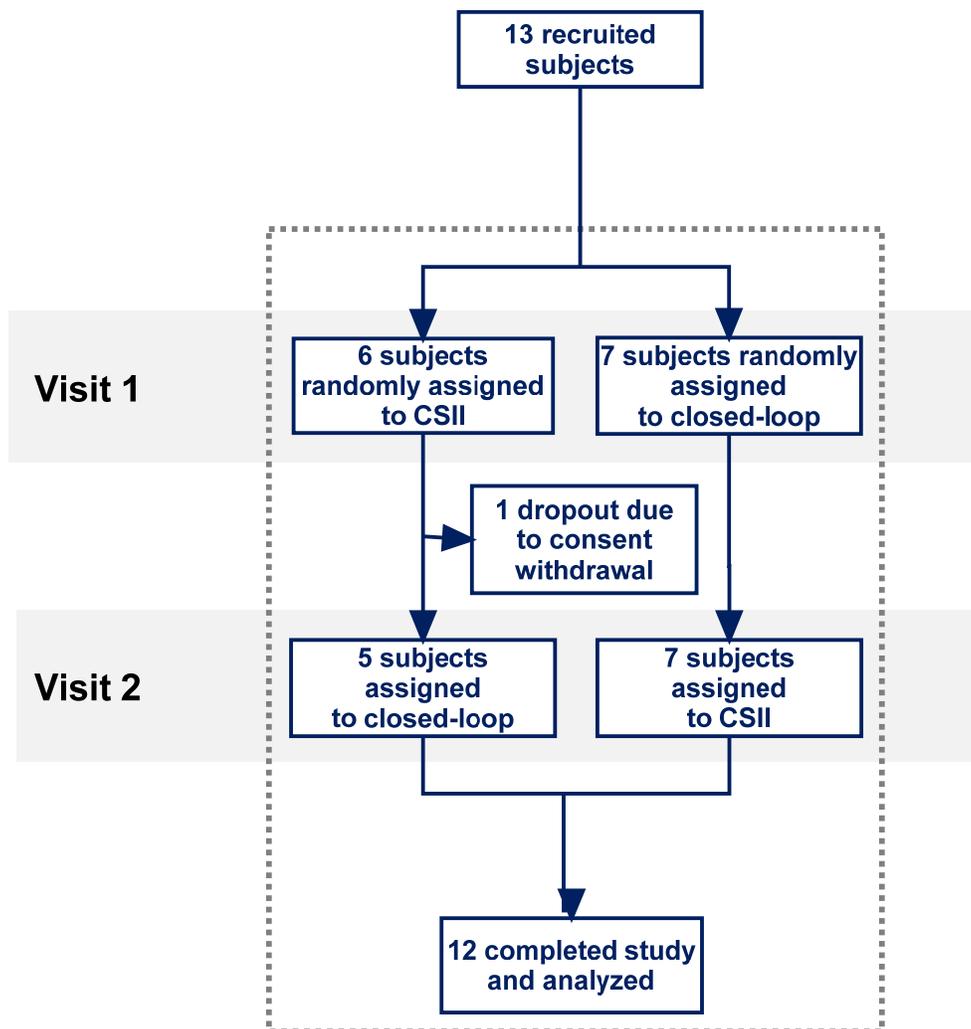
SUPPLEMENTARY DATA

Supplementary Table 4. Study outcomes during day-time (from 08:00 on Day 2 until midnight on Day 2) and night-time (first night: from midnight on Day 1 until 08:00 on Day 2; second night: from midnight on Day 2 until 08:00 on Day 3) based on continuous glucose monitoring glucose levels. Data are mean (SD) or median (interquartile range).

Outcome	First night		Day-time		Second night	
	Insulin pump therapy (n=12)	Closed-loop delivery (n=12)	Insulin pump therapy (n=12)	Closed-loop delivery (n=12)	Insulin pump therapy (n=12)	Closed-loop delivery (n=12)
Time in target 71 – 180mg/dl (%)	30 (5, 85)	100 (92, 100)	49 (32, 61)	55 (48, 71)	33 (2, 80)	96 (79, 100)
Mean glucose (mg/dl)	179 (85)	135 (20)	177 (51)	152 (19)	188 (78)	129 (21)
SD of glucose (mg/dl)	27 (18,43)	21 (15, 26)	56 (52, 71)	63 (48, 69)	23 (18, 38)	26 (18, 35)
Time in target 71 – 145mg/dl (%)	21 (0, 52)	73 (47, 87)	34 (18, 40)	38 (28, 49)	1 (0, 78)	77 (56, 94)
<i>Hypoglycemia:</i>						
Less or equal 70mg/dl (%)	0.0 (0.0, 4.4)	0.0 (0.0, 0.1)	8.2 (0.3, 12.5)	8.9 (5.6, 13.4)	0.0 (0.0, 2.4)	0.0 (0.0, 1.0)
Less or equal 63mg/dl (%)	0.0 (0.0, 1.7)	0.0 (0.0, 0.0)	2.7 (0.0, 9.7)	5.8 (3.2, 9.7)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)
Low blood glucose index (unitless)	0.0 (0.0, 1.7)	0.1 (0.0, 0.6)	1.5 (0.3, 2.7)	2.0 (1.5, 3.7)	0.0 (0.0, 1.2)	0.5 (0.1, 0.8)
<i>Hyperglycemia:</i>						
Greater than 180mg/dl (%)	35.0 (0.0, 95.4)	0.0 (0.0, 6.8)	41.4 (31.9, 61.3)	32.5 (21.7, 41.2)	64.6 (1.6, 97.5)	1.0 (0.0, 13.9)
Greater than 300mg/dl (%)	0.0 (0.0, 12.7)	0.0 (0.0, 0.0)	0.0 (0.0, 20.7)	0.0 (0.0, 2.1)	0.0 (0.0, 12.5)	0.0 (0.0, 0.0)

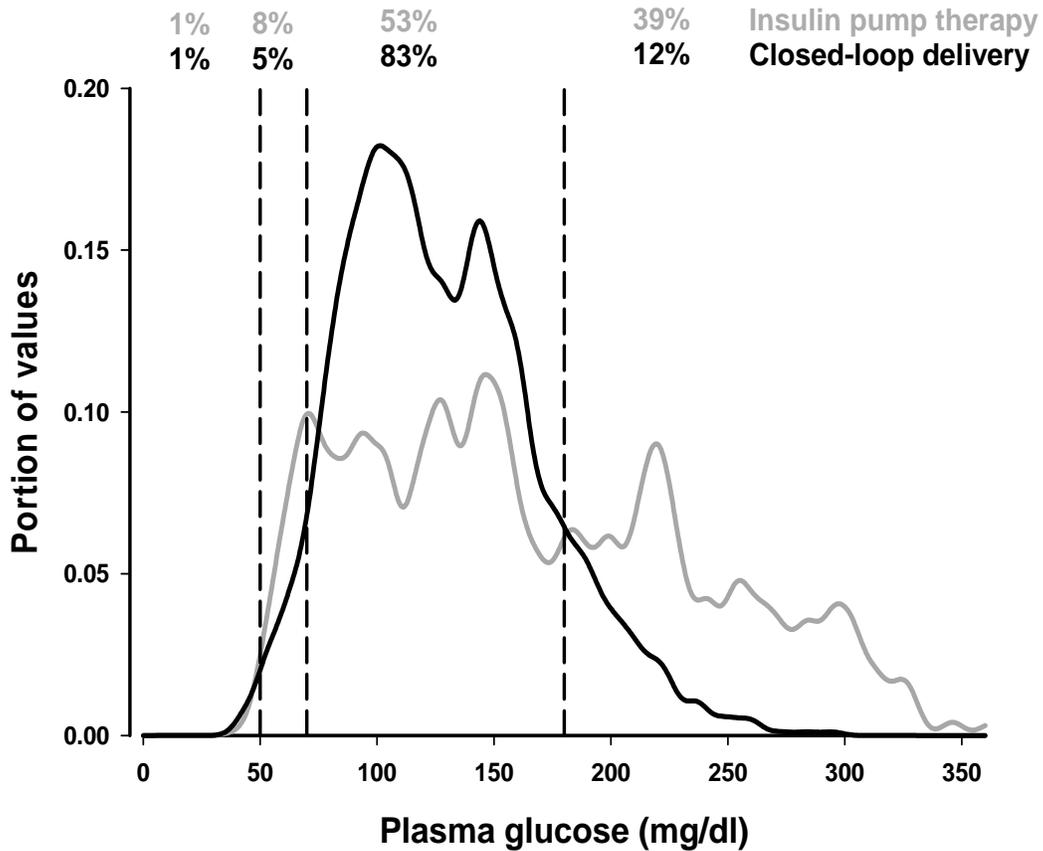
SUPPLEMENTARY DATA

Supplementary Figure 1. Flow of participants through the study comparing closed-loop basal insulin delivery with conventional insulin pump therapy over a 36 hour period.



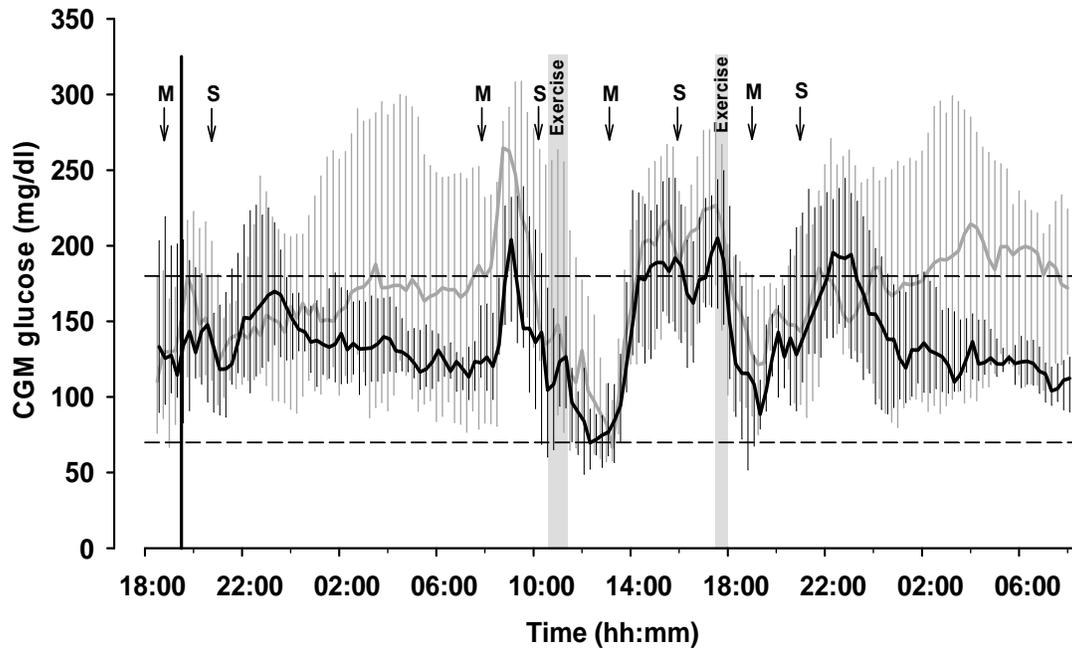
SUPPLEMENTARY DATA

Supplementary Figure 2. Plasma glucose distribution during conventional insulin pump therapy (grey solid line) and closed-loop basal insulin delivery (solid black line) using data collected from midnight on Day 1 until 08:00 on Day 3. Vertical dashed lines denote thresholds of 50, 70, and 180mg/dl. Percentage of glucose values below, within, and above thresholds are shown at the top.



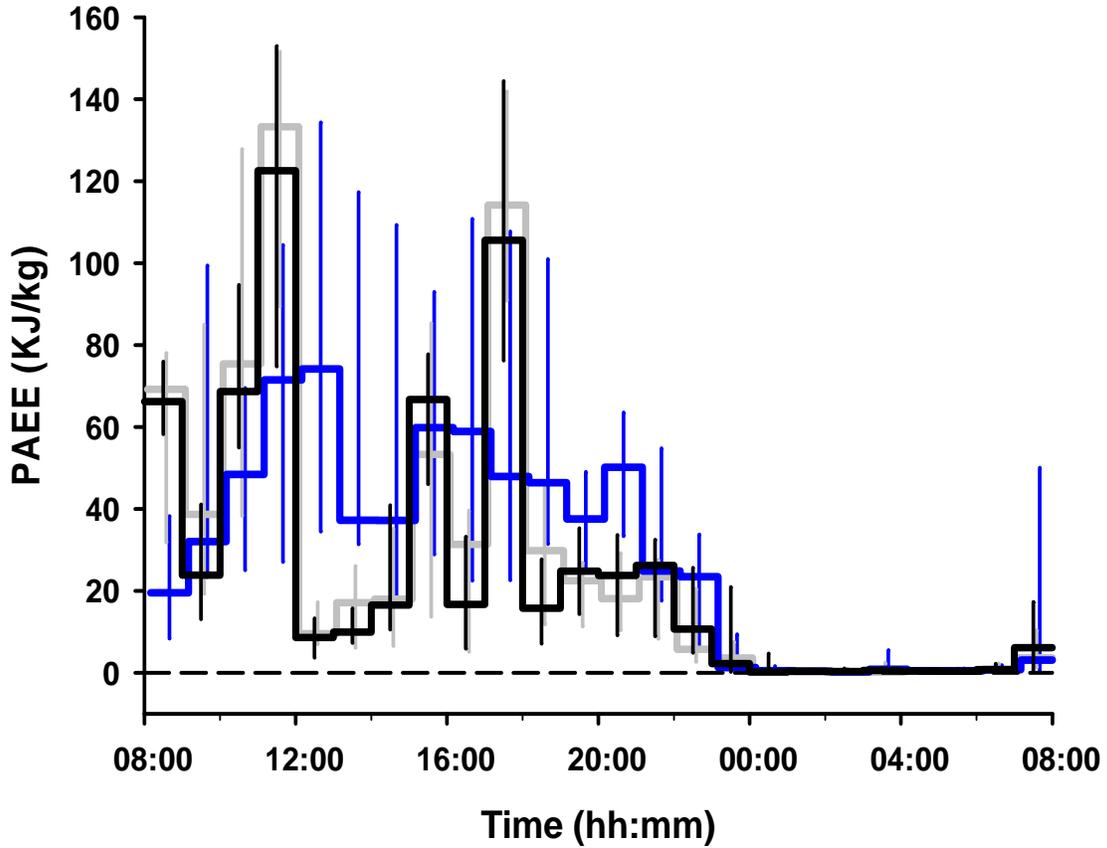
SUPPLEMENTARY DATA

Supplementary Figure 3. Continuous glucose monitoring (CGM) levels [median (interquartile range)] during conventional insulin pump therapy (grey line) and closed-loop delivery (black line). Meals (M) and snacks (S) are shown by vertical arrows. Exercise sessions are illustrated by shaded bars.



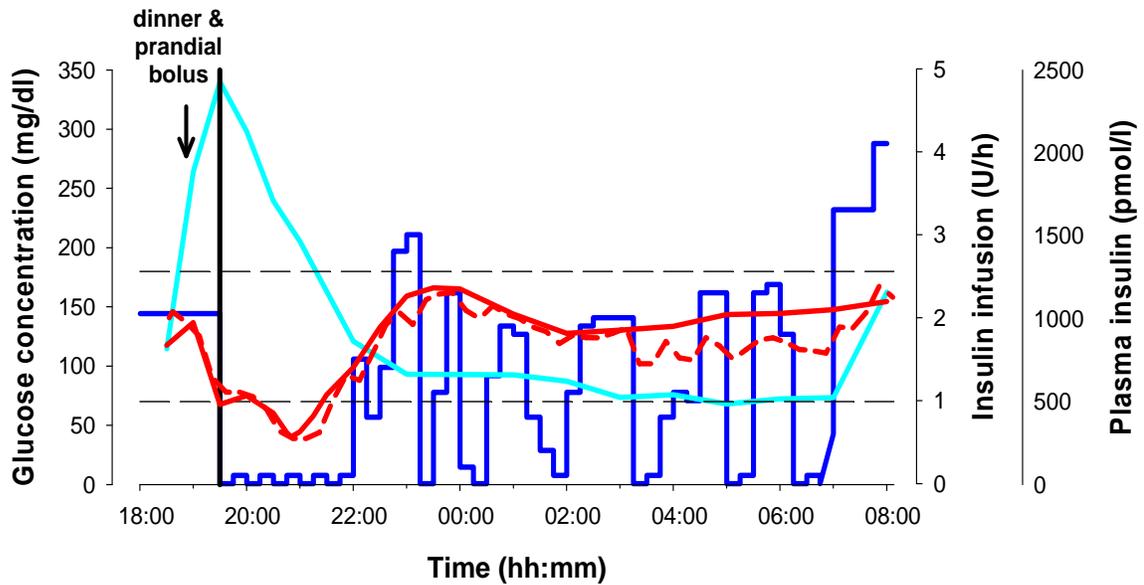
SUPPLEMENTARY DATA

Supplementary Figure 4. Median (interquartile range) physical activity energy expenditure (PAEE) (KJ/kg) over 24 hour (Day 2 08:00 to Day 3 08:00) during conventional insulin pump therapy (continuous grey line), closed-loop delivery (continuous black line) and during comparable period at home settings (continuous blue line).



SUPPLEMENTARY DATA

Supplementary Figure 5. An example of closed-loop study when plasma glucose levels (continuous red line) dropped to 44mg/dl 2hours after the meal. An insulin bolus of 16 units was administered 10 minutes before the evening meal consumed at 19:00. The bolus was calculated using the subject's pump bolus calculator for 80g carbohydrate meal. Insulin infusion (dark blue line) was virtually suspended by the control algorithm from the start of closed-loop at 19:30 for 2.5 hours. The resulting plasma insulin concentrations are shown by the light blue line. The sensor glucose levels (dashed red line) are also illustrated. The vertical line illustrates the time when closed-loop started. The horizontal dashed lines indicate glucose target range.



SUPPLEMENTARY DATA

APPENDIX B

Individual profiles

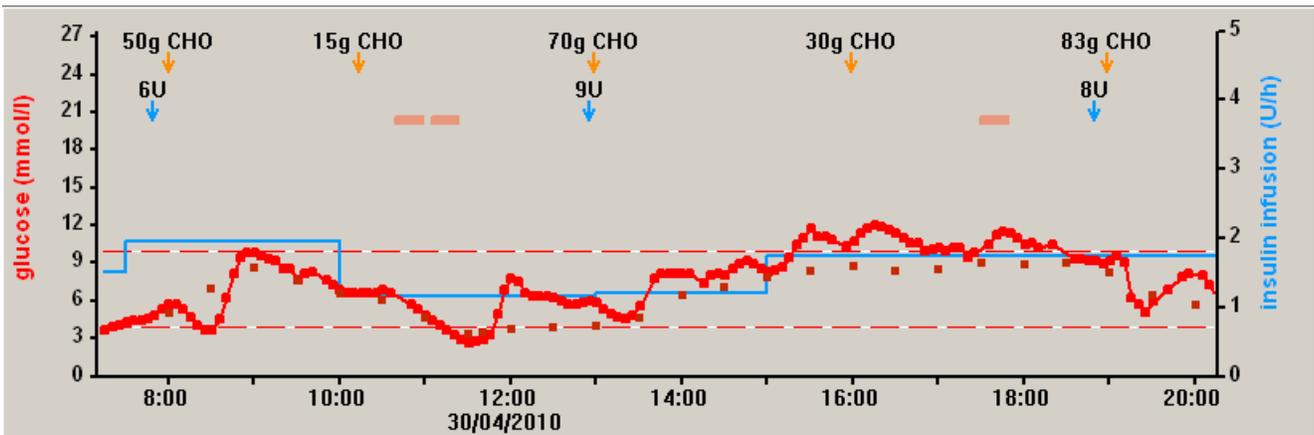
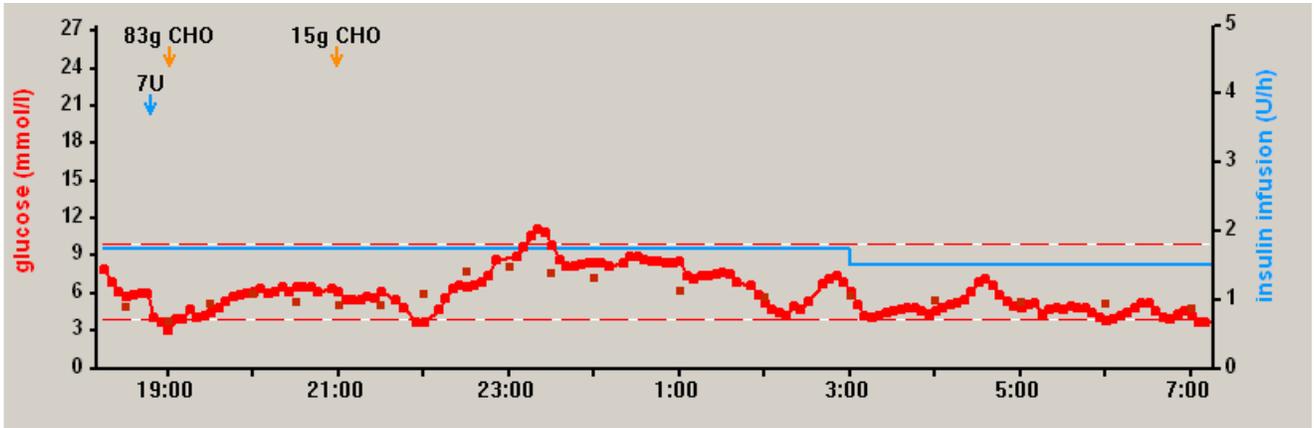
The following section includes the single glucose and insulin profiles observed in each subject on the two occasions (closed-loop delivery and insulin pump therapy).

The red thick line illustrates continuous glucose readings, whereas the dark red squares indicate the plasma glucose reference as measured by YSI Stat Analyser. Insulin infusion rates during closed-loop delivery are shown by the blue thick line and the thin blue line indicates the pre-programmed basal insulin infusion rates. Vertical arrows indicate when meals or snacks (orange arrow) and the insulin boluses (blue arrow) were given. Carbohydrate content of the meal/snack and insulin doses (unit, U) are also shown. Horizontal orange bars illustrate the bike exercise sessions. Red dashed lines illustrate the target range of 3.9 to 10mmol/l (71 to 180mg/dl). Closed-loop glucose control started at 19:00 on Day 1 and ran until 08:00 two days later.

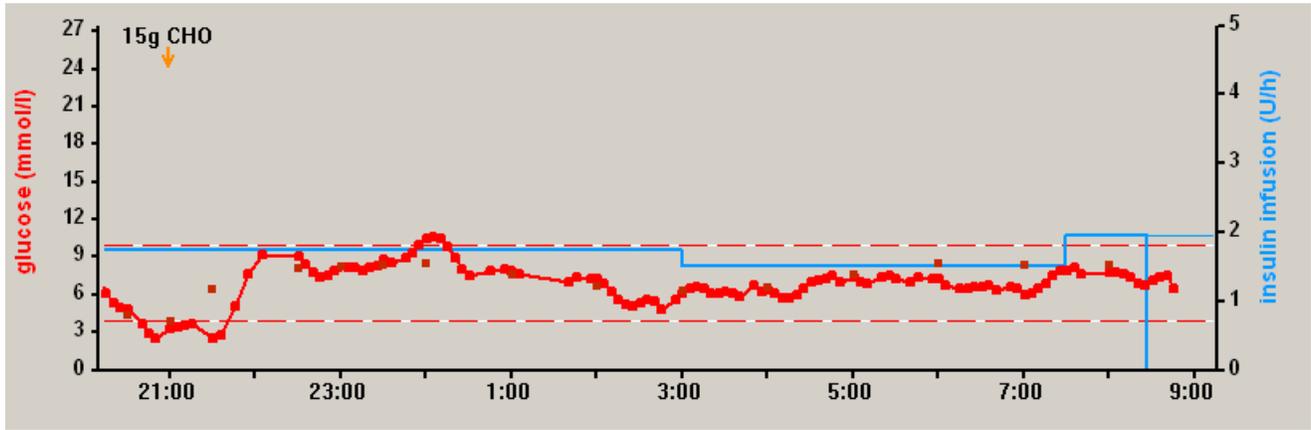
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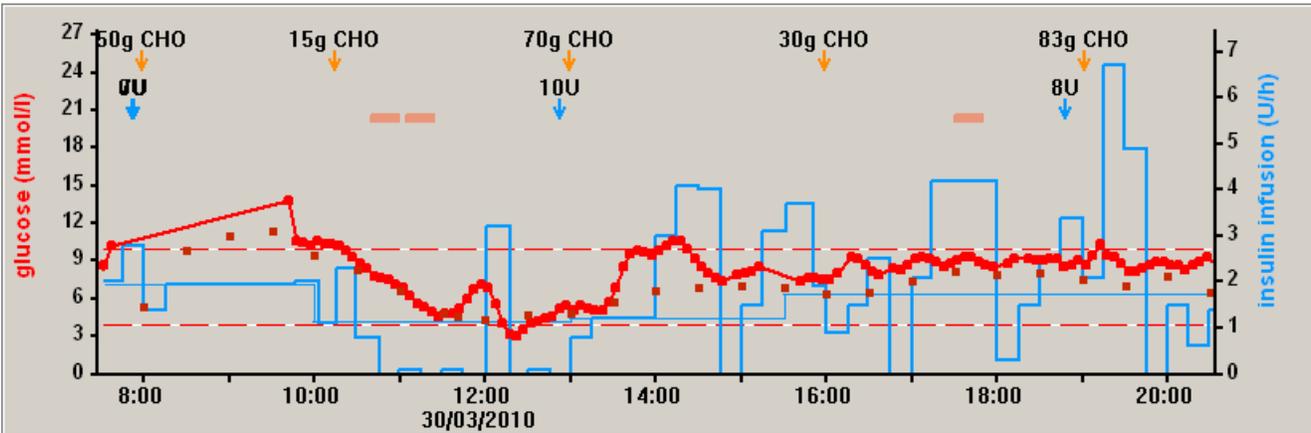
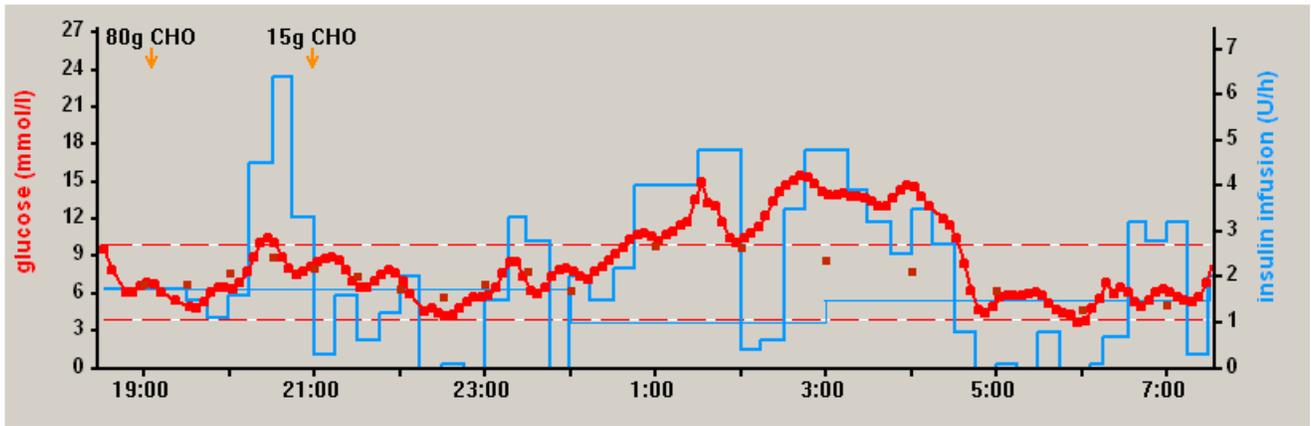
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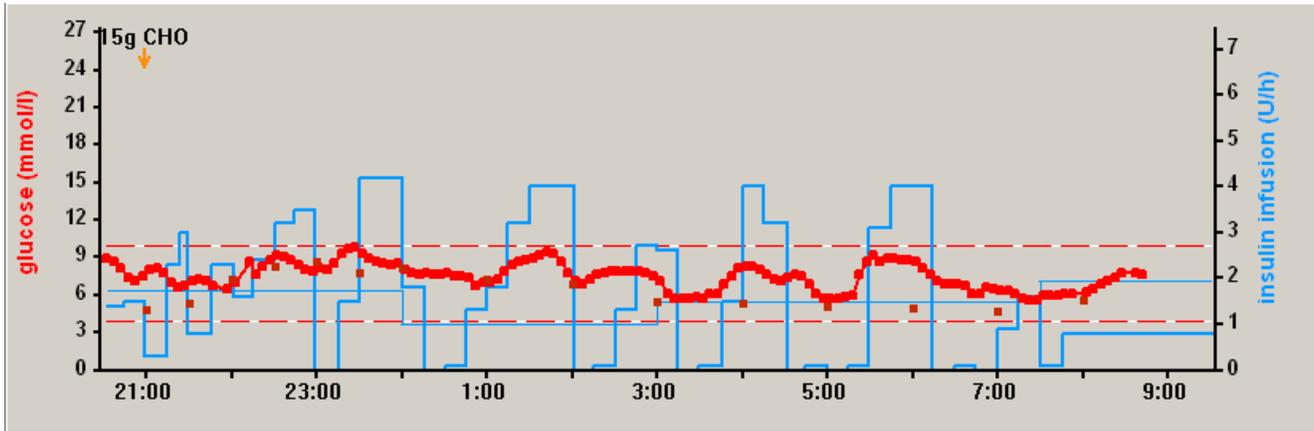
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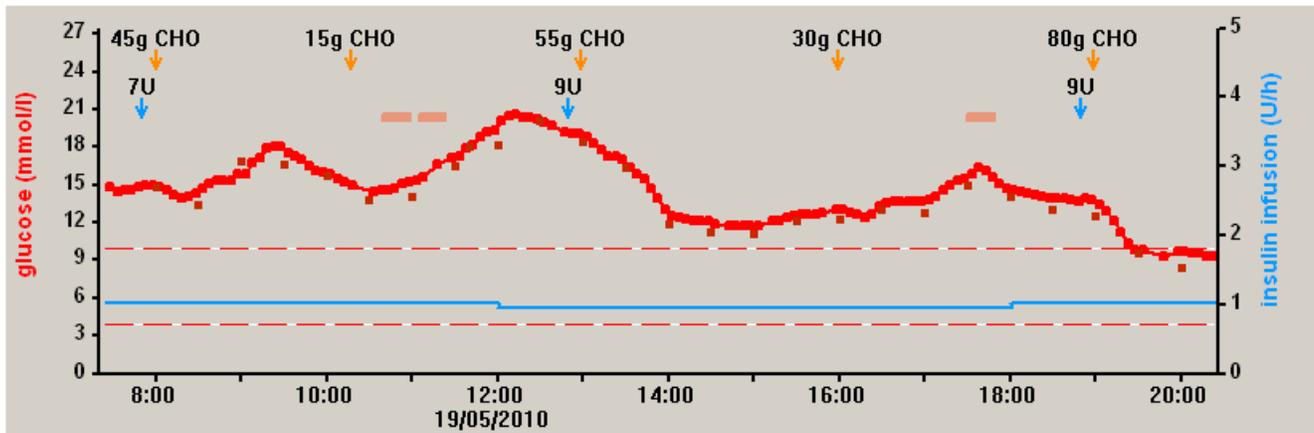
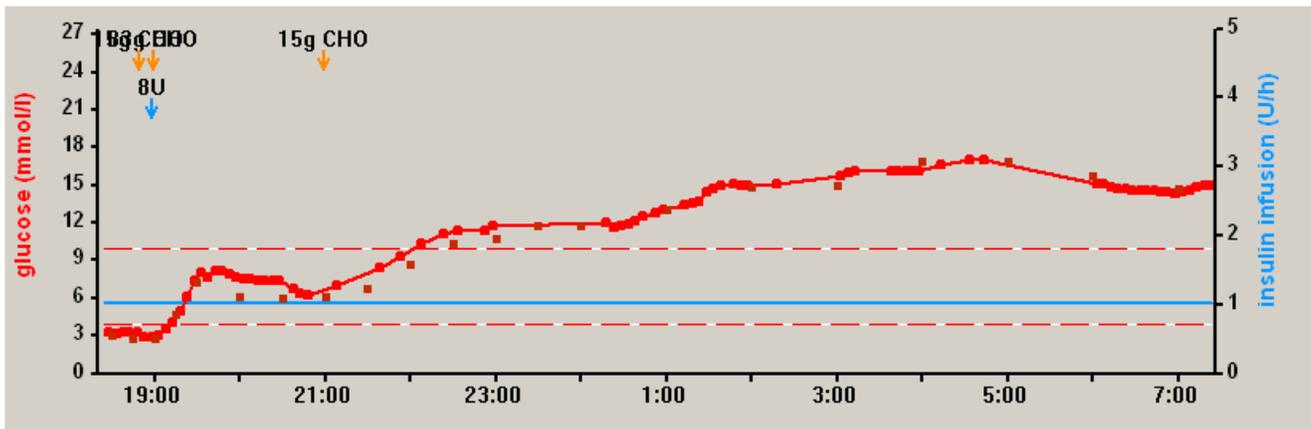


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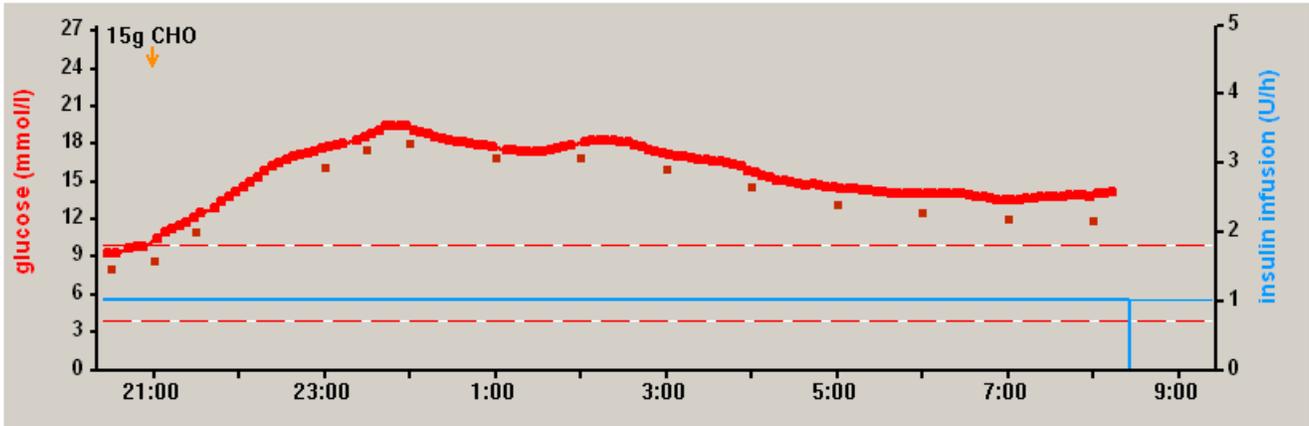


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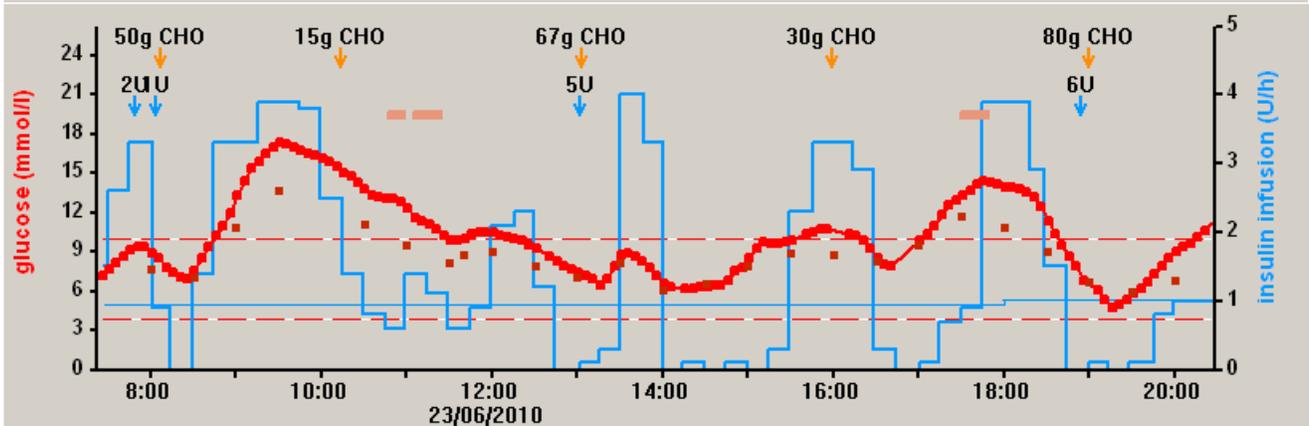
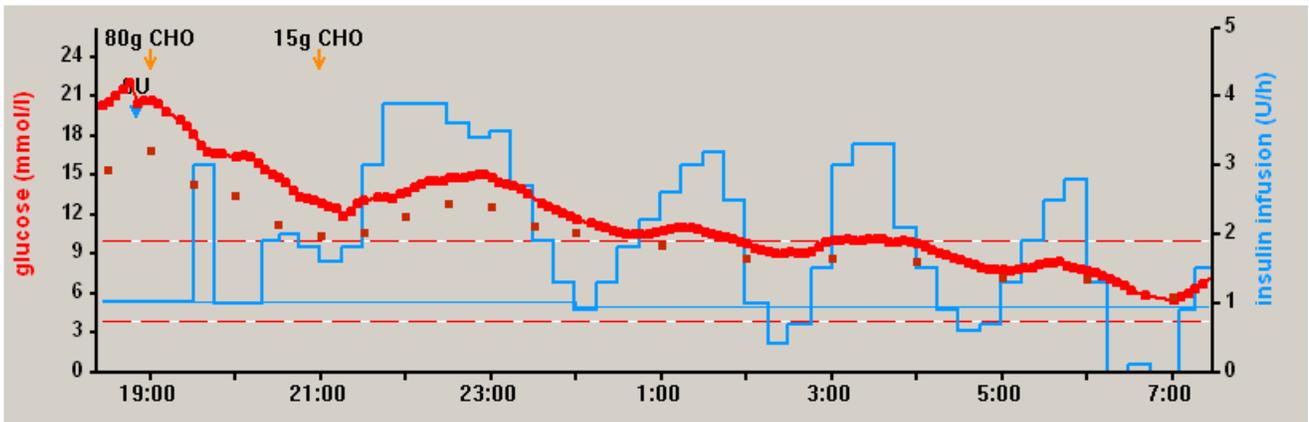
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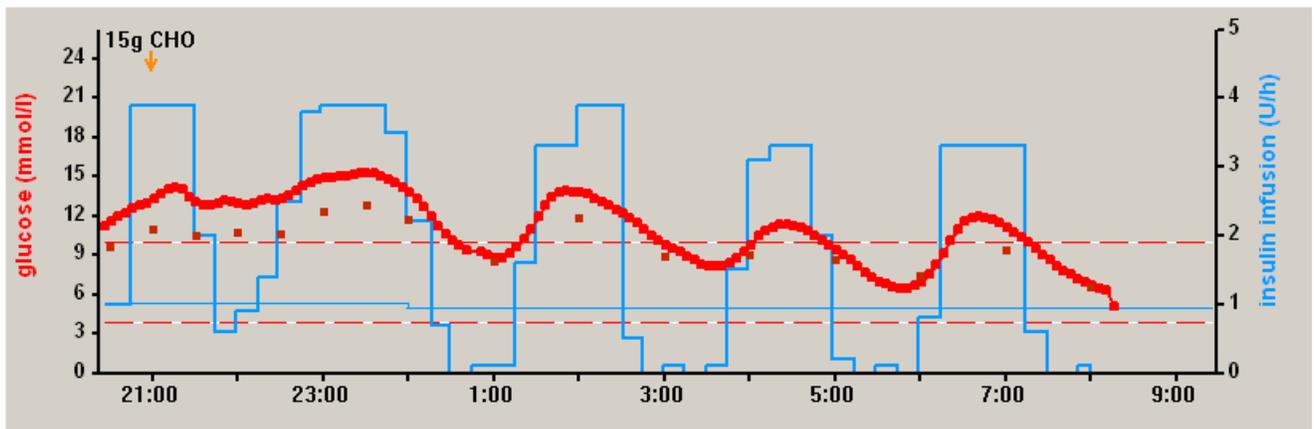
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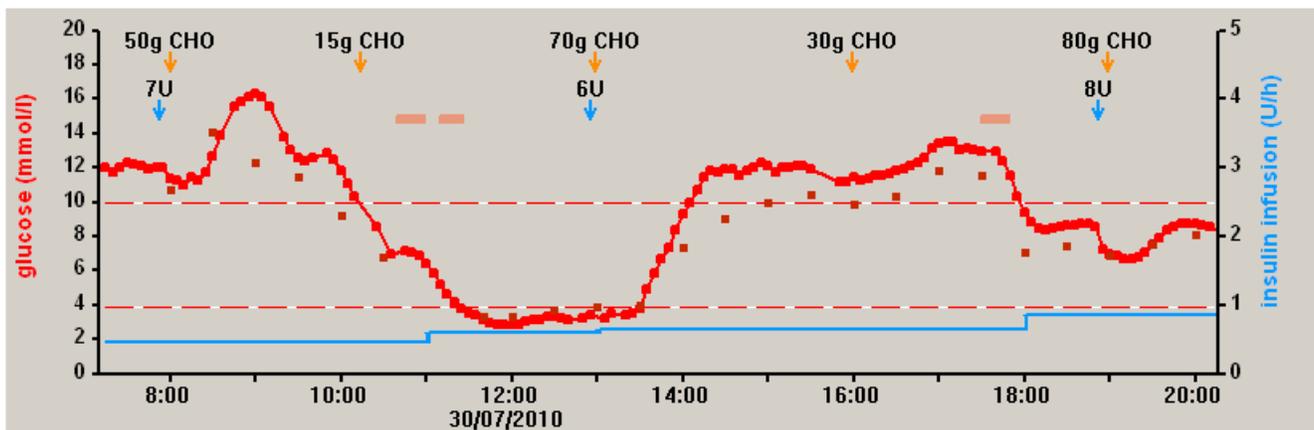
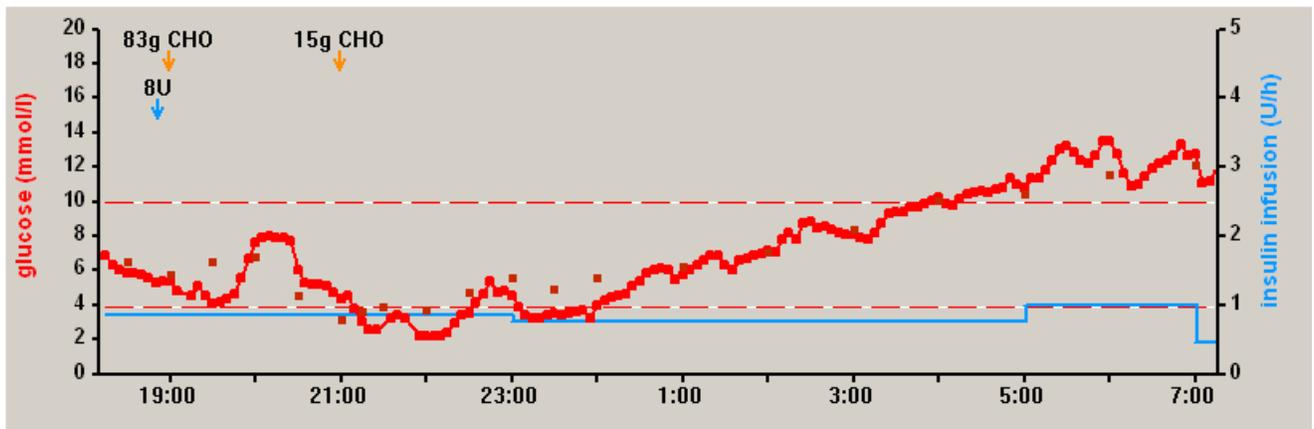


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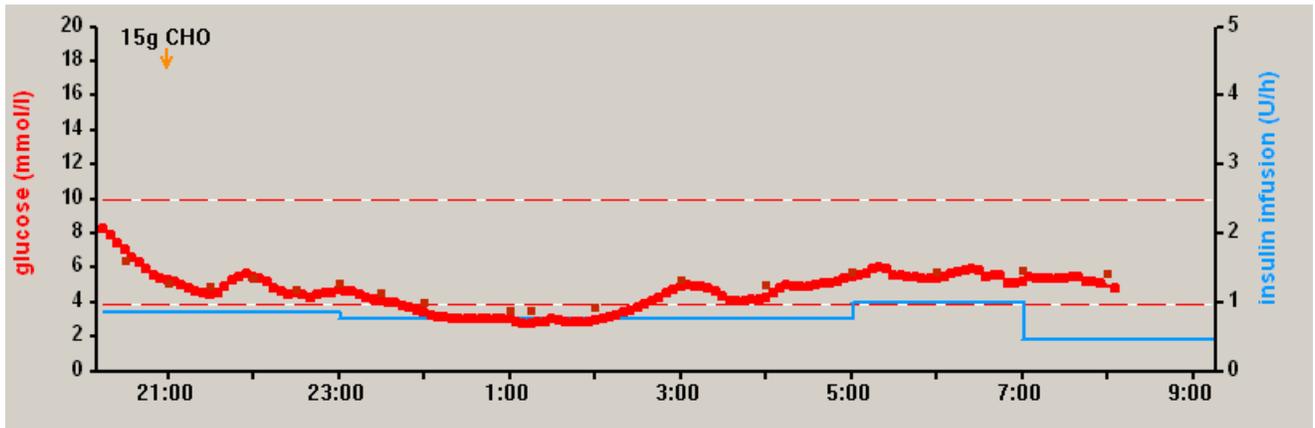


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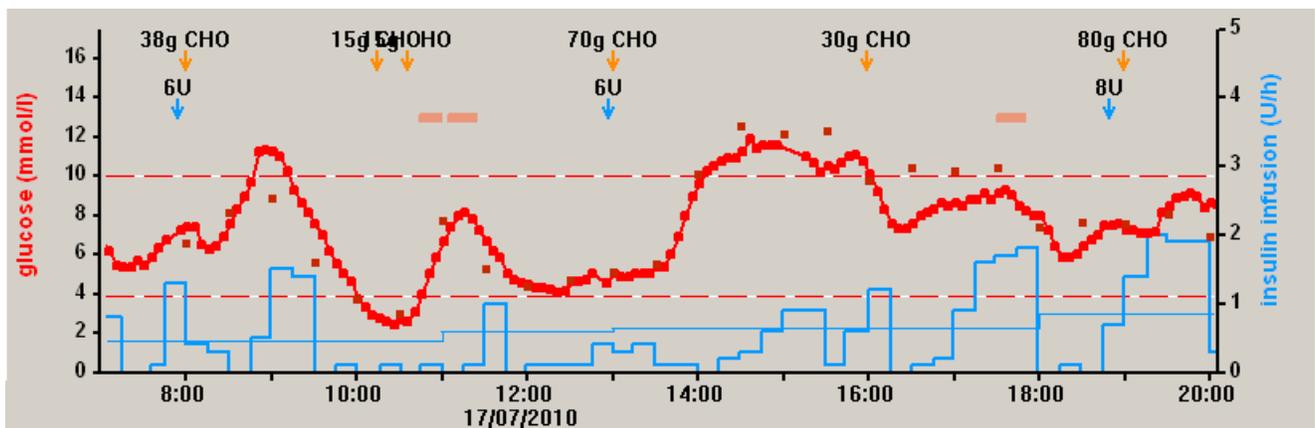
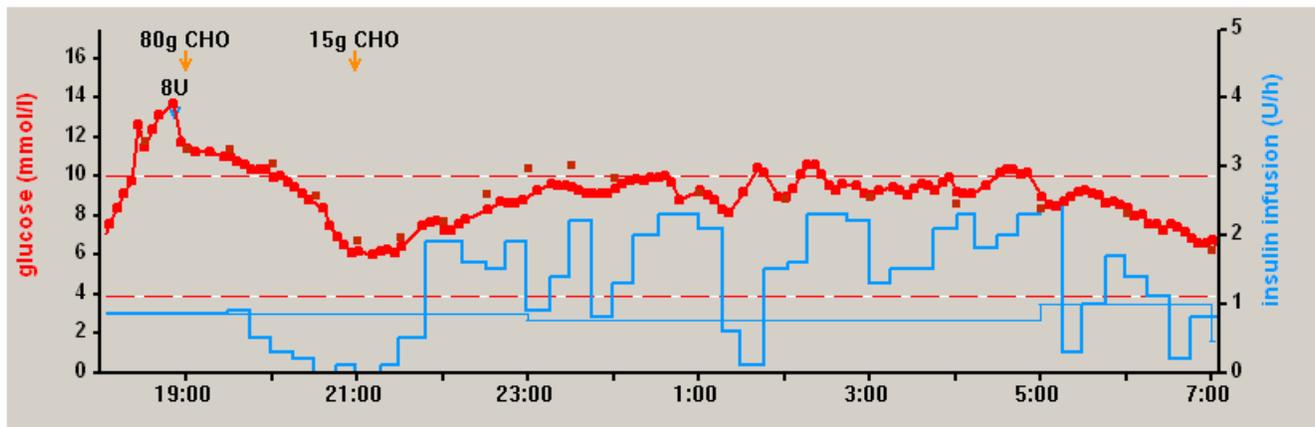
- Insulin pump therapy



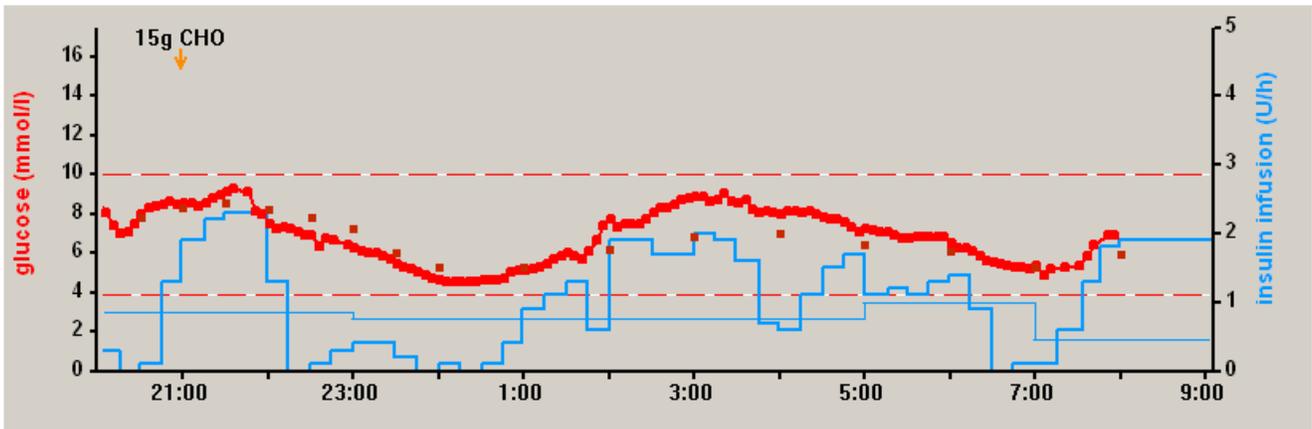
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• Closed-loop delivery

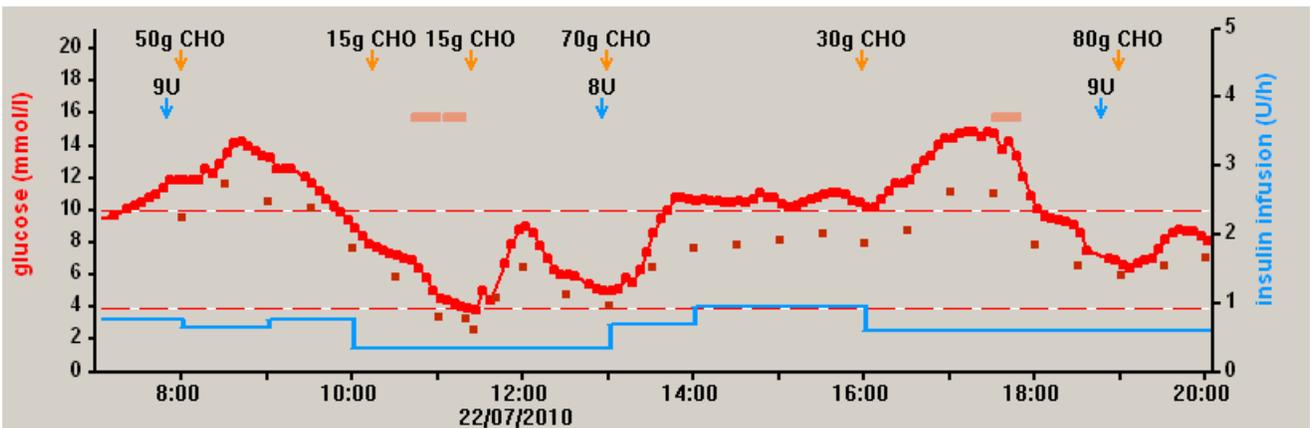
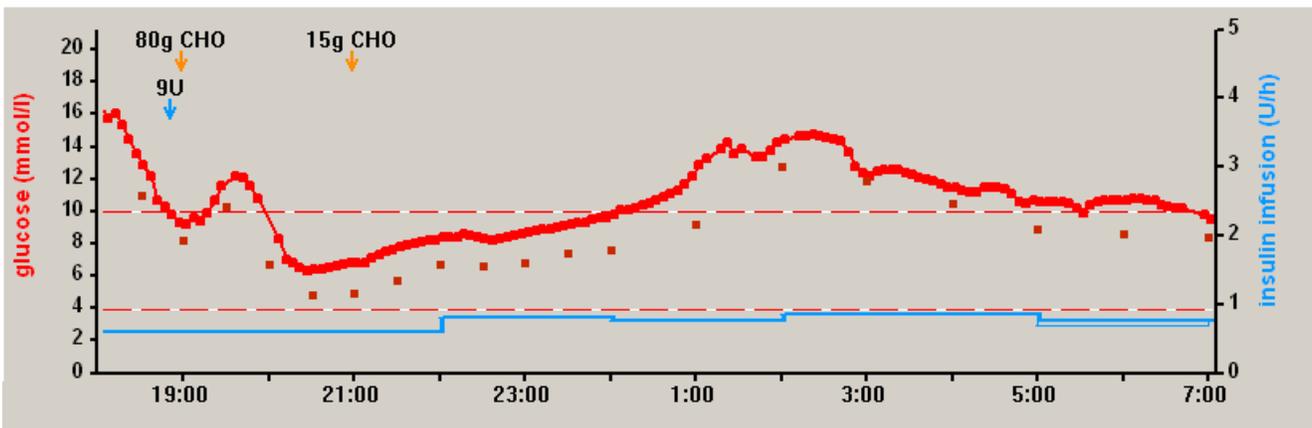


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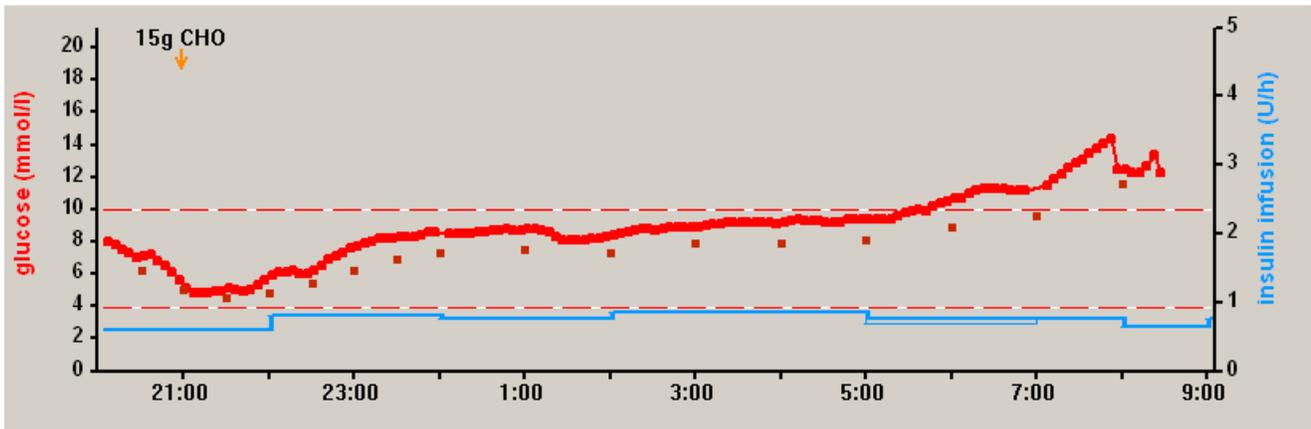


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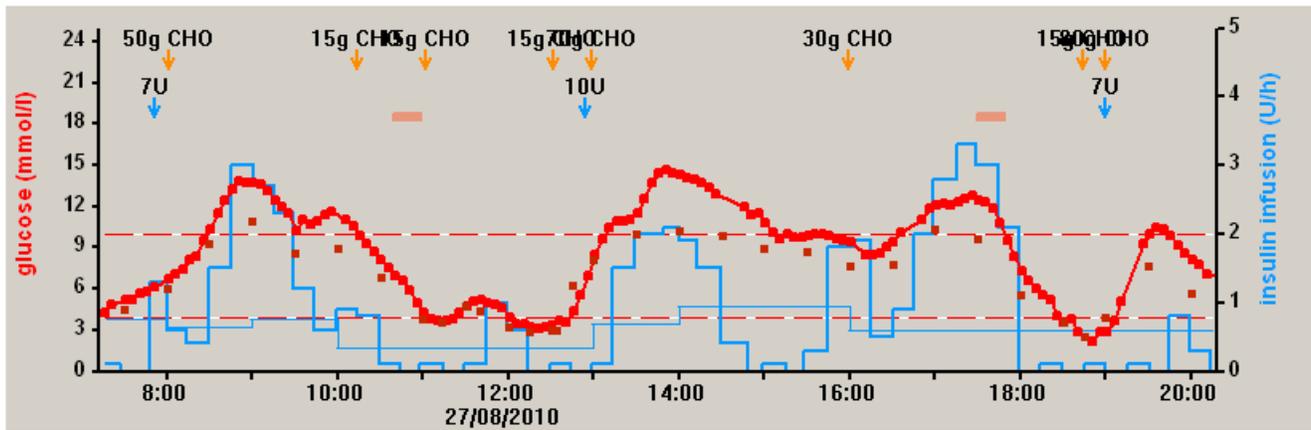
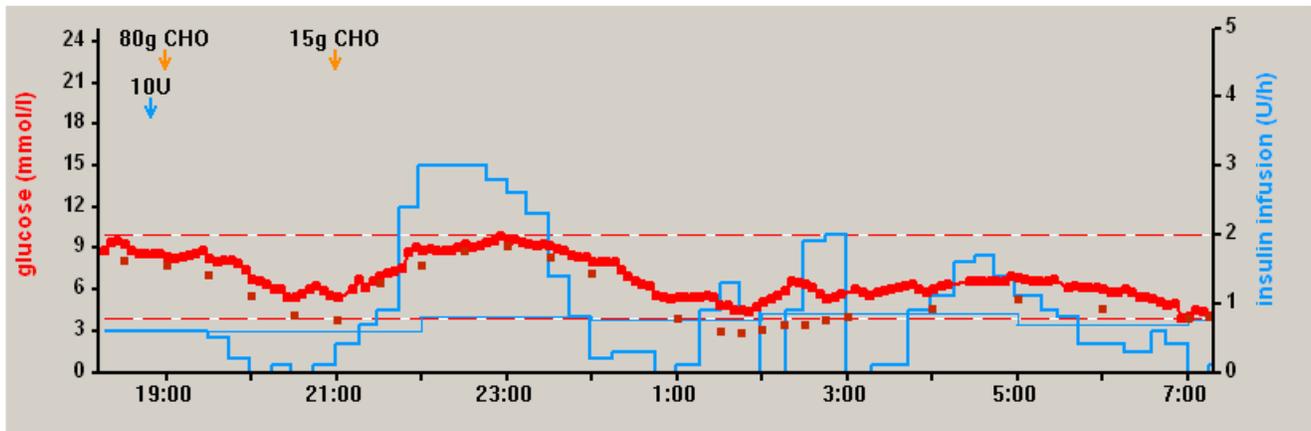
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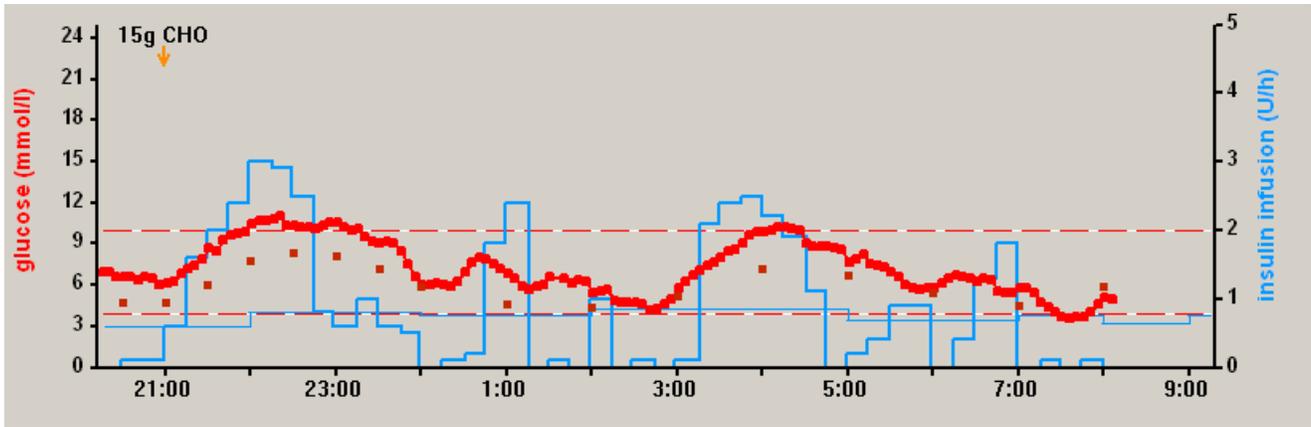
SUPPLEMENTARY DATA



• Closed-loop delivery

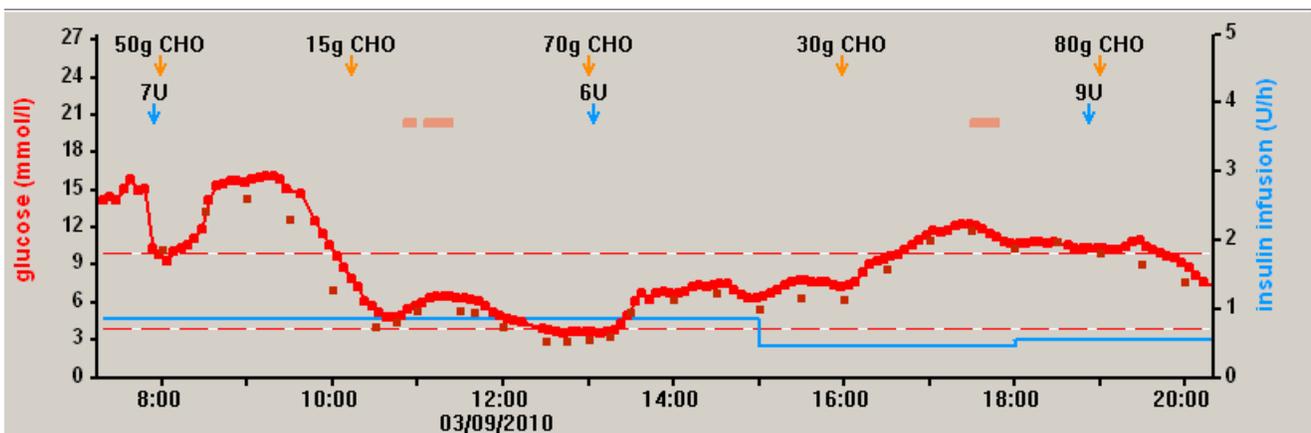
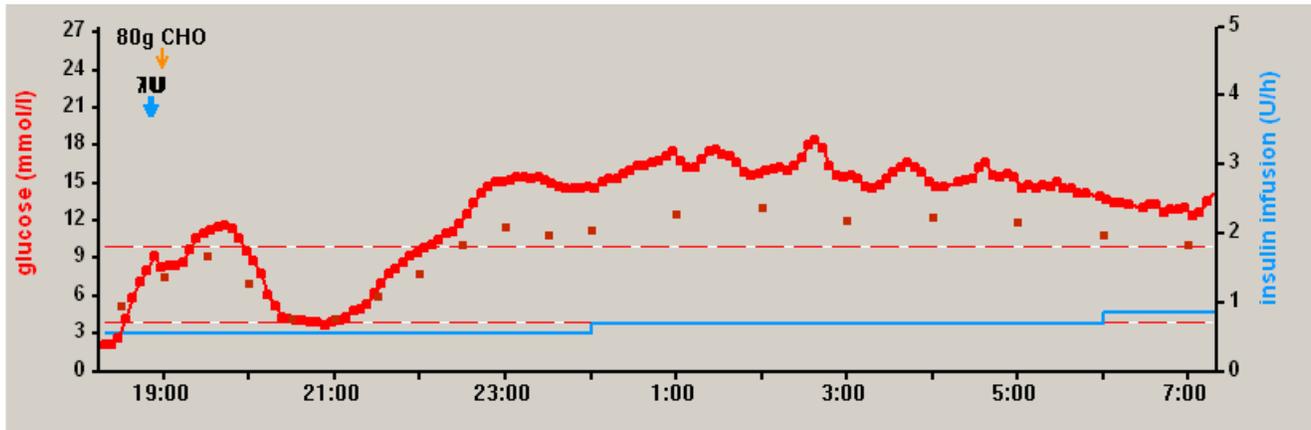


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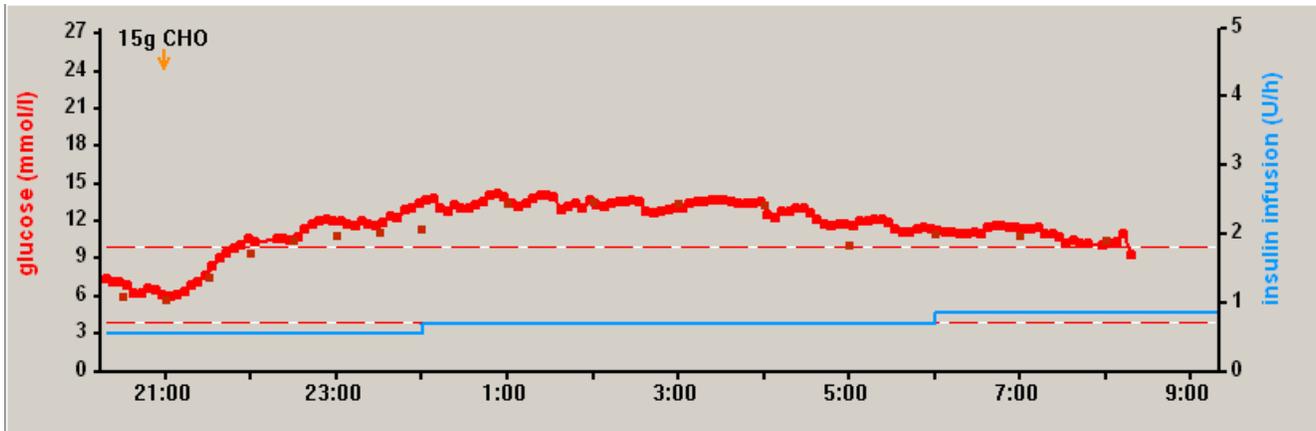


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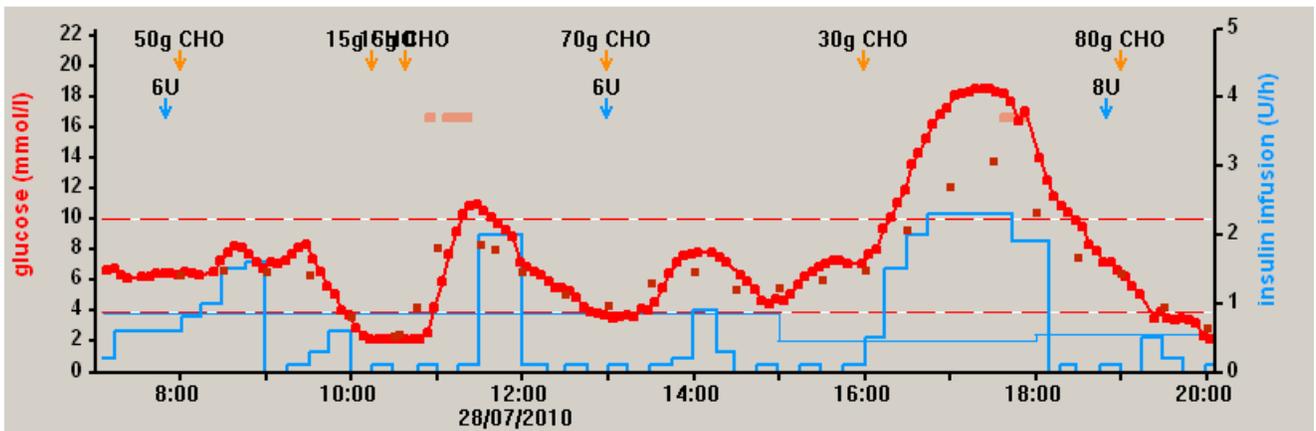
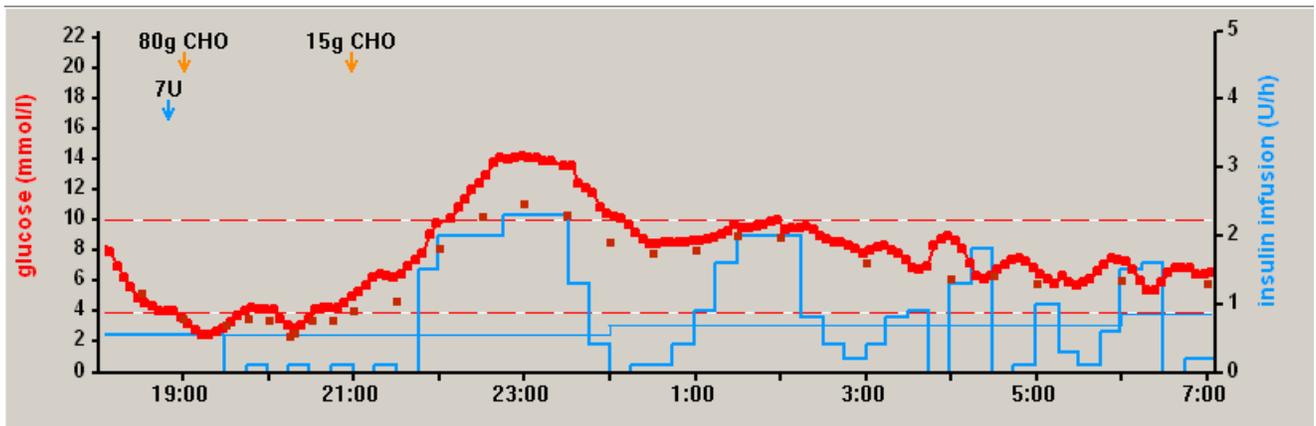
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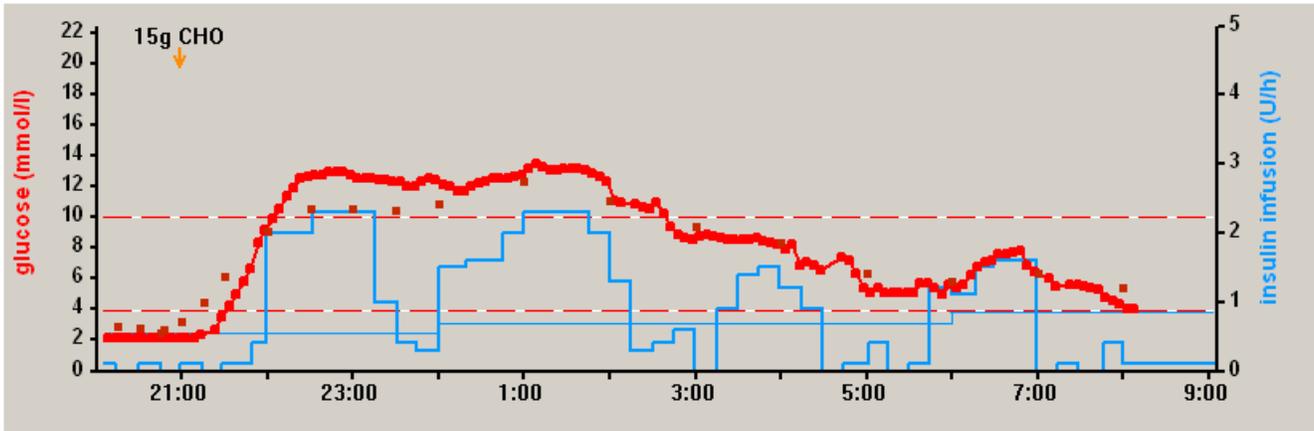
SUPPLEMENTARY DATA



• Closed-loop delivery

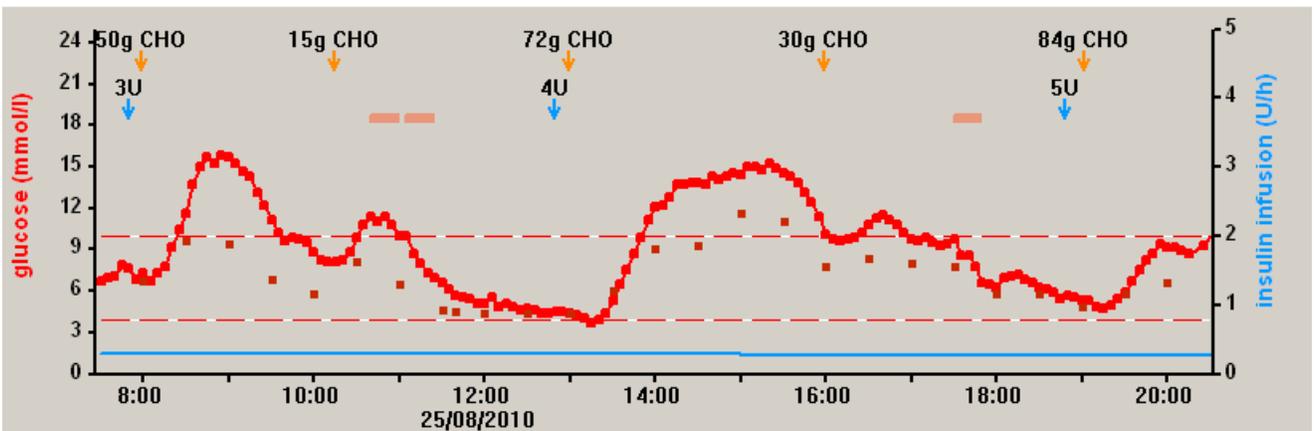
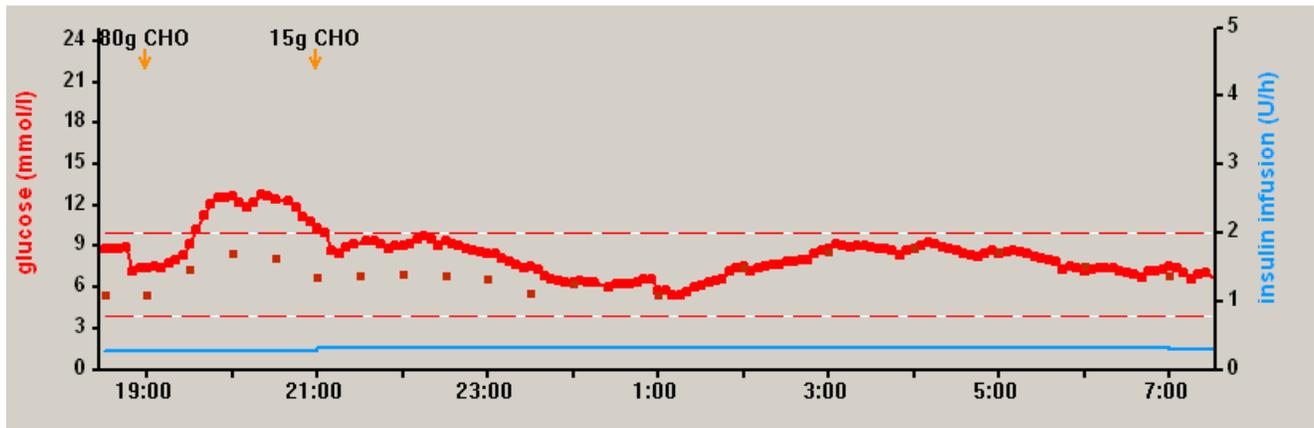


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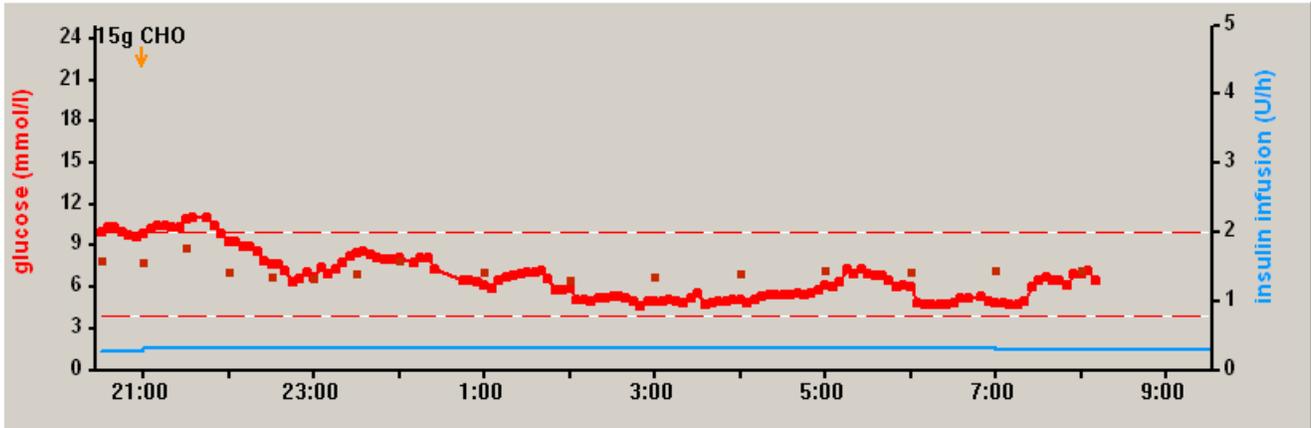


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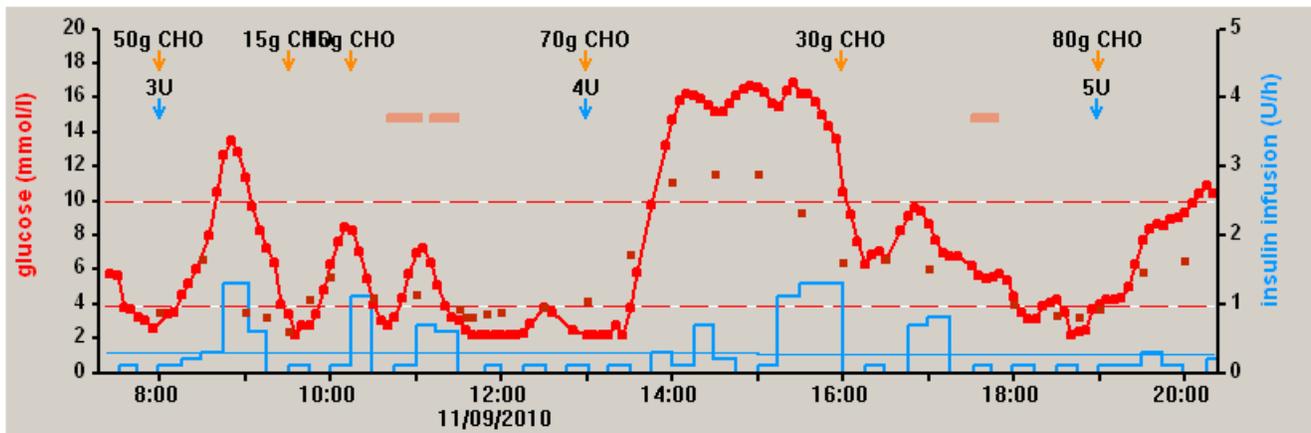
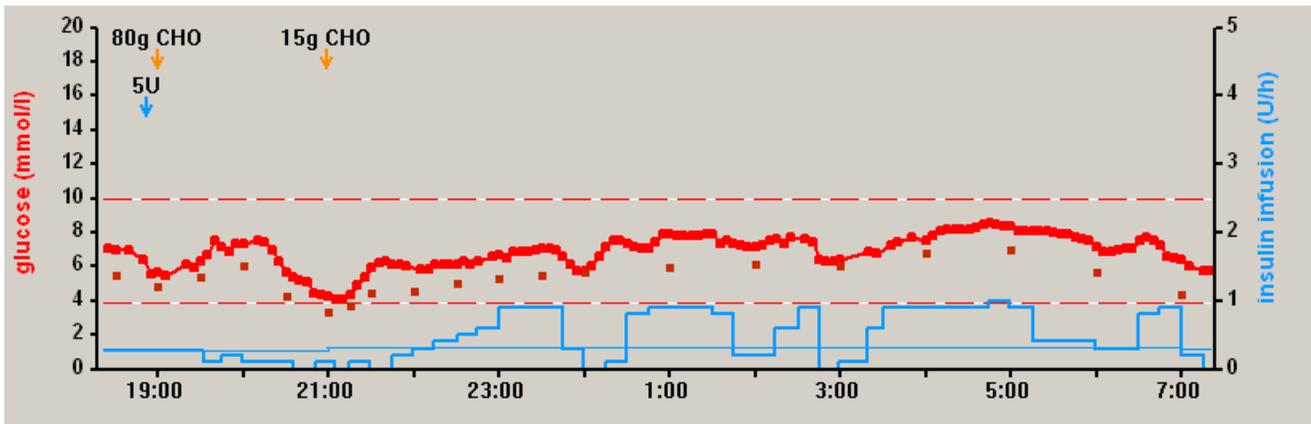
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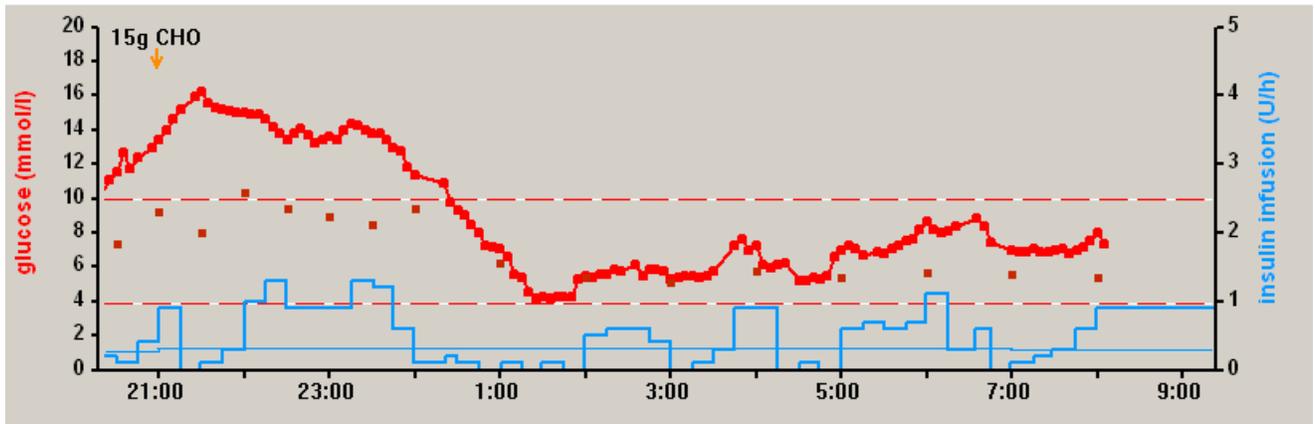
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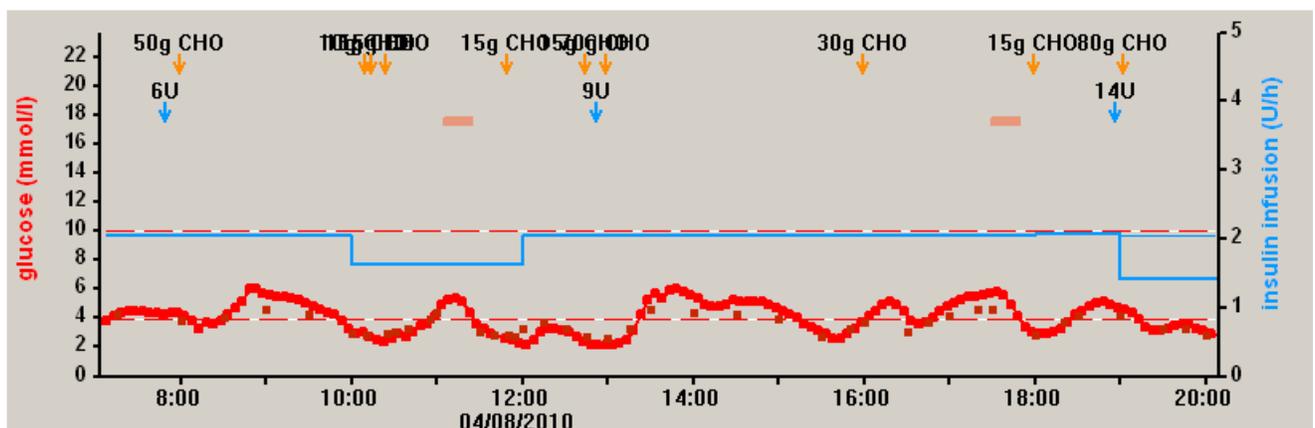
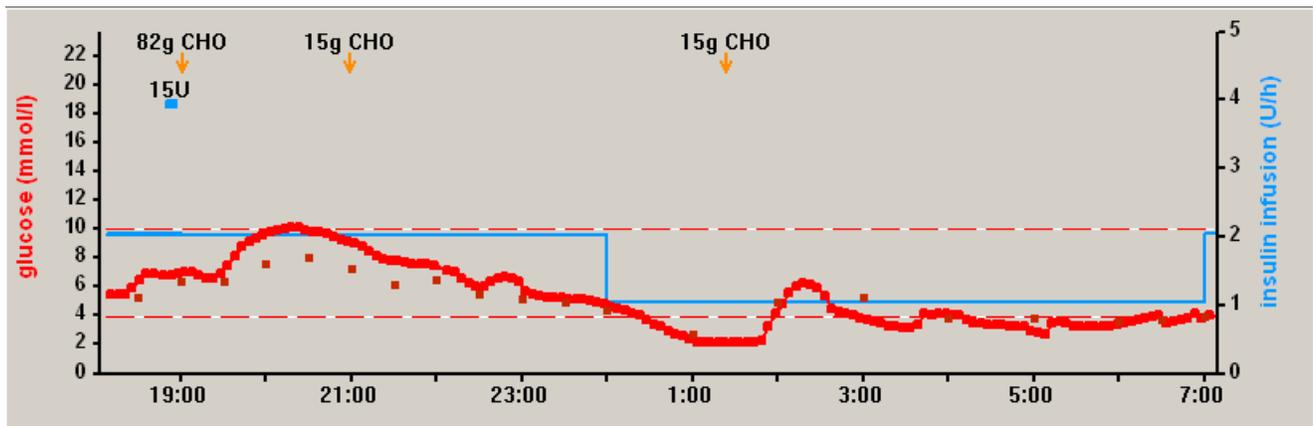


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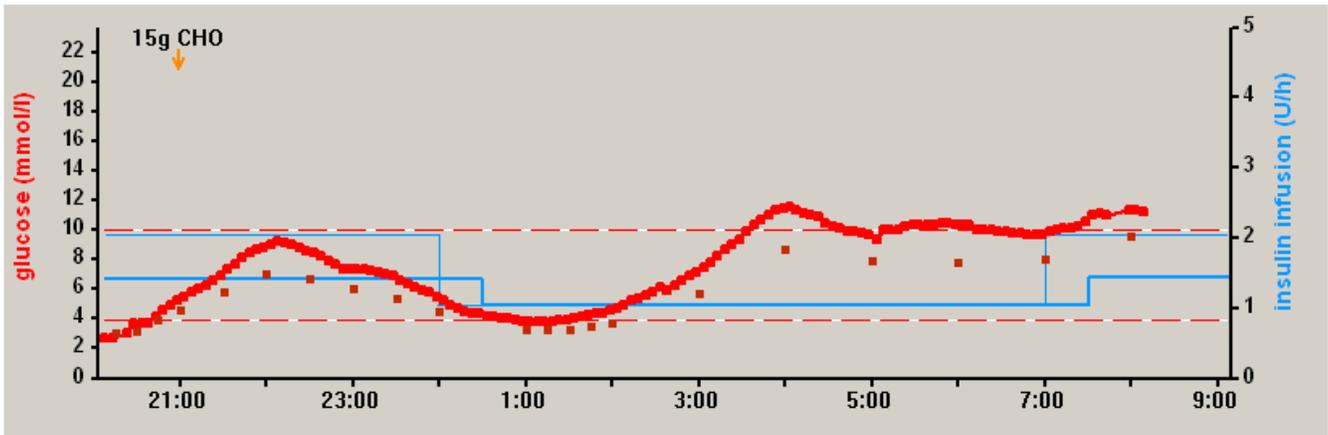


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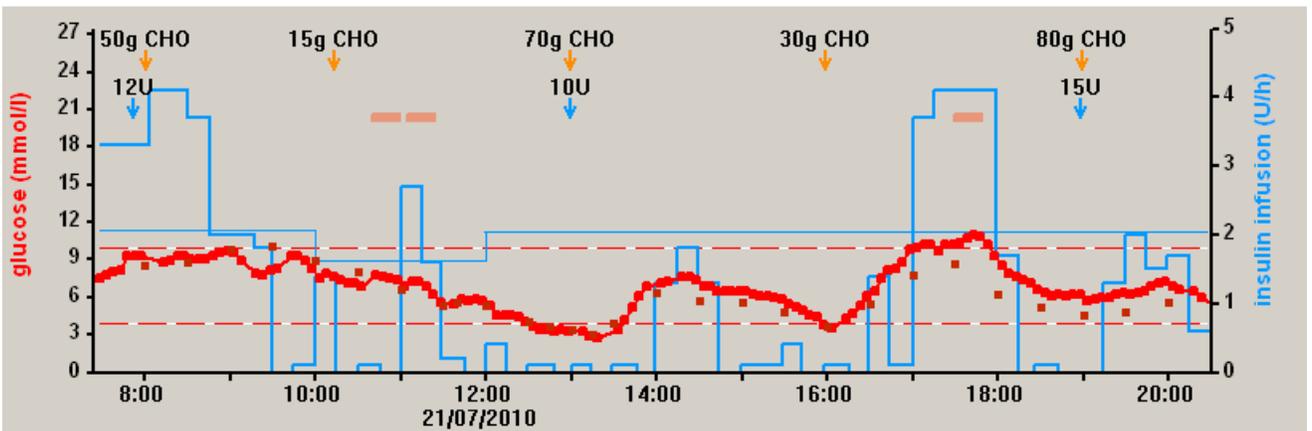
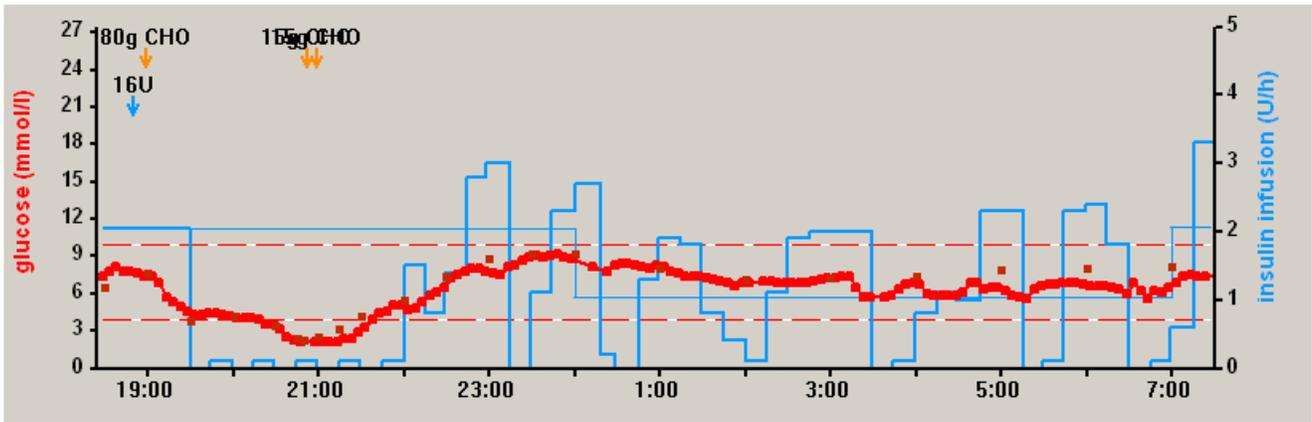
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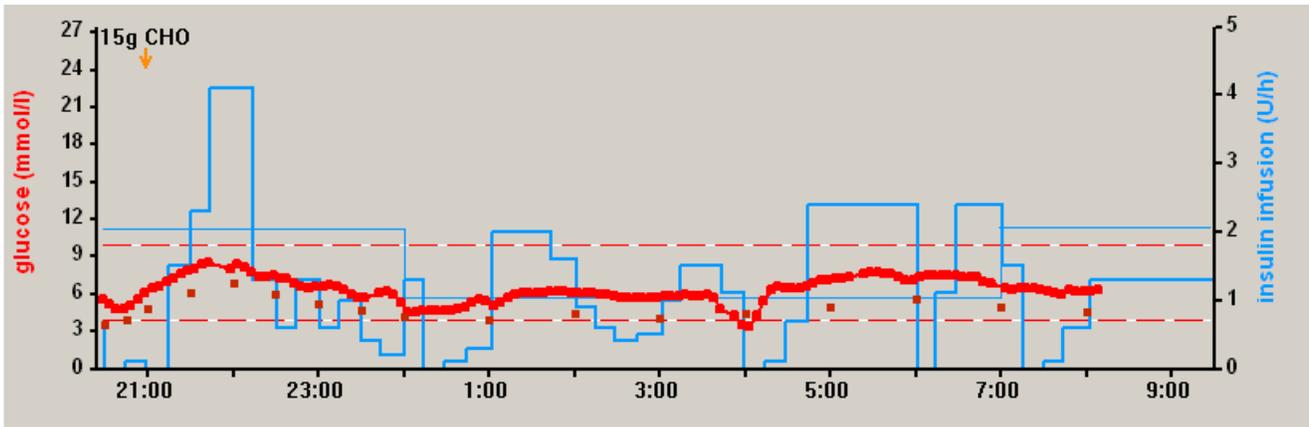
SUPPLEMENTARY DATA



• Closed-loop delivery

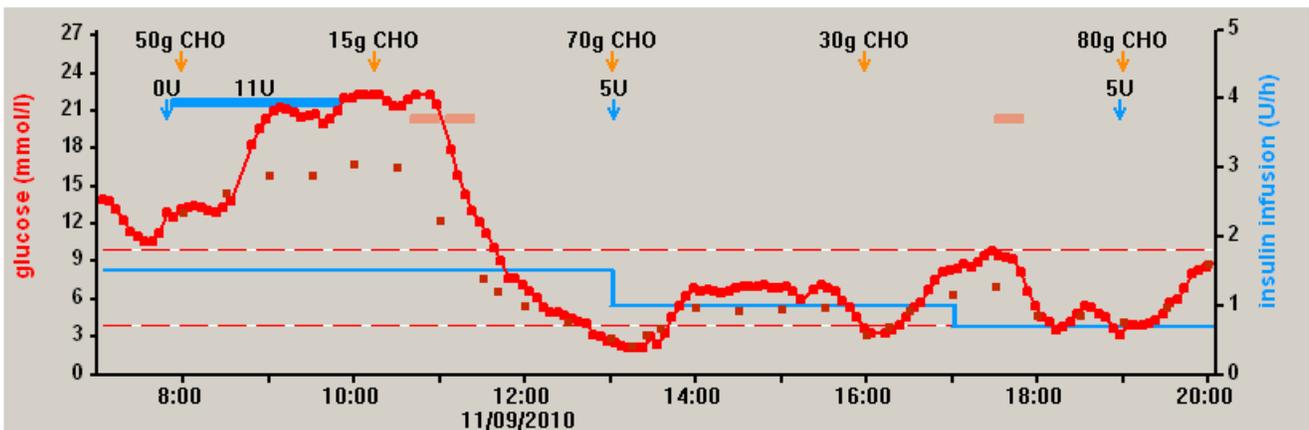
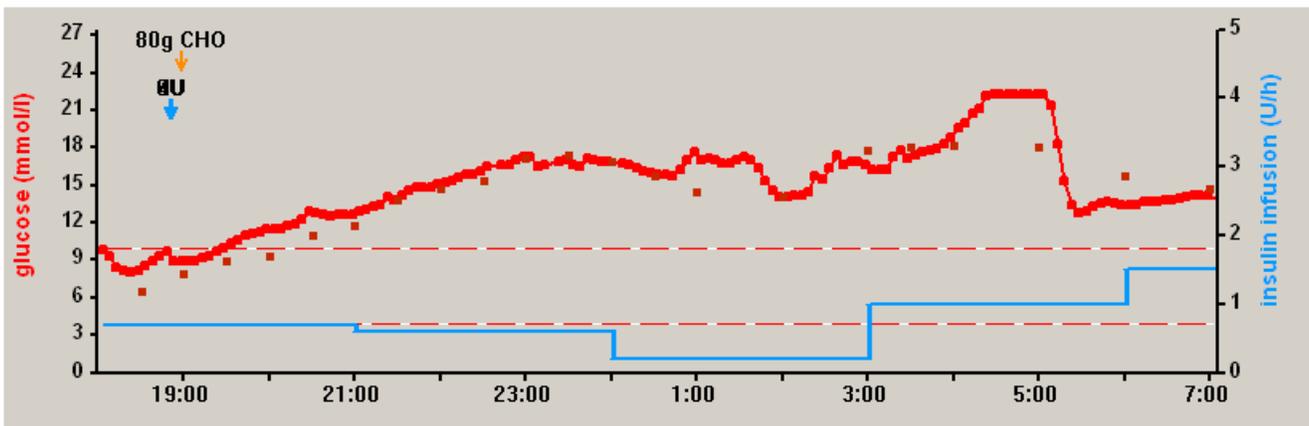


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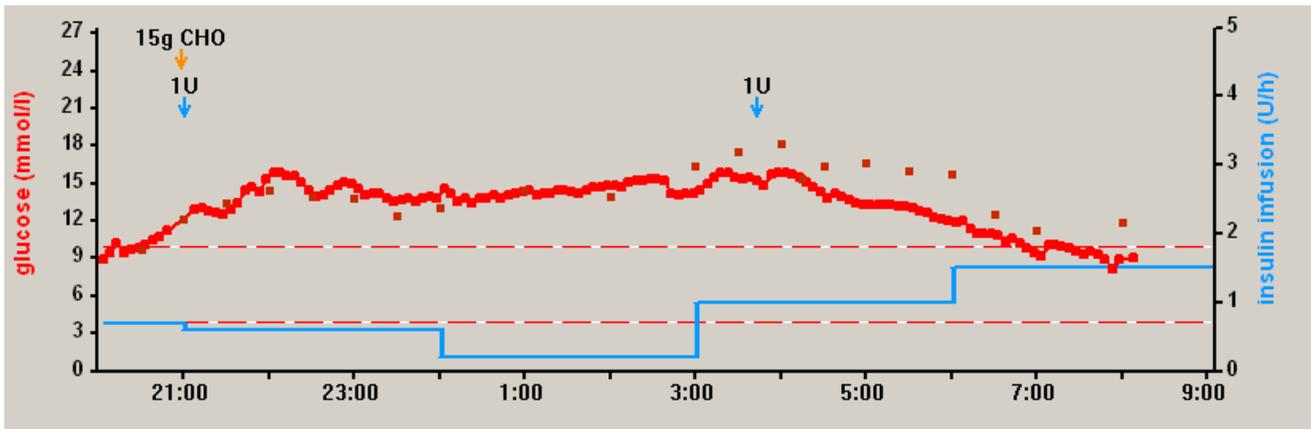


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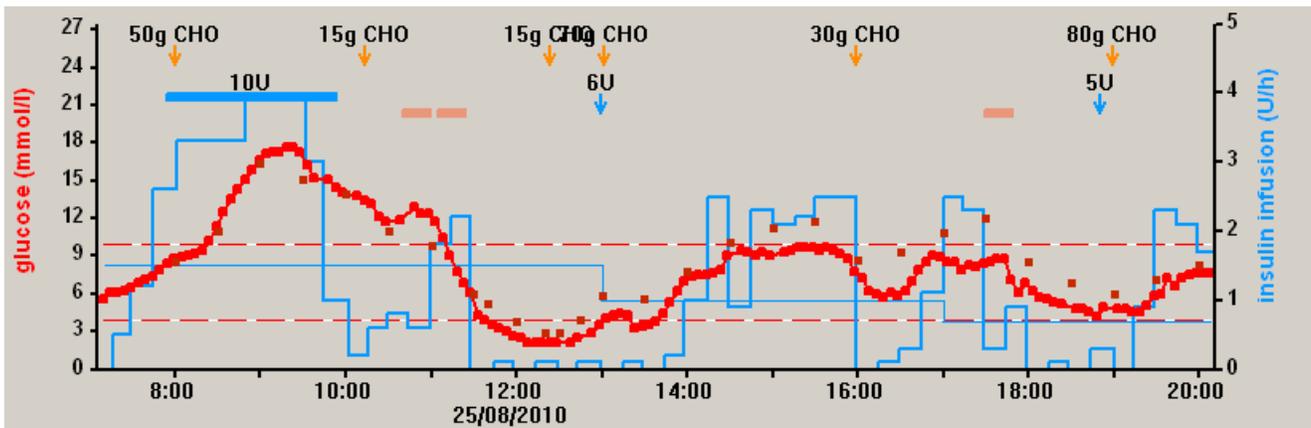
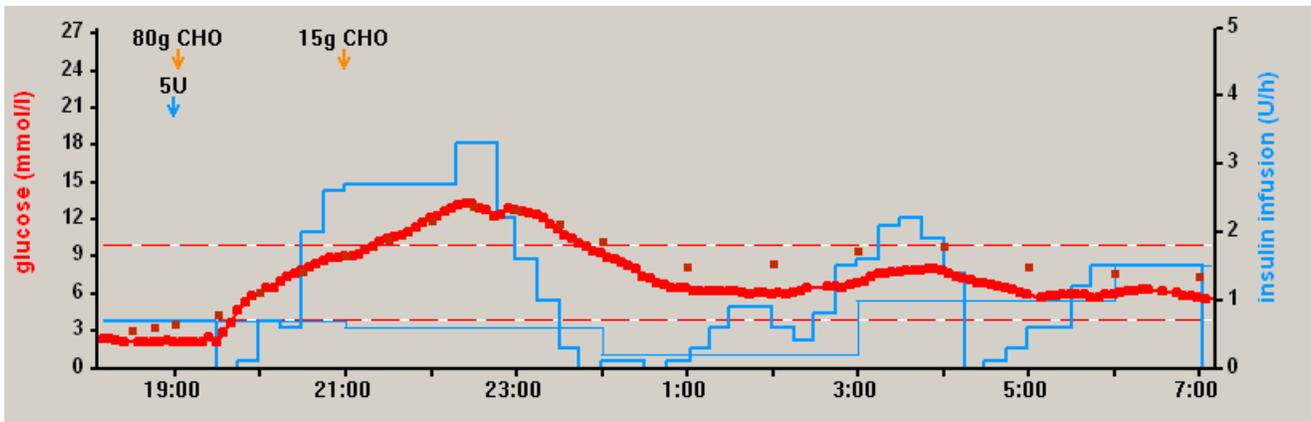
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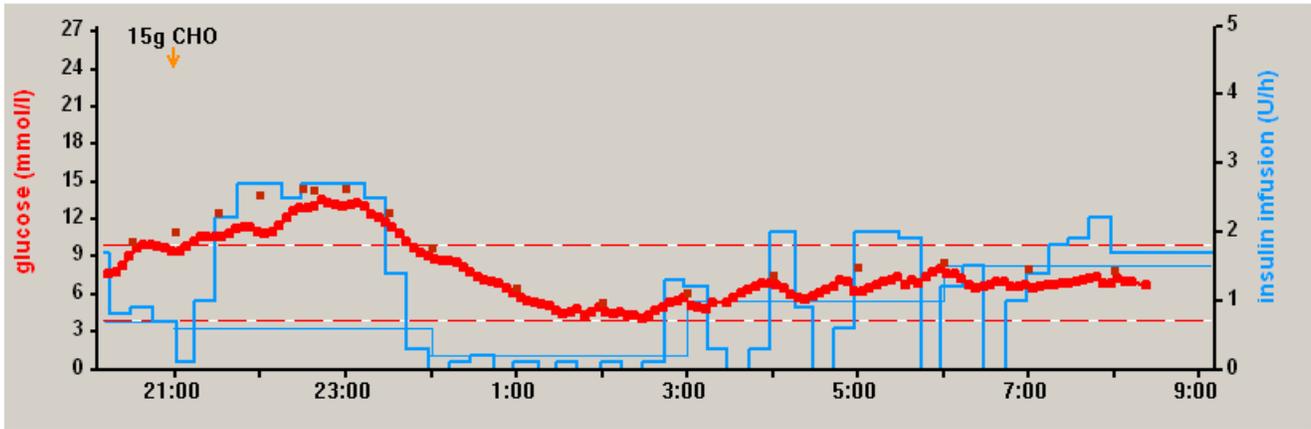
SUPPLEMENTARY DATA



• Closed-loop delivery

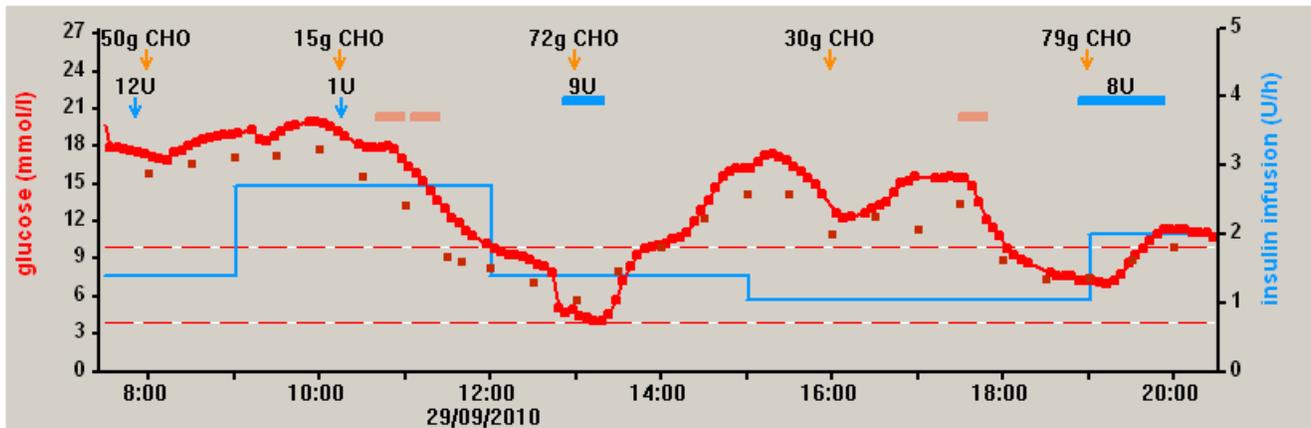
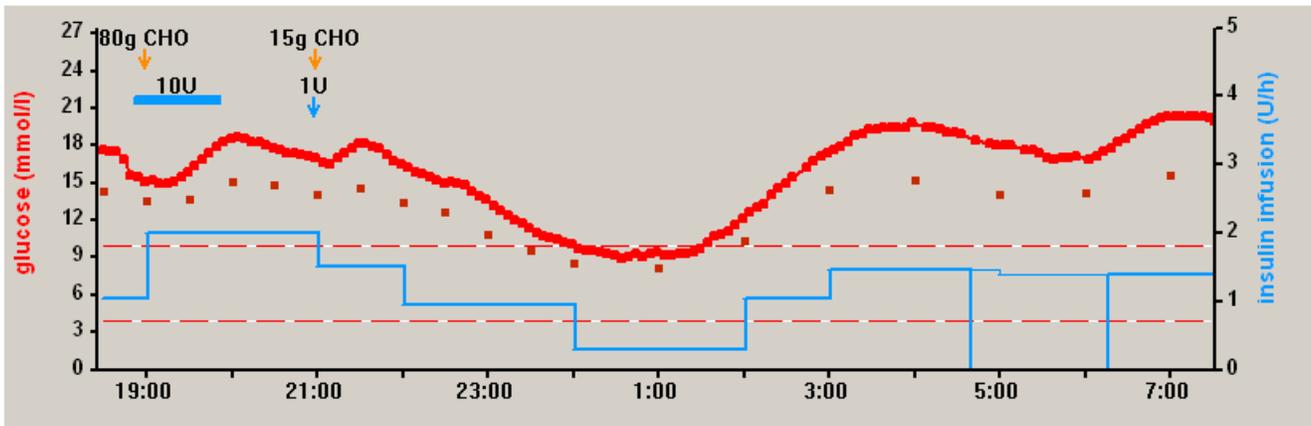


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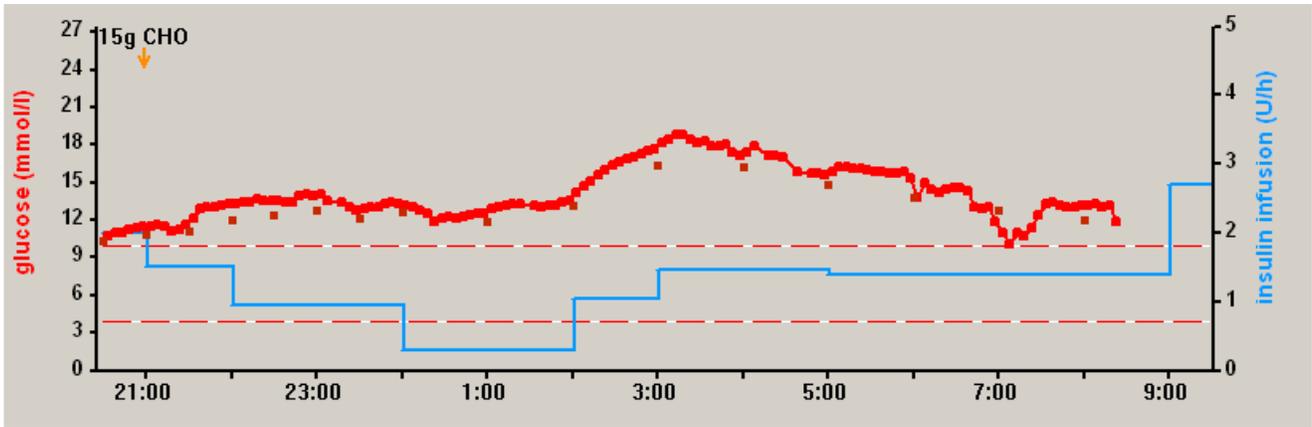


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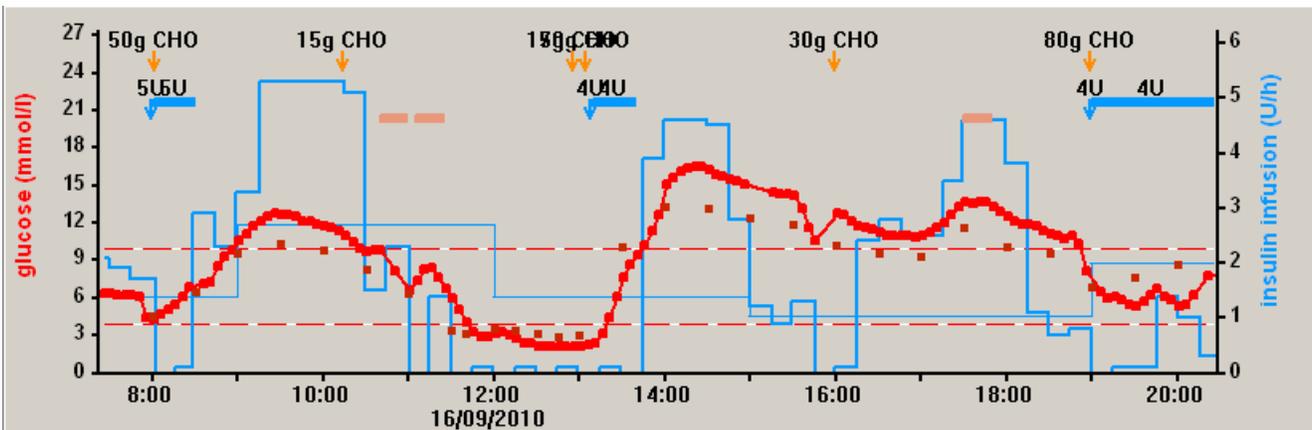
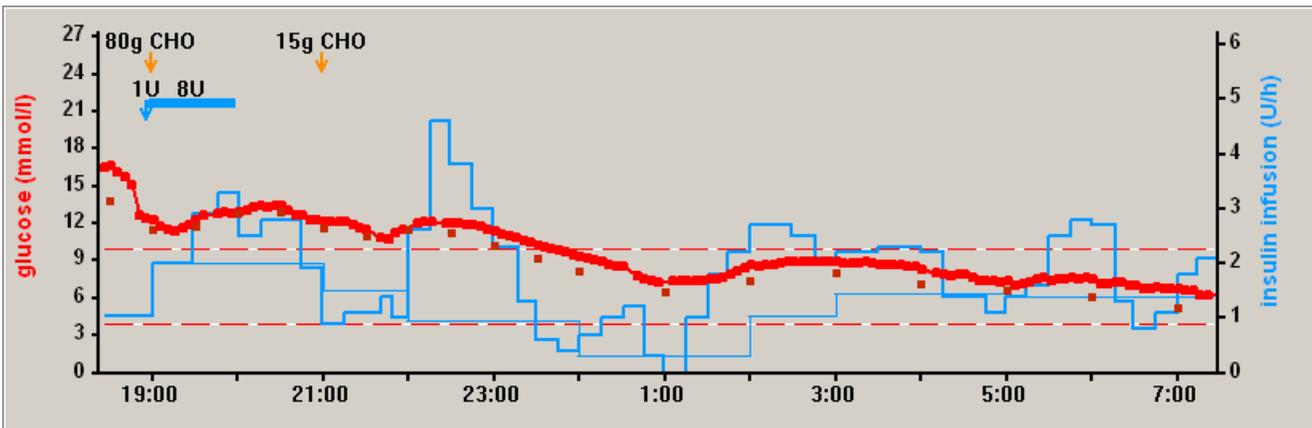
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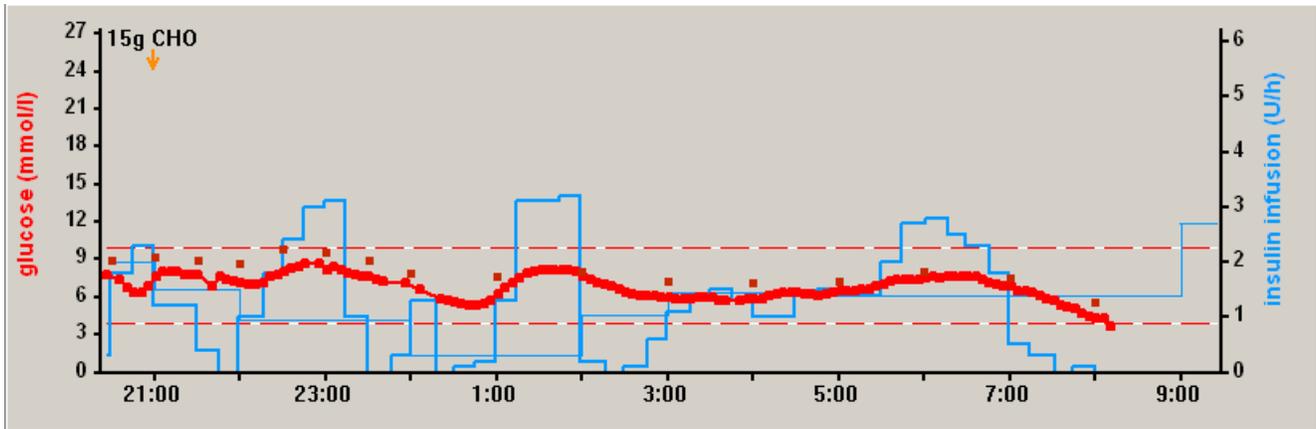
SUPPLEMENTARY DATA



• Closed-loop delivery

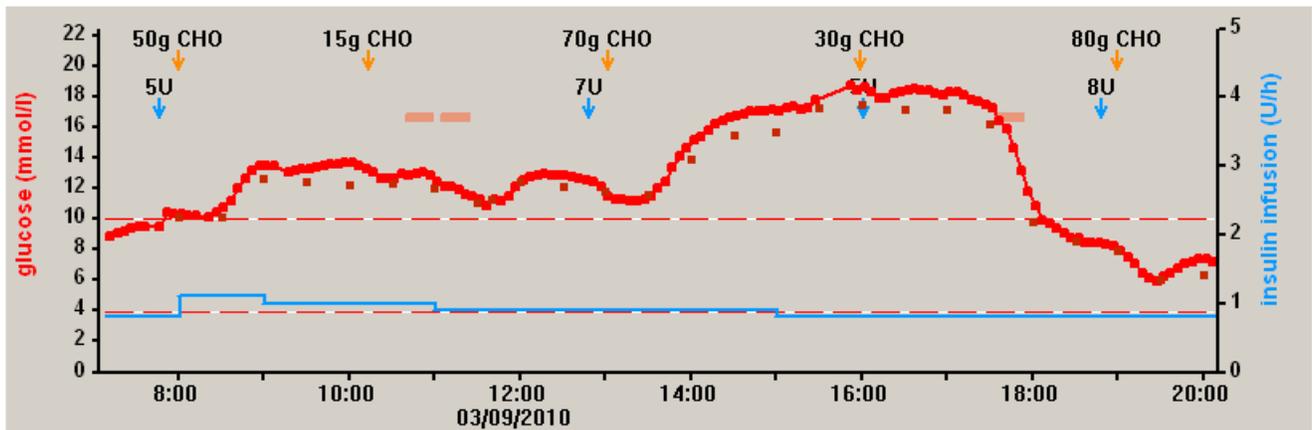
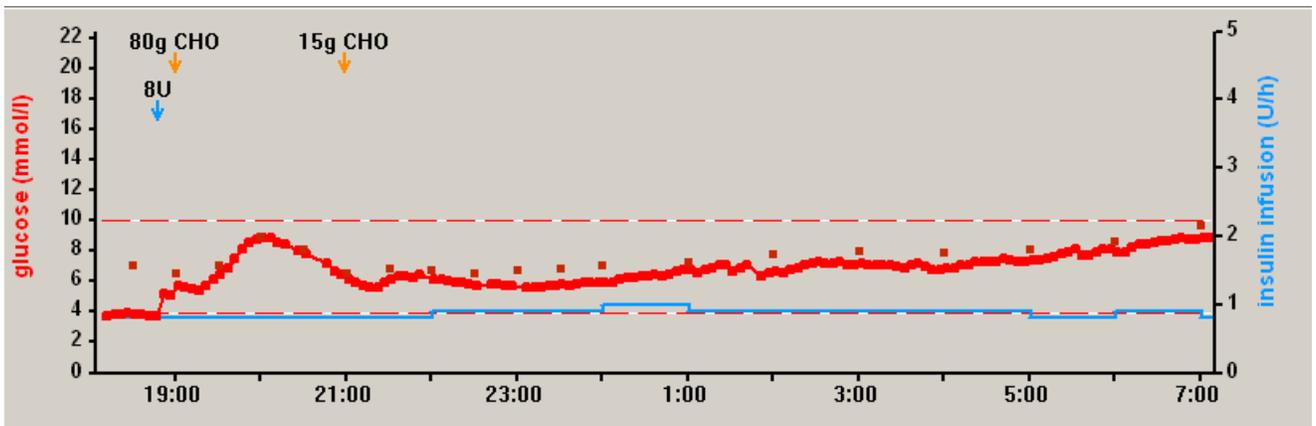


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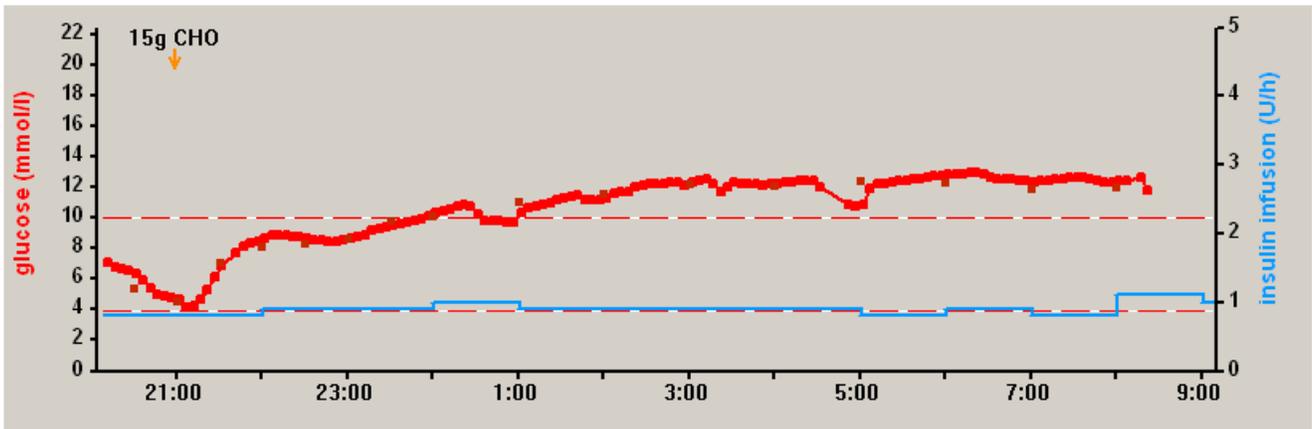


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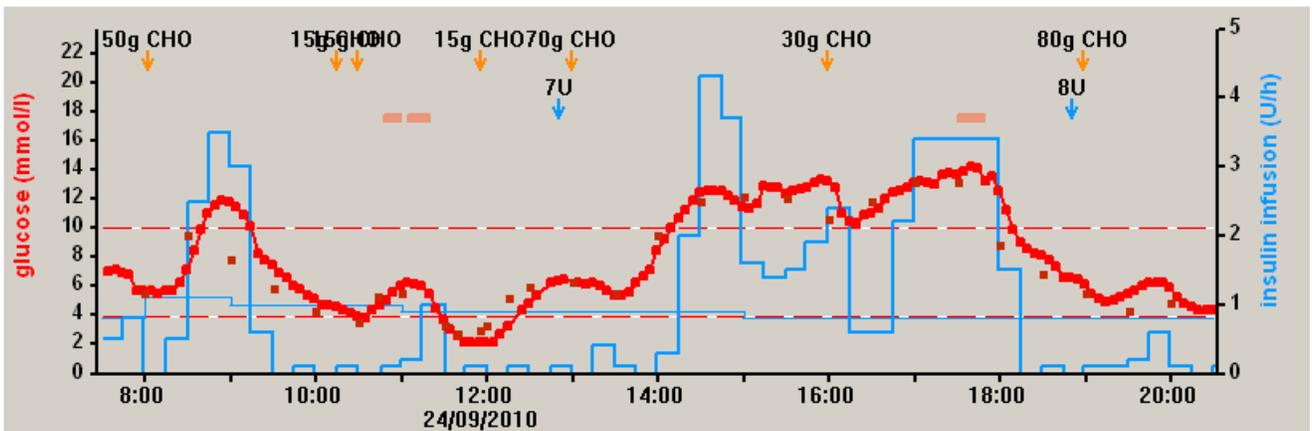
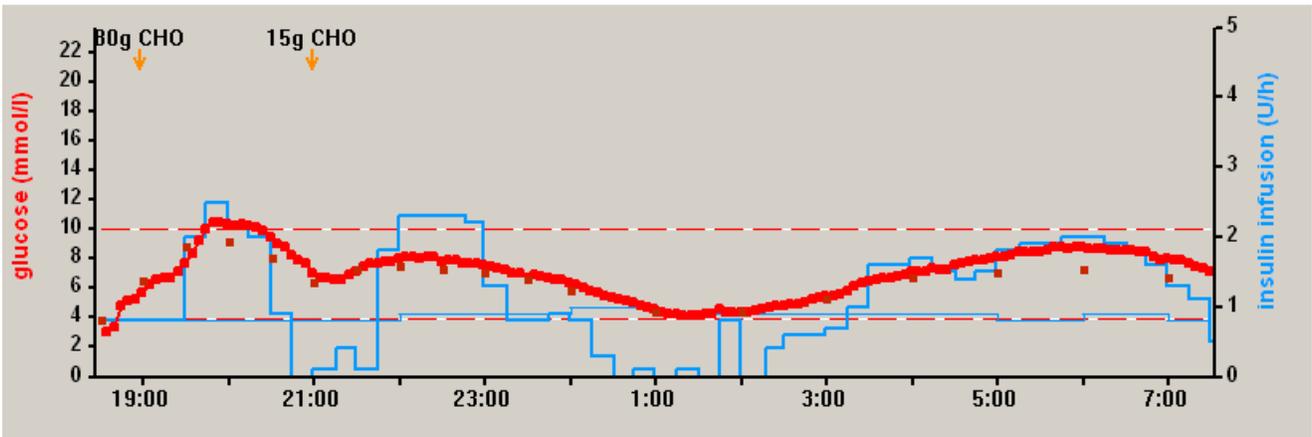
- Insulin pump therapy



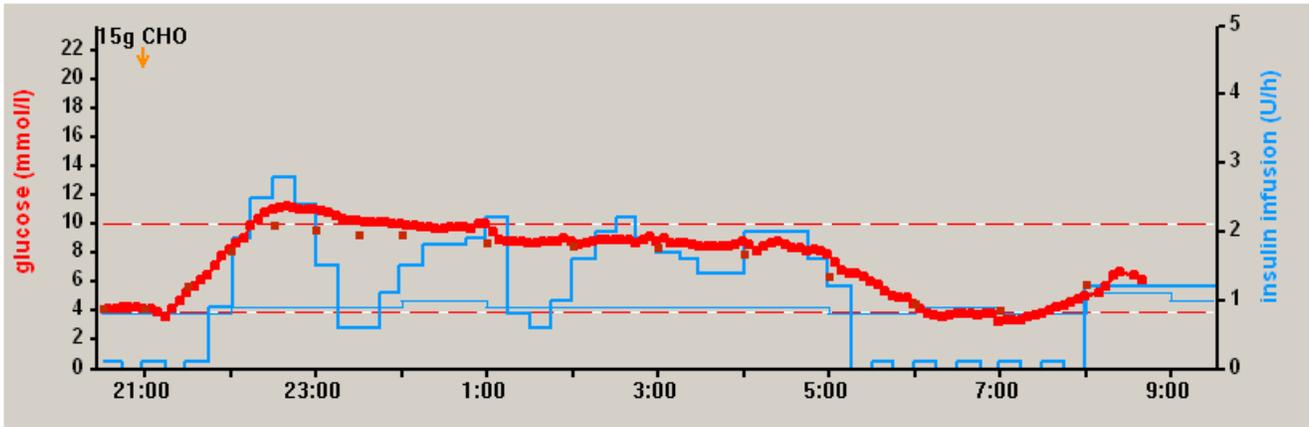
SUPPLEMENTARY DATA



• Closed-loop delivery

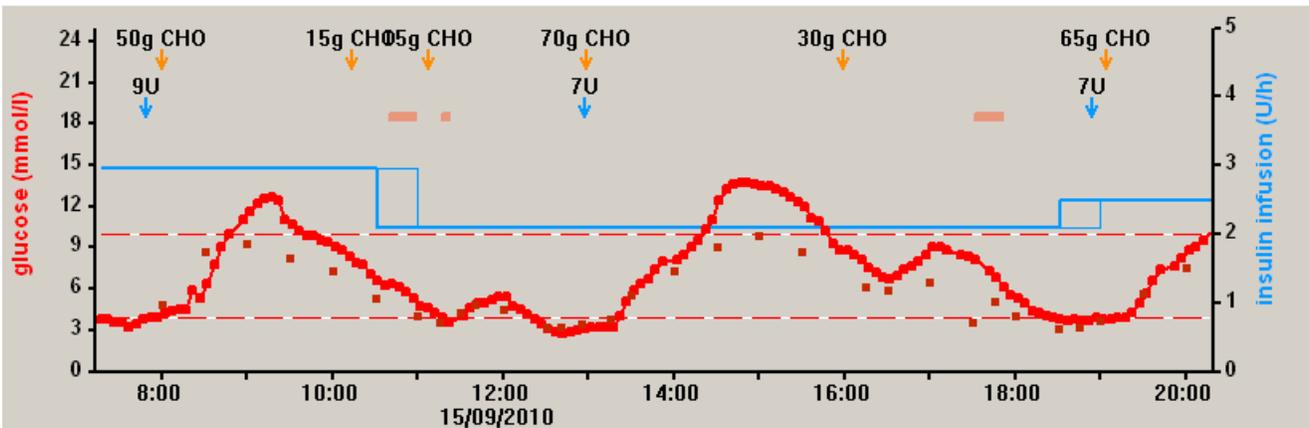
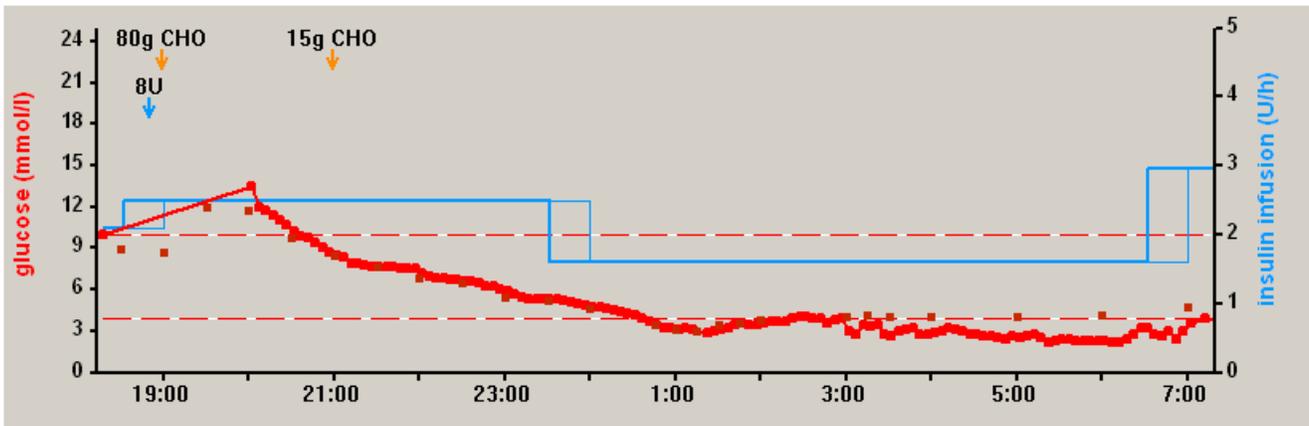


SUPPLEMENTARY DATA

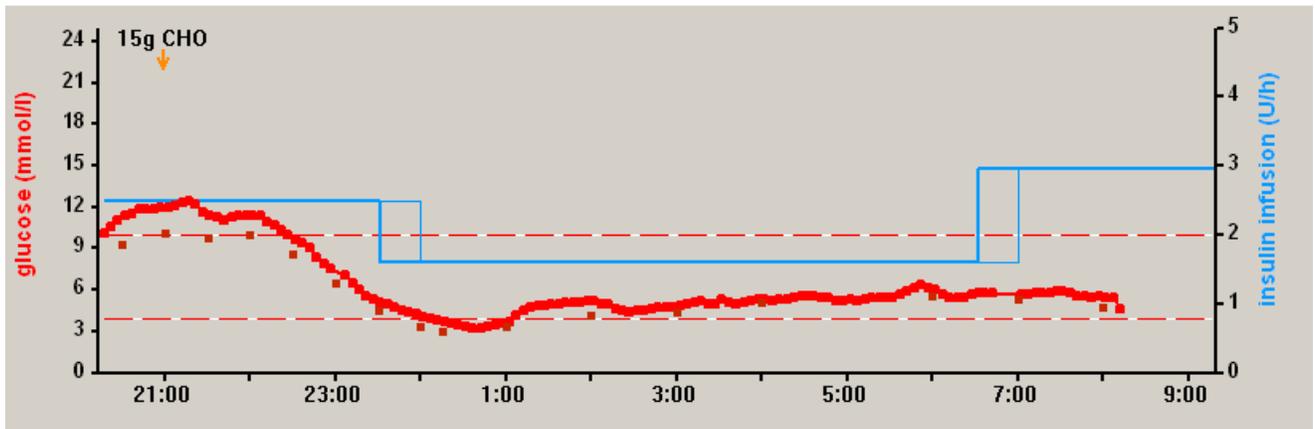


11. Subject 11

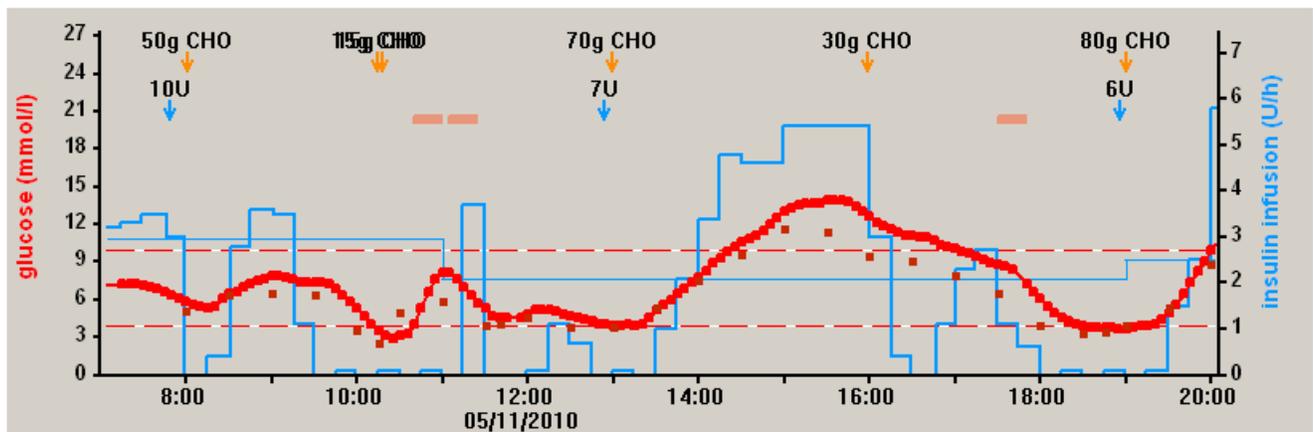
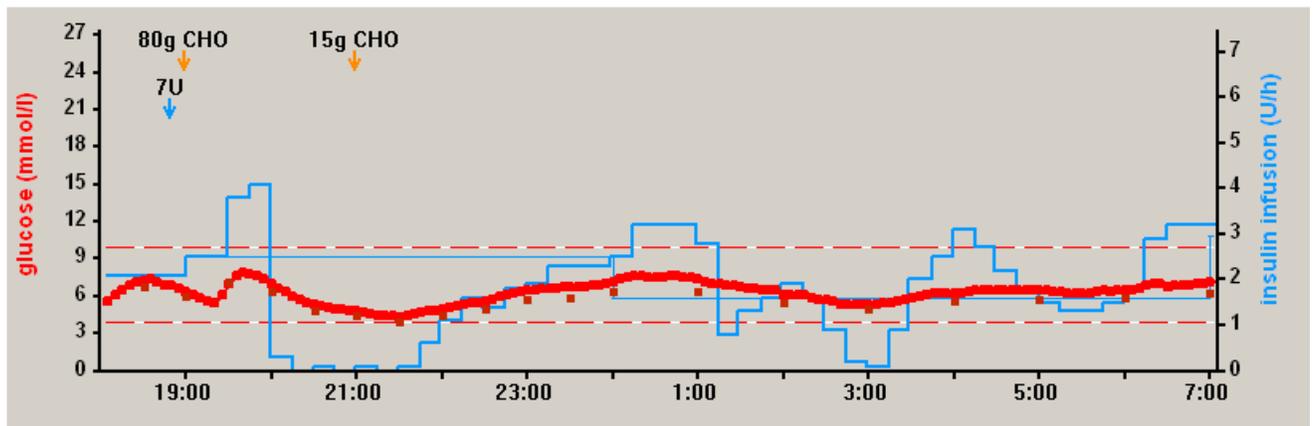
- Insulin pump therapy



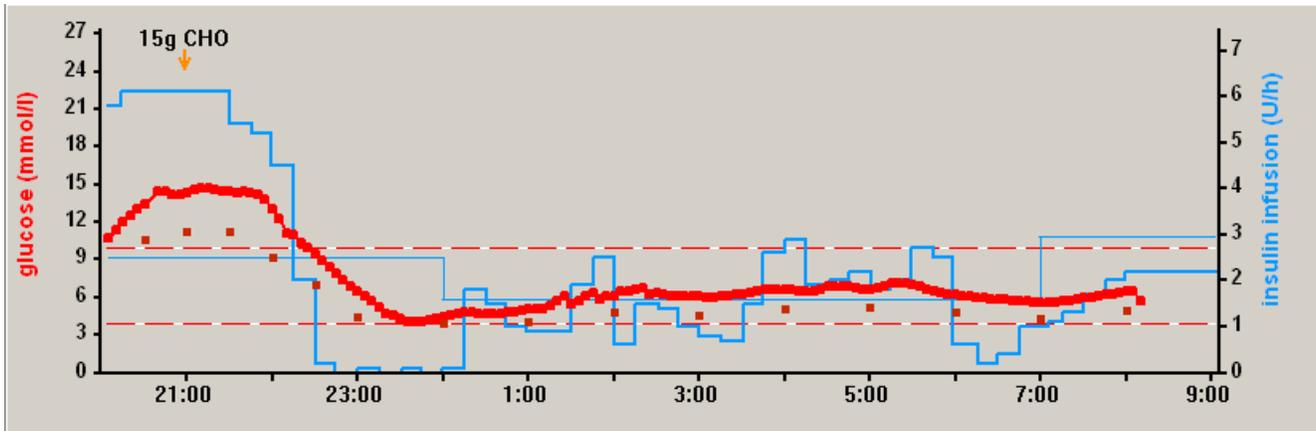
SUPPLEMENTARY DATA



• Closed-loop delivery

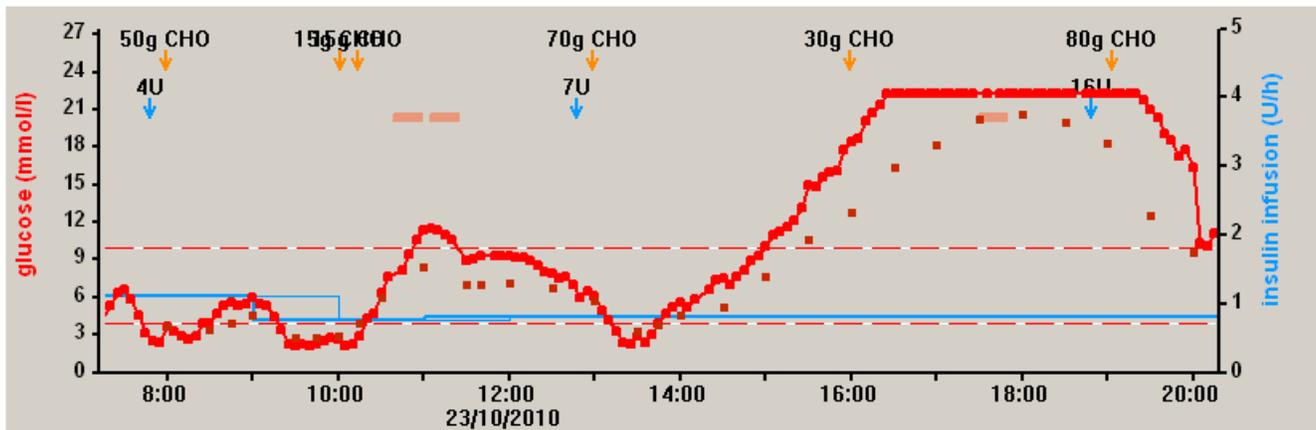
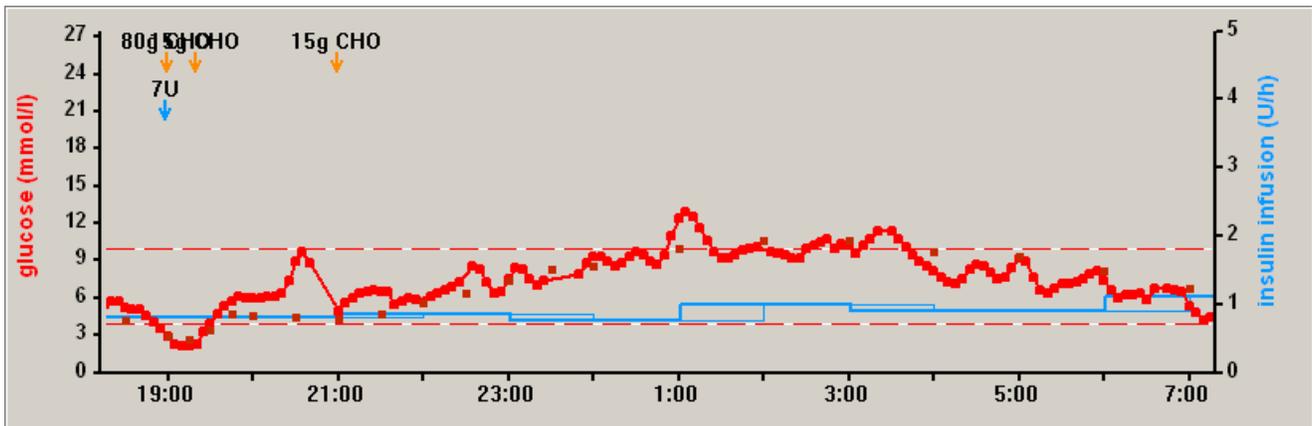


SUPPLEMENTARY DATA

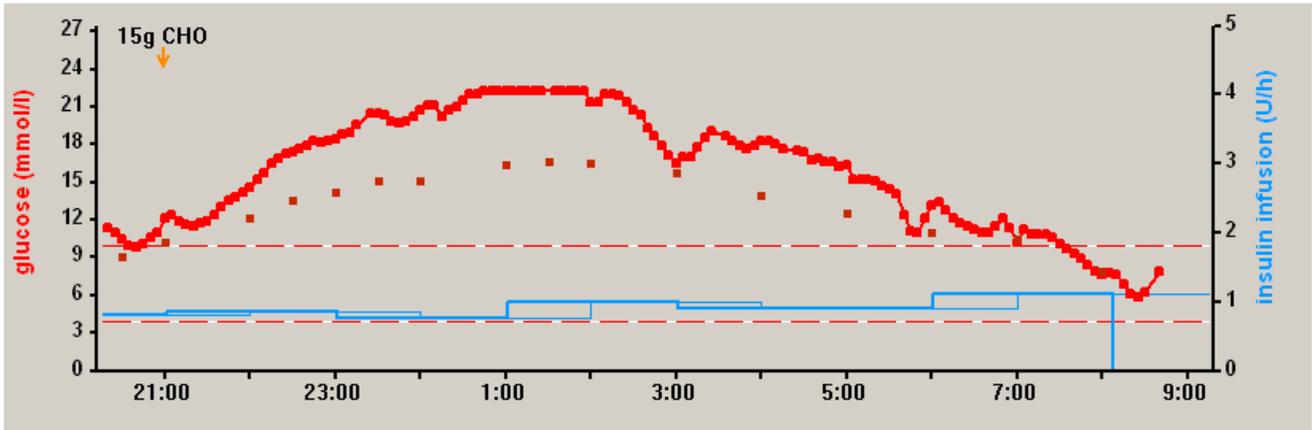


12. Subject 12

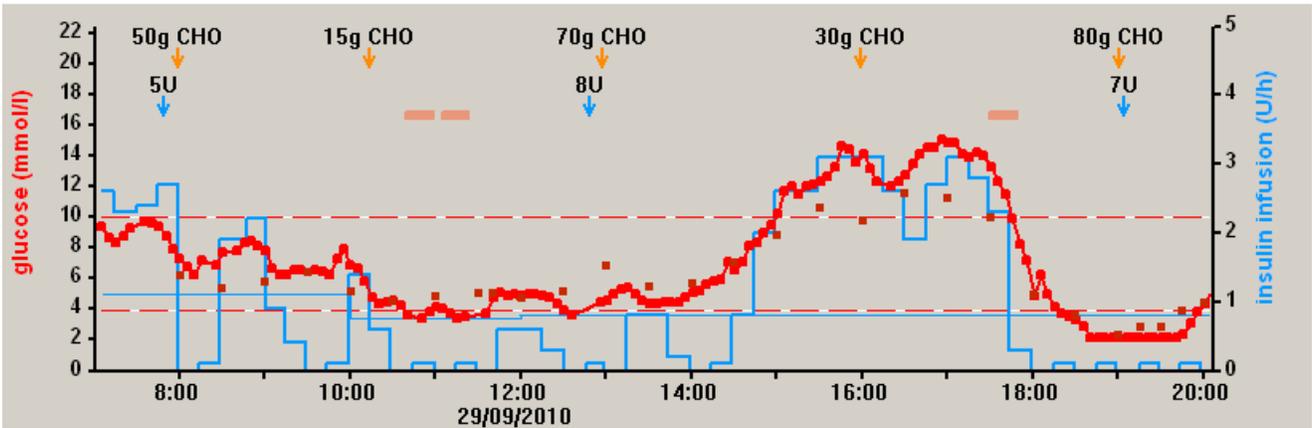
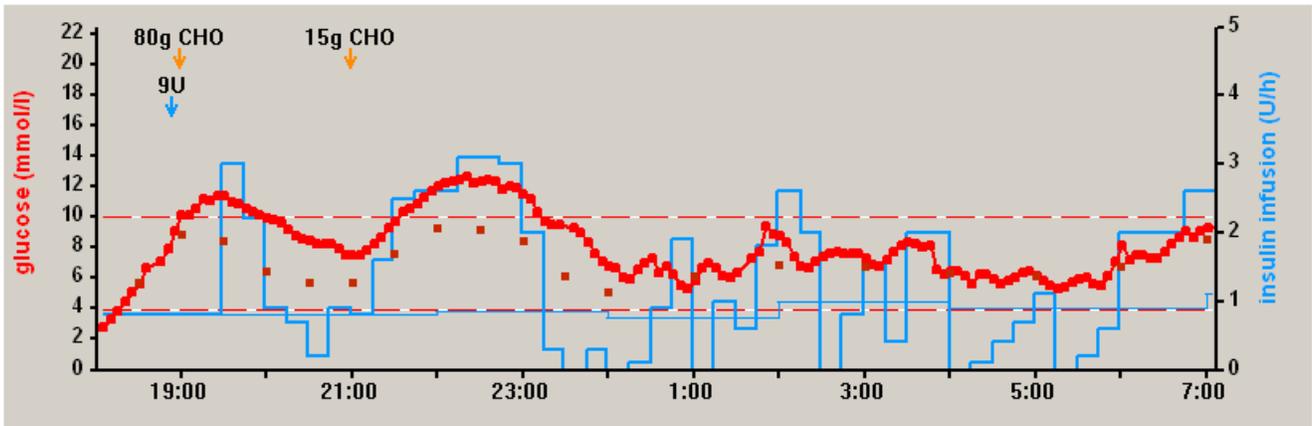
- Insulin pump therapy



SUPPLEMENTARY DATA



• Closed-loop delivery



SUPPLEMENTARY DATA

