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SESSIONS

WASHINGTON, DC • JUNE 25–29, 2021

Performance of a Dual-Hormone Closed-Loop System versus an Insulin-Only Closed-Loop System during Challenging Inpatient Conditions

- A Single-Blinded Randomized Controlled Crossover Study

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Presenter disclosures

Ajenthn G. Ranjan

Disclosed no conflict of interest

Photography allowed

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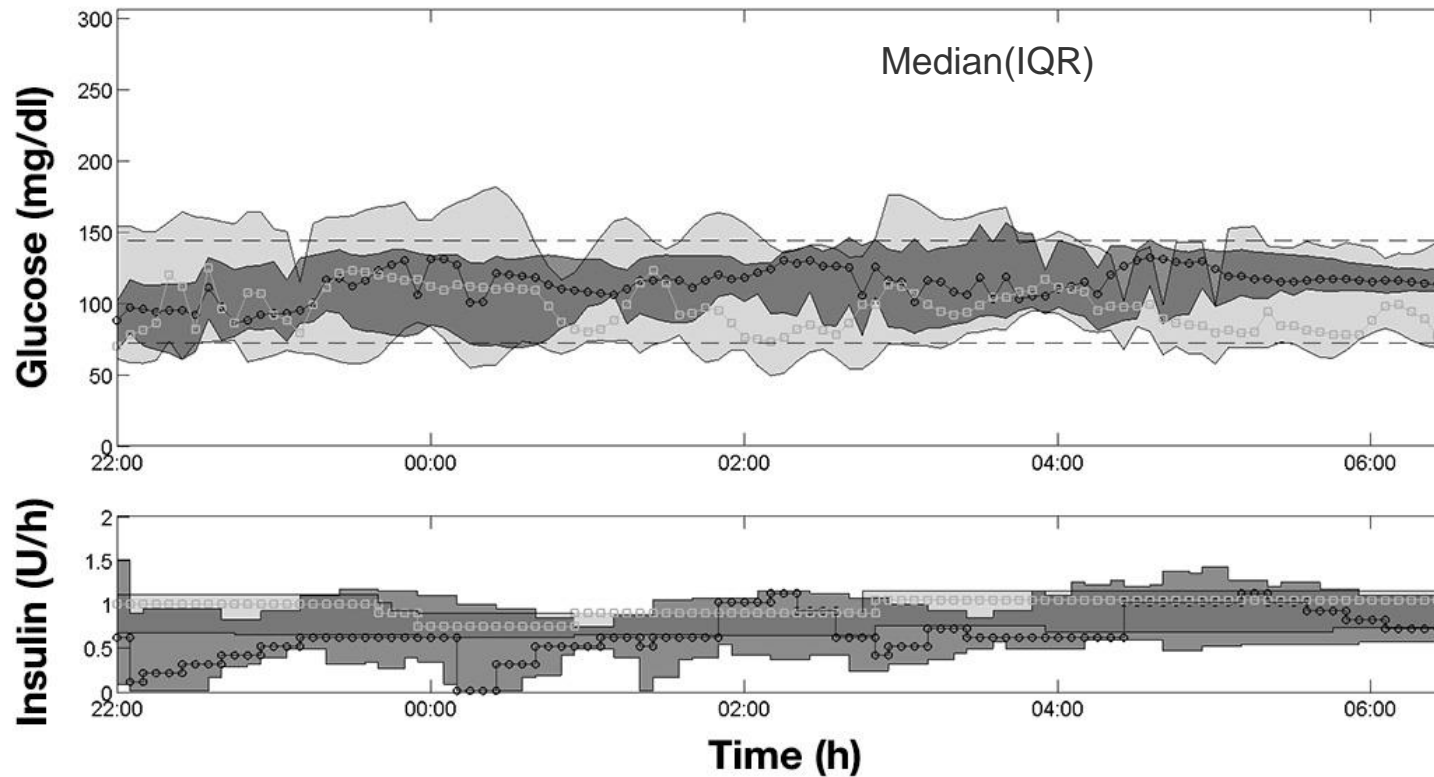


Background

- The most technologically advanced therapy for people with type 1 diabetes is a closed-loop system
- Closed-loop systems perform better than any other technologically approaches
- Hypoglycemia remains an issue especially during challenging conditions, e.g overbolusing and exercise
- Dual-hormone closed-loop system including glucagon infusion may overcome these challenges and reduce the risk for hypoglycemia

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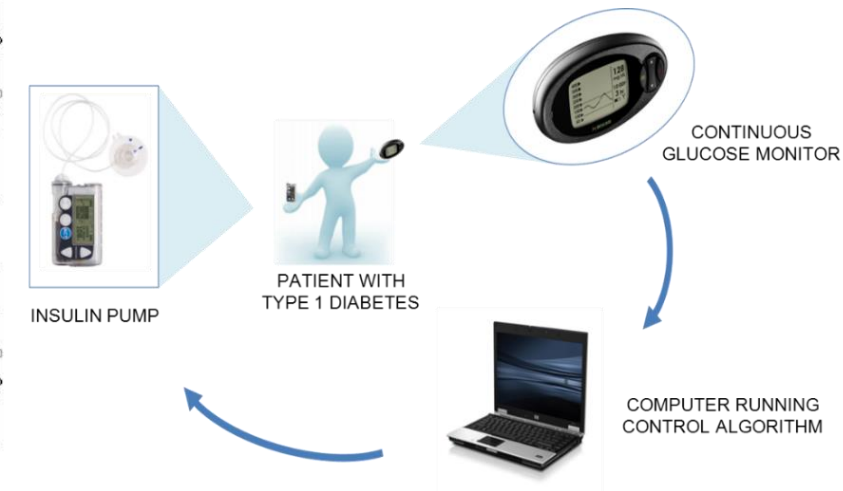
Previous overnight study



Time in range %

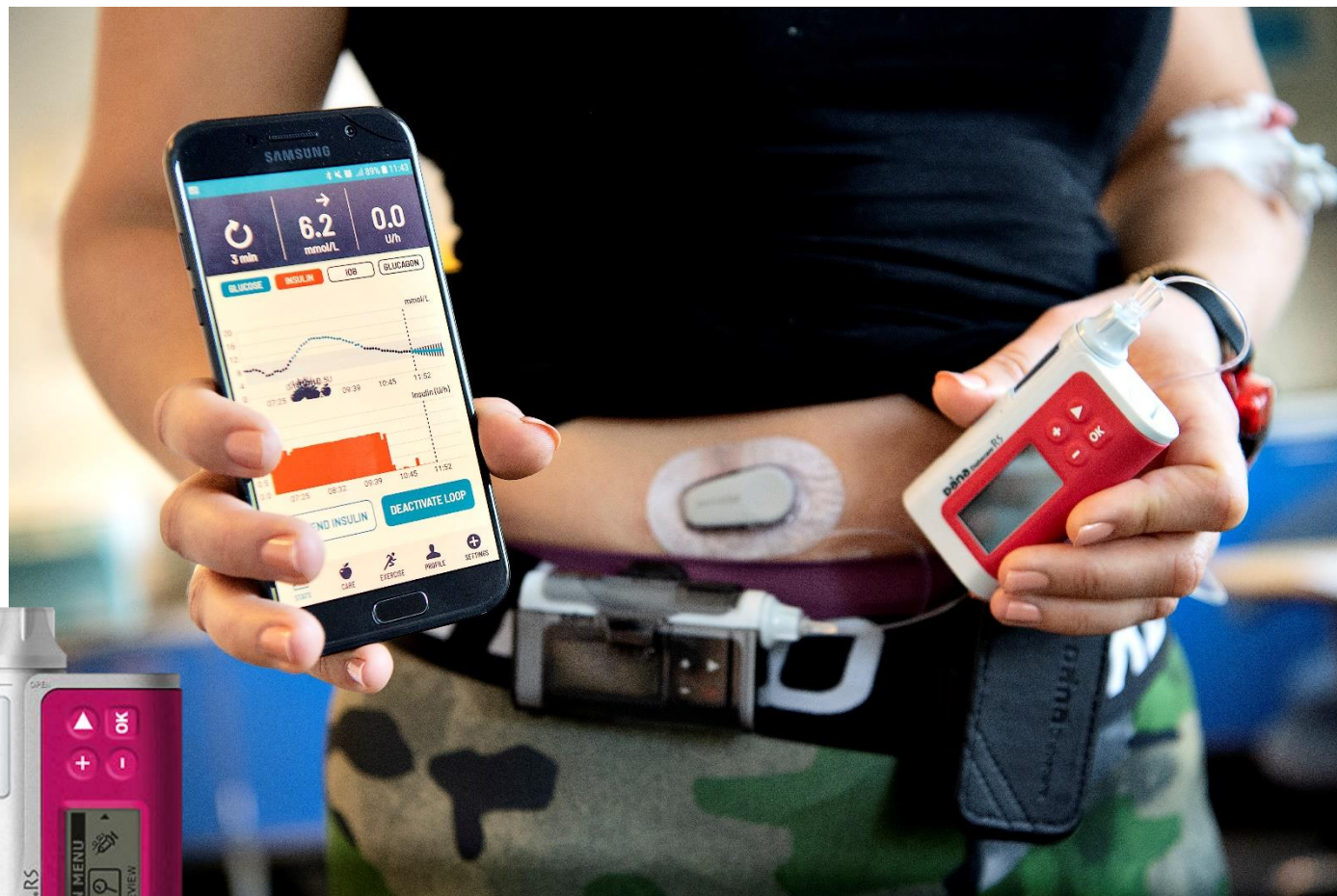
Conventional 67.9 (12.1–90.0)

Closed Loop 90.4 (84.7–99.3)



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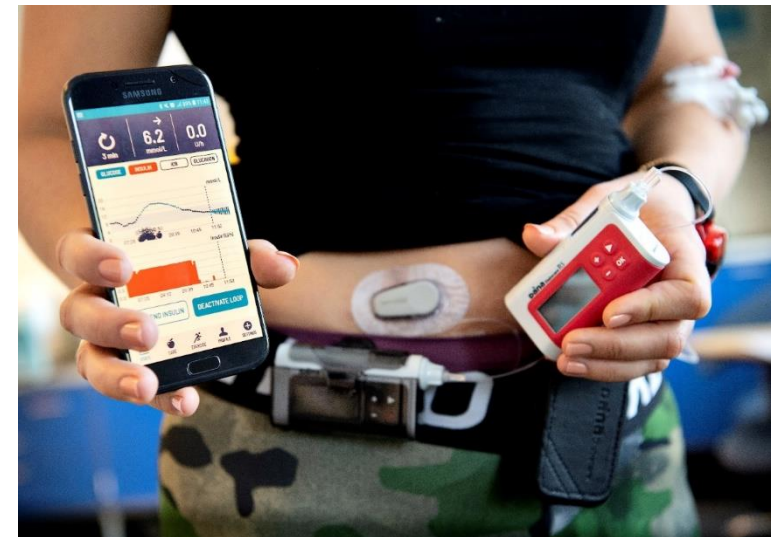
DiaCon APS

- Model fitting based on 3-days CGM and insulin data
- Information put into the system before initiation
 - Average basal rate
 - Insulin to carbohydrate ratio
 - Insulin sensitivity
- Upper limit on basal rate, meal bolus and glucagon bolus
- Meal announcement (gram carbohydrate)
- Autocorrections only allowed for 2 hours postprandially
- No exercise announcement
- No co-administration of insulin and glucagon



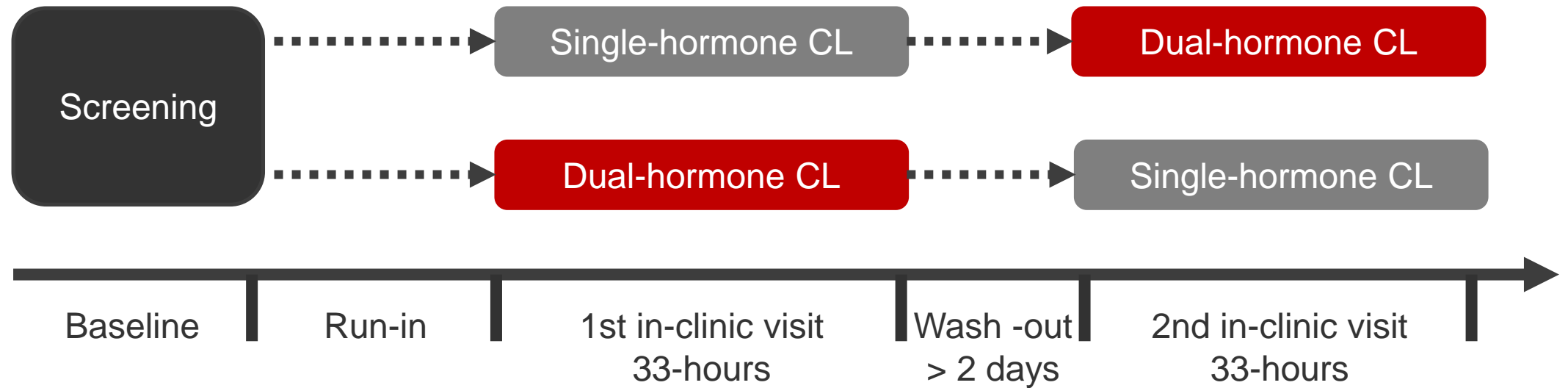
Aim

To assess the **efficacy and safety** of an insulin-glucagon dual-hormone (DHCL) closed-loop system compared with an insulin-only single-hormone (SHCL) closed-loop system



Design

Single-Blinded Randomized Controlled Crossover Study



Single-hormone Closed-loop:
Dual-hormone Closed-loop:

FiAsp and Placebo ("dummy")
FiAsp and GlucaGen



Eligibility criteria

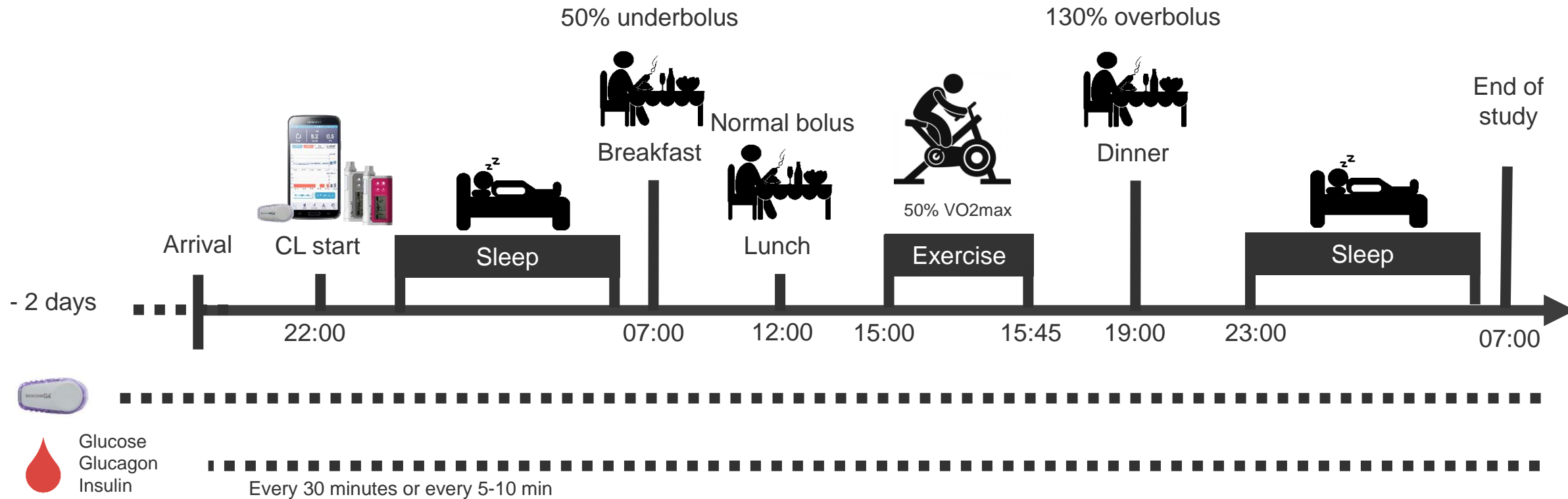
Inclusion criteria

- Age \geq 18 years
- T1D \geq 2 years
- Insulin pump therapy \geq 1 years
- Currently treated with FiAsp-insulin
- HbA1c \leq 8.5% (69 mmol/mol)

Exclusion criteria

- Pregnancy or nursing
- Inability to comply with procedures
- Hypoglycemia unawareness
- Use of anti-diabetic medicine (not insulin)
- History of coronary artery disease

Study visit



Outcomes

Primary outcome

- Percentage of time with CGM < 3.9 mmol/l
- Number of rescue carbohydrates to hypoglycemia (PG < 3.0 mmol/l)

Secondary outcomes

- Mean glucose level
- Glucose variability
- Number of hypoglycemic events

Sample size calculation (N=13)

- Clinical effect size = 2.3%-points (30 min)
- Standard deviation = 2.7%-points¹
- 80% power
- 5% significance level

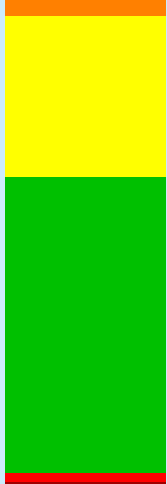
1) Haidar A. Diabetes 2014; 63 Suppl 1: A238–OR.

Baseline Characteristic

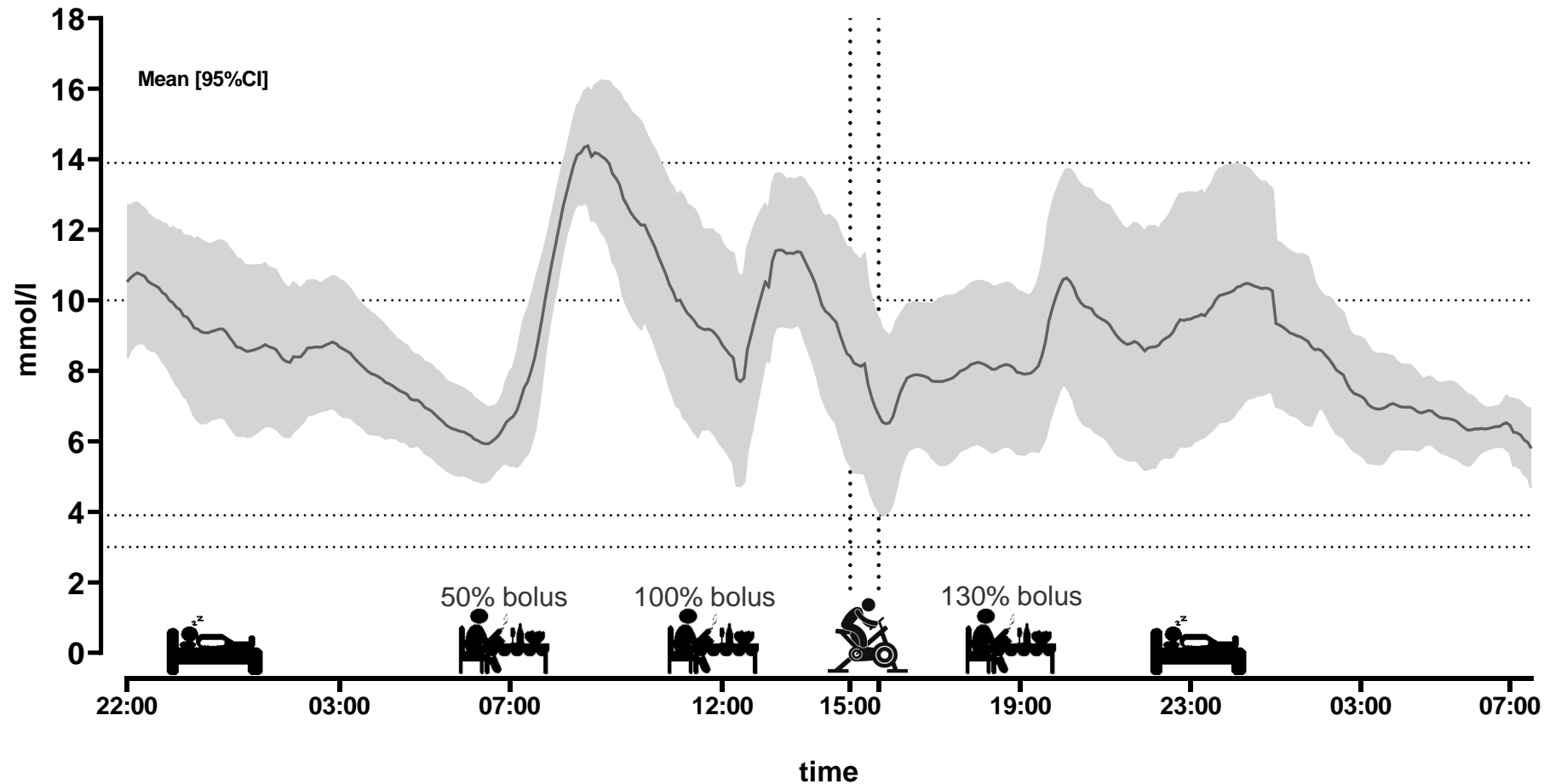
Characteristics	Mean (range)
No. of females/total	7/13
Age, years	48 (26-64)
BMI, kg/m ²	28 (22.2-36.6)
HbA1c, mmol/mol	56 (44-69)
HbA1c, %	7.3 (6.2-8.5)
Diabetes duration, years	29 (17-45)
Insulin pump duration, years	8 (2-15)
CGM duration, years	4 (0-11)
Total daily insulin dose, units	46 (26-74)
Basal, %	51 (49-58)

Continuous Glucose Monitor (CGM)

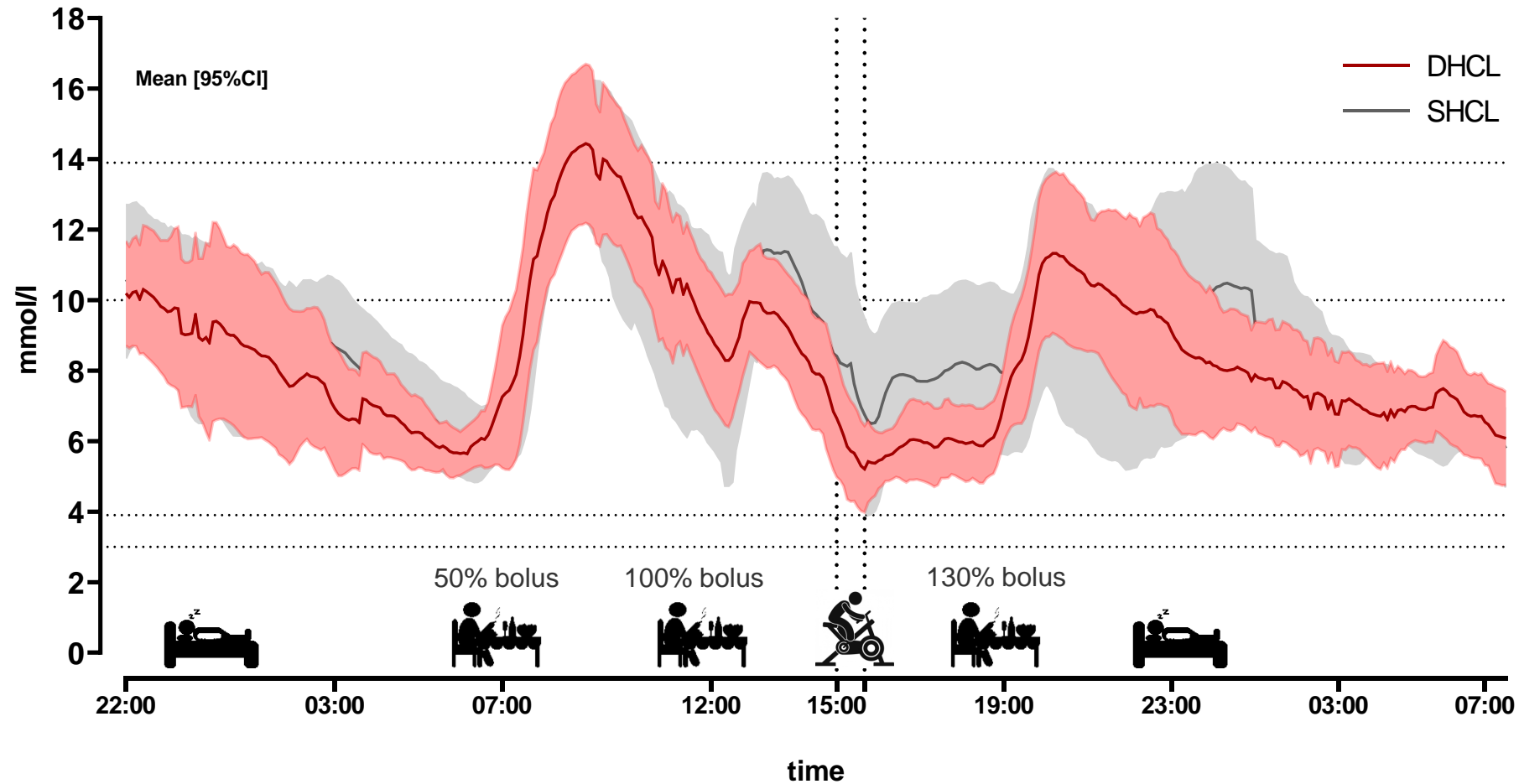
<u>Time in Ranges</u>	<u>Mean (range)</u>
>13.9 mmol/L	9.2 (2.32-32.6)
>10 mmol/L	33.2 (15.8-56.7)
3.9-10 mmol/L	61.0 (39.3-76.3)
<3.9 mmol/L	2.0 (0.3-4.3)
<3.0 mmol/L	0.5 (0.0-1.7)



Sensor Glucose profiles

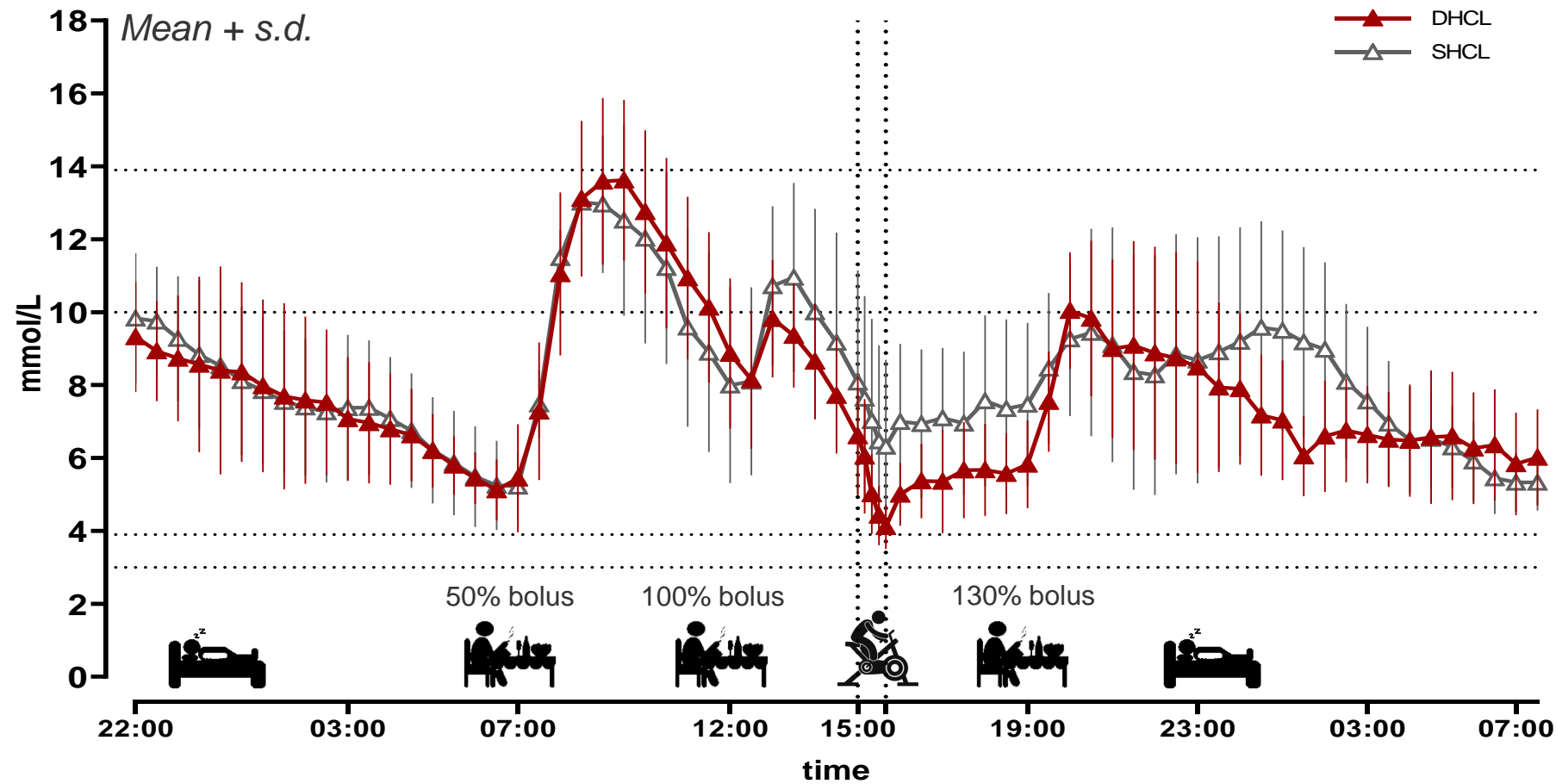


Sensor Glucose profiles



$$P_{\text{treatment*time}} = 0.23$$

Plasma Glucose Profile

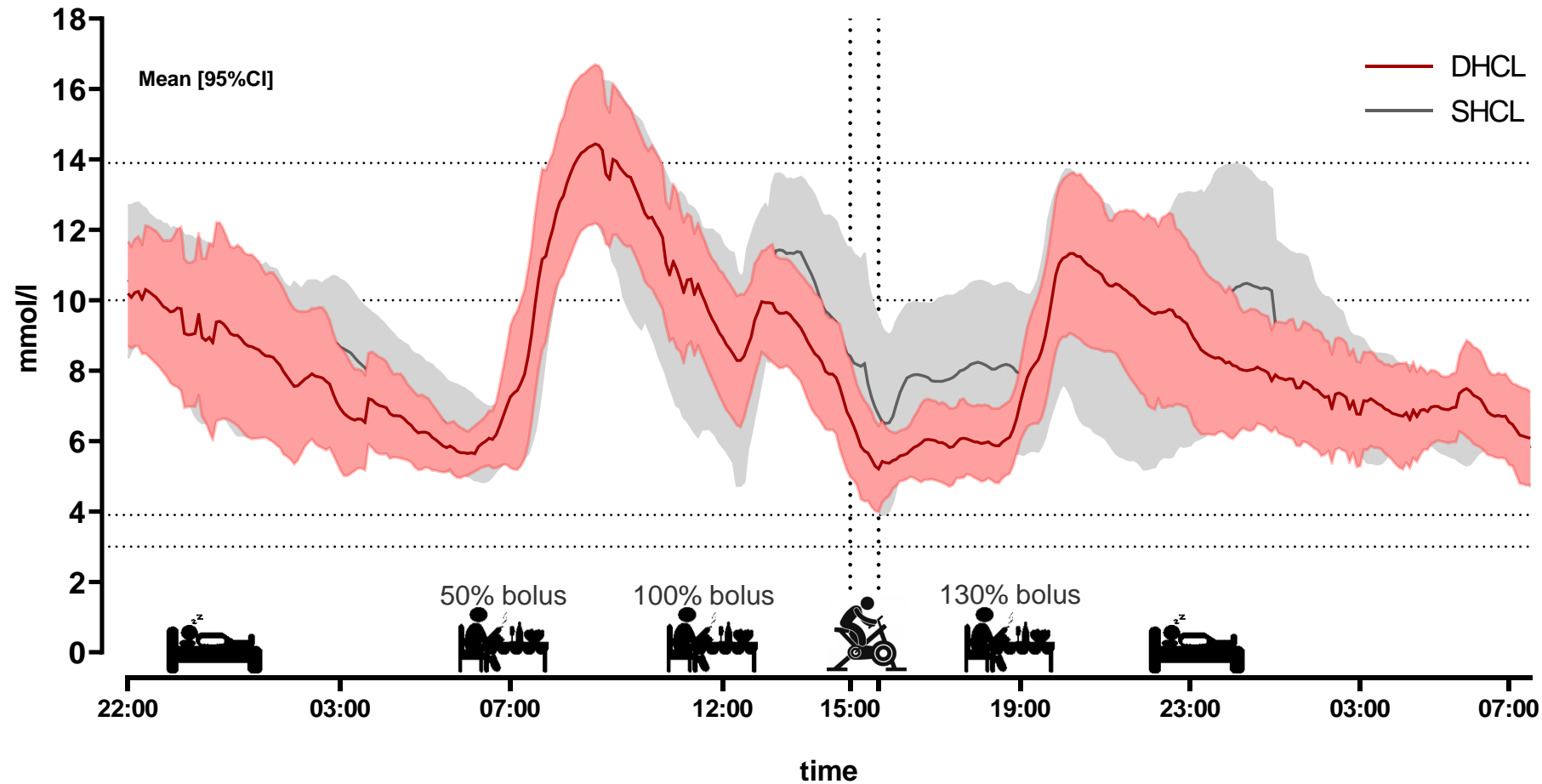


$$P_{\text{treatment*time}} = 0.31$$
$$P_{\text{AUC}} = 0.38$$

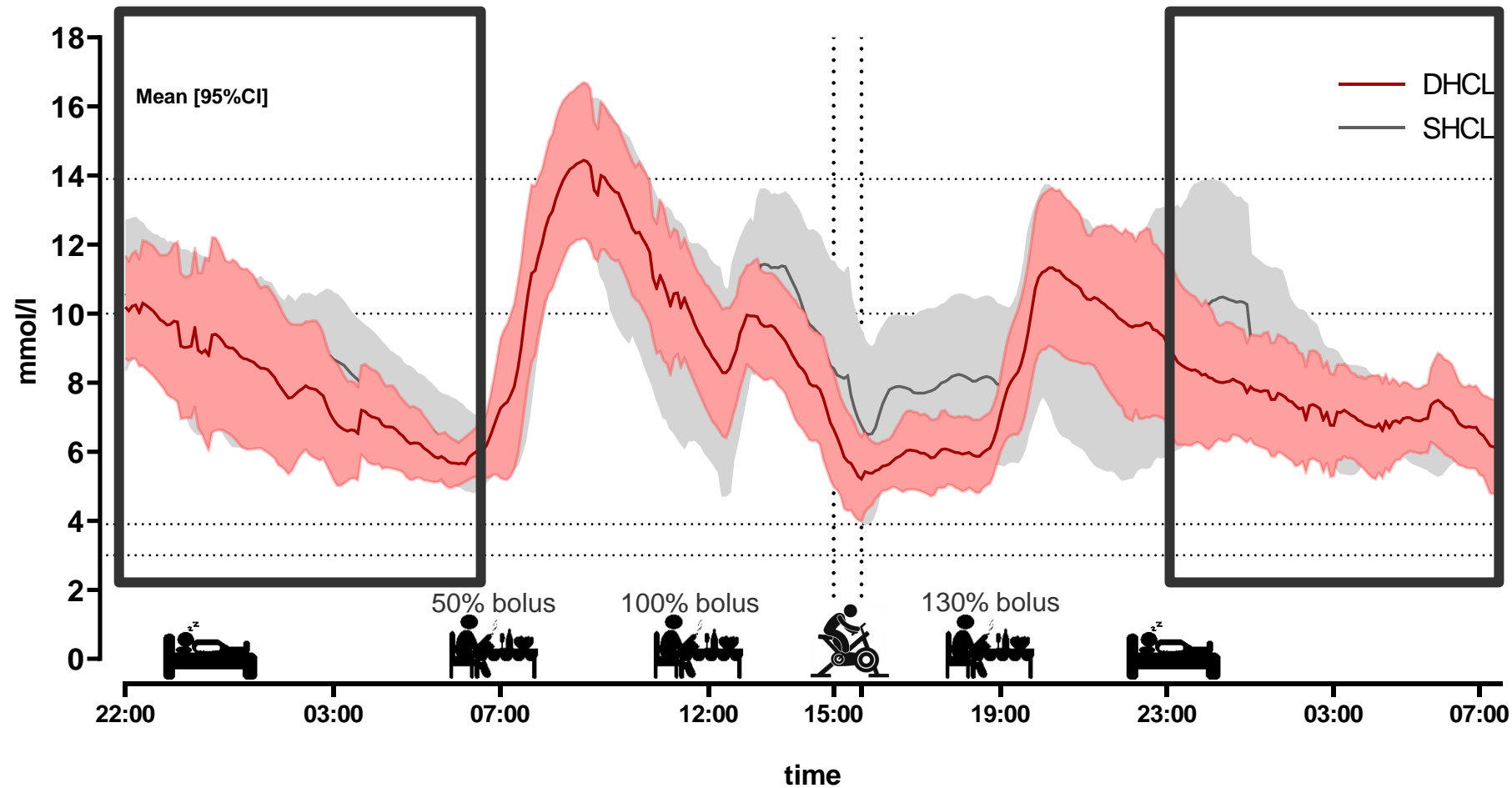
Glucose parameters

	Mean + sd	SHCL		DHCL		P-value
Sensor glucose	TAR-L2 (>13.9 mmol/L), %	11.7	6.7	8.16	6.6	0.26
	TAR-L1 (>10.0 mmol/L), %	29.2	10.4	27.5	14.8	0.46
	TIR (3.9-10.0 mmol/L), %	66.9	10.2	68.8	14.9	0.41
	TBR-L1 (<3.9 mmol/L), %	3.9	3.1	3.7	2.5	0.49
	TBR-L2 (<3.0 mmol/L), %	0.6	0.5	0.6	0.7	0.46
	Mean, mmol/L	8.62	1.0	8.32	1.2	0.30
	CV, %	39%	9%	39%	5%	0.30

Glucose profiles

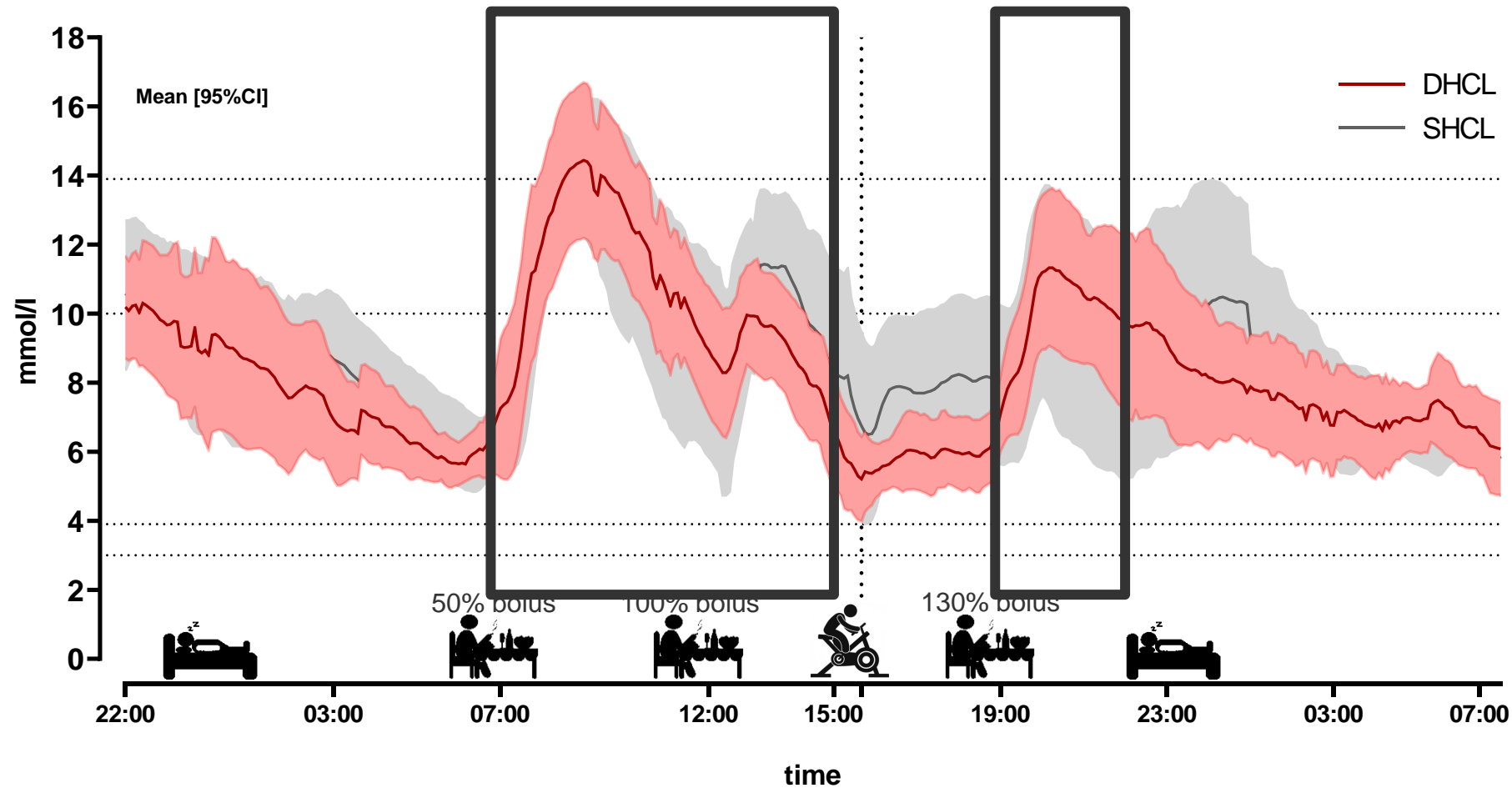


Glucose profiles



No difference
 1. Overall
 2. Overnight

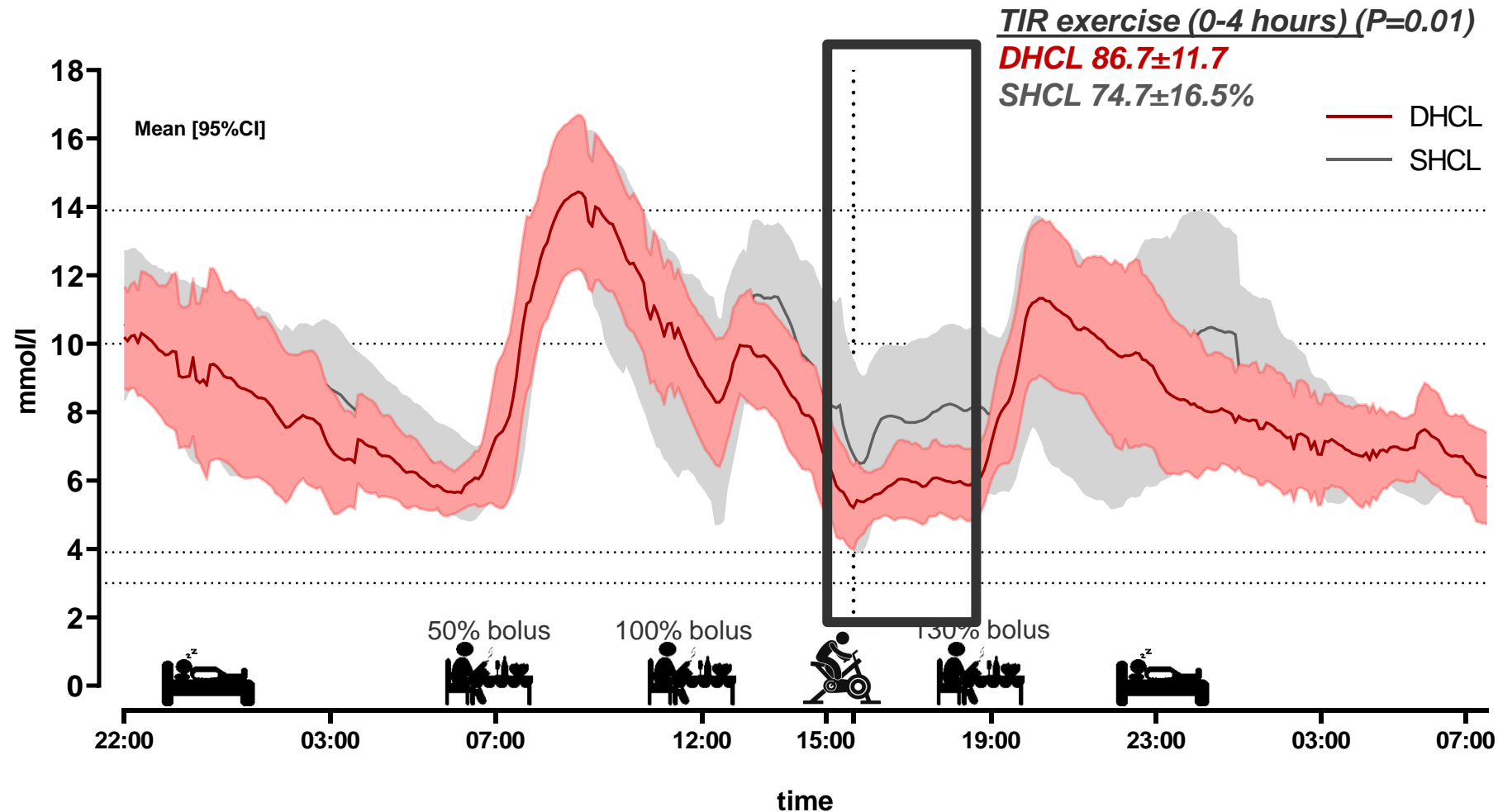
Glucose profiles



No difference

1. Overall
2. Overnight
3. Postprandial (3 hours)

Glucose profiles



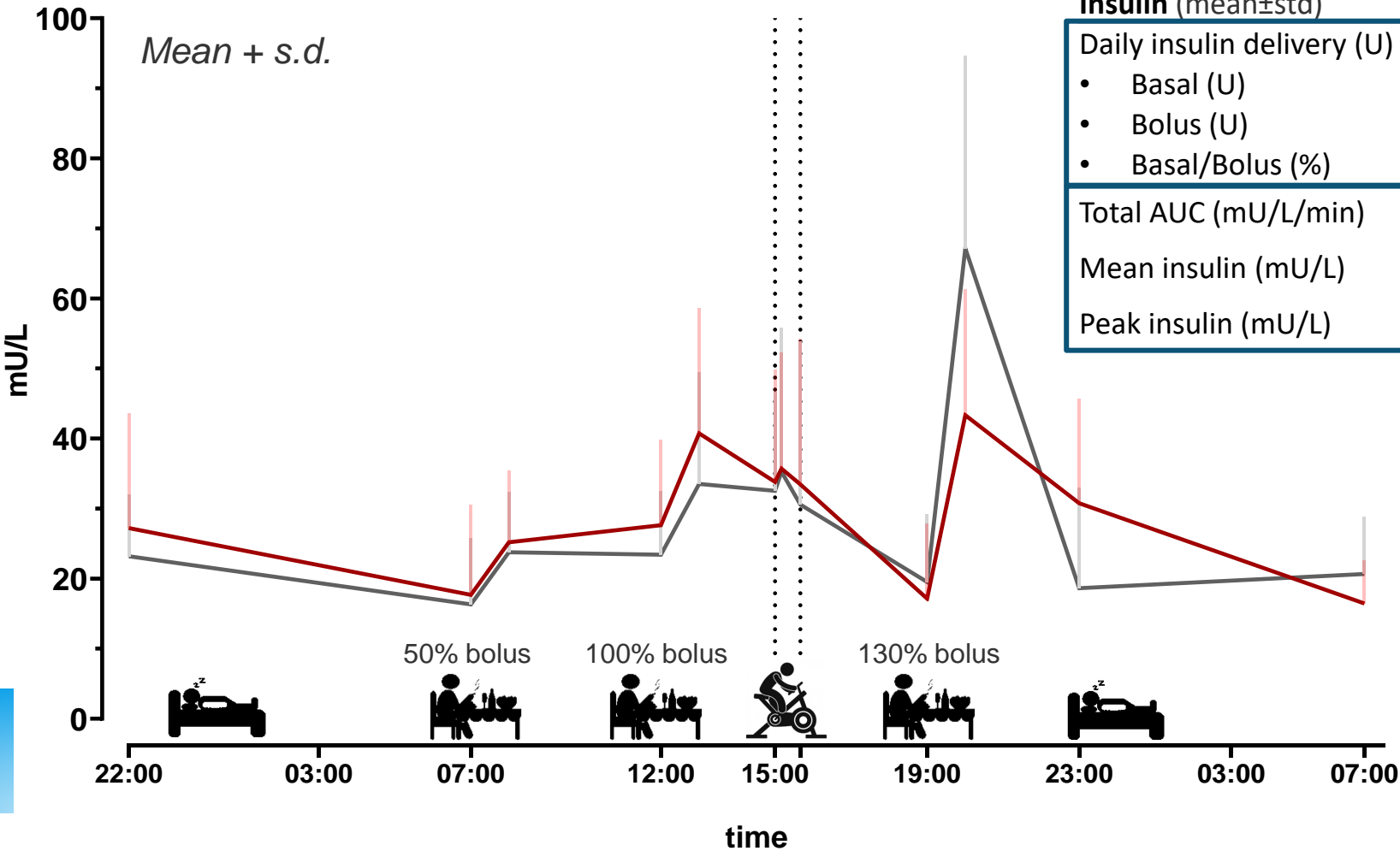
No difference

1. Overall
2. Overnight
3. Postprandial (3 hours)

Difference

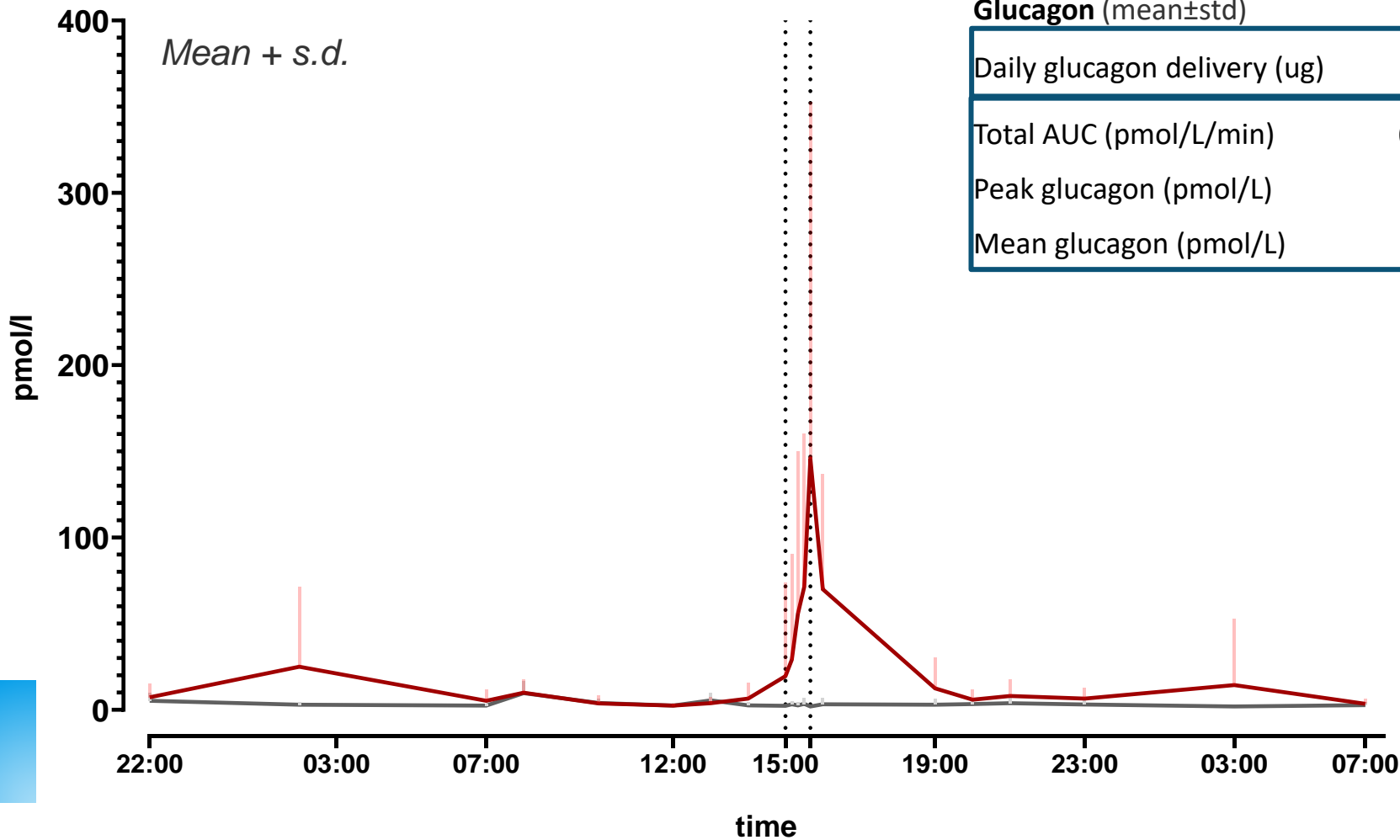
1. Exercise (45 min)
2. Post-exercise (0-3 hours)

Insulin



Insulin (mean±std)	SHCL	DHCL	P-value
Daily insulin delivery (U)	45.5 ± 11.8	40.9 ± 13.8	0.07
• Basal (U)	31.0 ± 8.3	28.8 ± 9.5	0.18
• Bolus (U)	14.5 ± 5.9	12.2 ± 6.2	0.17
• Basal/Bolus (%)	68 / 32	70/30	0.3
Total AUC (mU/L/min)	44833 ± 14153	47318 ± 19728	0.91
Mean insulin (mU/L)	27.8 ± 7.9	29.1 ± 8.8	0.72
Peak insulin (mU/L)	69.8 ± 233.9	55.9 ± 17.1	0.12

Glucagon



Glucagon (mean±std)	SHCL	DHCL	P-value
Daily glucagon delivery (ug)	--	379±13.8 (17-889)	-
Total AUC (pmol/L/min)	6342 ± 2271	28823 ± 15922	<0.0001
Peak glucagon (pmol/L)	12 ± 5.8	182 ± 194.3	<0.0001
Mean glucagon (pmol/L)	3.5 ± 1.3	25.2 ± 19.0	<0.0001

Adverse events

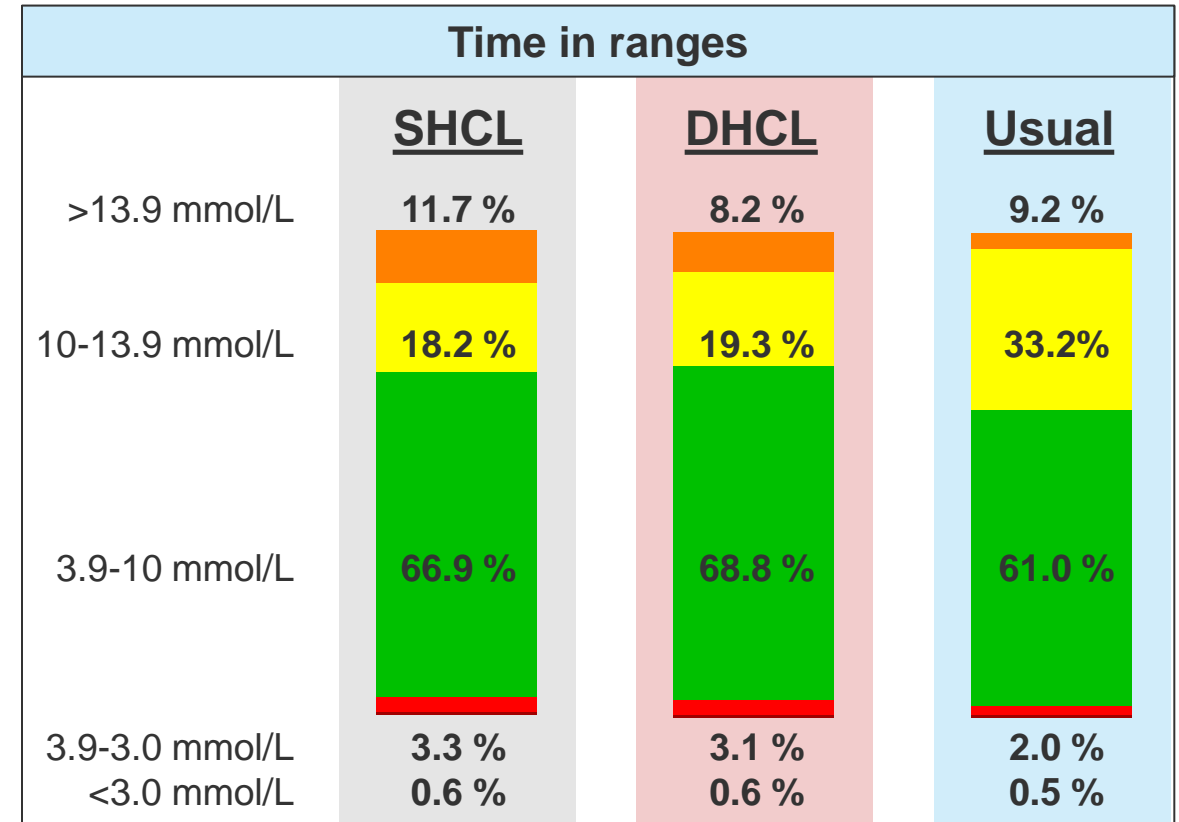
		SHCL	DHCL	P-value
Side effects*	Nausea, no.	4	5	0.73
	Headache, no.	23	17	0.28
	Vomiting, no.	1	0	0.80
	Palpitation, no.	5	1	0.09
	Hunger, no.	37	35	0.76

(*Visual analog scale (0-100) performed 7 times per visit. 1 event = visual analog scale > 10.)

Conclusion

Compared with DiaCon's SHCL, the DHCL

- Had similar TBR
- Had similar TIR
- Reduced the need for rescue carbohydrate
- Had an increased TIR from 0-4 hours after exercise start
- Did not result in more adverse outcomes



Perspectives

- Ongoing adolescents study
- Adjustment in insulin dosing algorithm
- Autocorrection
- Exercise announcement
- Adjustment in the limits of insulin and glucagon delivery



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