SUPPLEMENTARY DATA

Power simulation protocol for supplemental appendix

We conducted power simulations using a database consisting of 165 patients under standard treatment at home. The patients in the database were aged 12-65 years, had a history of type 1 diabetes for at least one year and had used insulin pump therapy for at least three months. They had glycated hemoglobin levels (A1c) of 6.5-10% and Body Mass Index for age below the 97th percentile. The database contains sensor values for several nights for each patient while treated with sensor augmented pump treatment (define as "control" for this study). Since the present study was a crossover study, and since we used non-parametric tests to compare groups, we used the within patient variability observed in the database to estimate the number of patients needed to achieve power for each primary outcome.

The procedure for the power simulations is as follows:

1) We will define a significance level of α=0.05
2) We will calculate the power for a study with *n* patients; while *n* is changing from 10 in jumps of 2 patients. For example, n_1=10, n_2=12... n_{21}=50.
3) For each n_i we will conduct 1000 iterations according to the following procedure:

a) We will randomly choose n_i patients without return from the database.
b) For each chosen patient, we will randomly select 39 nights for MD-Logic arm and other 39 nights for control nights.
c) We will calculate the value of the endpoint from the reference data specifically for each night (per arm).
d) We will estimate that the MD-Logic system impact on the endpoint will be reduction by 30% and enforce it on the endpoint outcome for nights in MD-Logic arm.
e) Valid night for analysis is night which has at least 67% of sensor data. Based on previous experience it is estimated that only 70% of the nights are marked as valid. Therefore, for each patient and for each night we will draw a number between 0-1 to determine if a specific night is marked as valid. If the drawn number is below 0.70, then it is a valid night otherwise this night will be marked as not valid.
f) Each patient will enter into data analysis only if he/she has more than 19 nights (i.e. ~50% of the total 39 nights) on each arm. Patient that does not meet this criterion will be removed from analysis.
g) For each valid patient we will average the results of the endpoint over valid night per arm.
h) We will calculate the P-value from comparing control arm to estimate MD-Logic arm using the non-parametric Wilcoxon sign rank test.

4) For each n_i , we thus obtained 1000 simulated P values, defined as *P_ValueSet*. We will calculat the power for each n_i as follows:

$$Power_{ni} = [\sum P\_ValueSet < 0.05]/1000$$

5) We will plot the $Power_{ni}$ against n_i and choose n_i to deliver power of 80%
6) In case the curve achieved do not do not provide n_i that reach the requested power, we will perform the following steps:

a) We will use the $Power_{ni}$ to calculate the inverse normal scale of 1- $Power_{ni}$, i.e. $Z_{(1-power)}$.
b) We will create a new data set of $Z_{(1-power)} = f(\sqrt{n})$ and fit a linear line to the data points.
c) In the resulting equation, we will calculate the value of $\sqrt{n}$ by inputing enter Z=-0.8416 (the inverse normal scale for 1- power of 80%).
d) We will eliminate the square root and get the N that needed for the requested power.
In this way our power calculation reflects the actual level of variability in outcomes according to the study design and the statistical test that was chosen.

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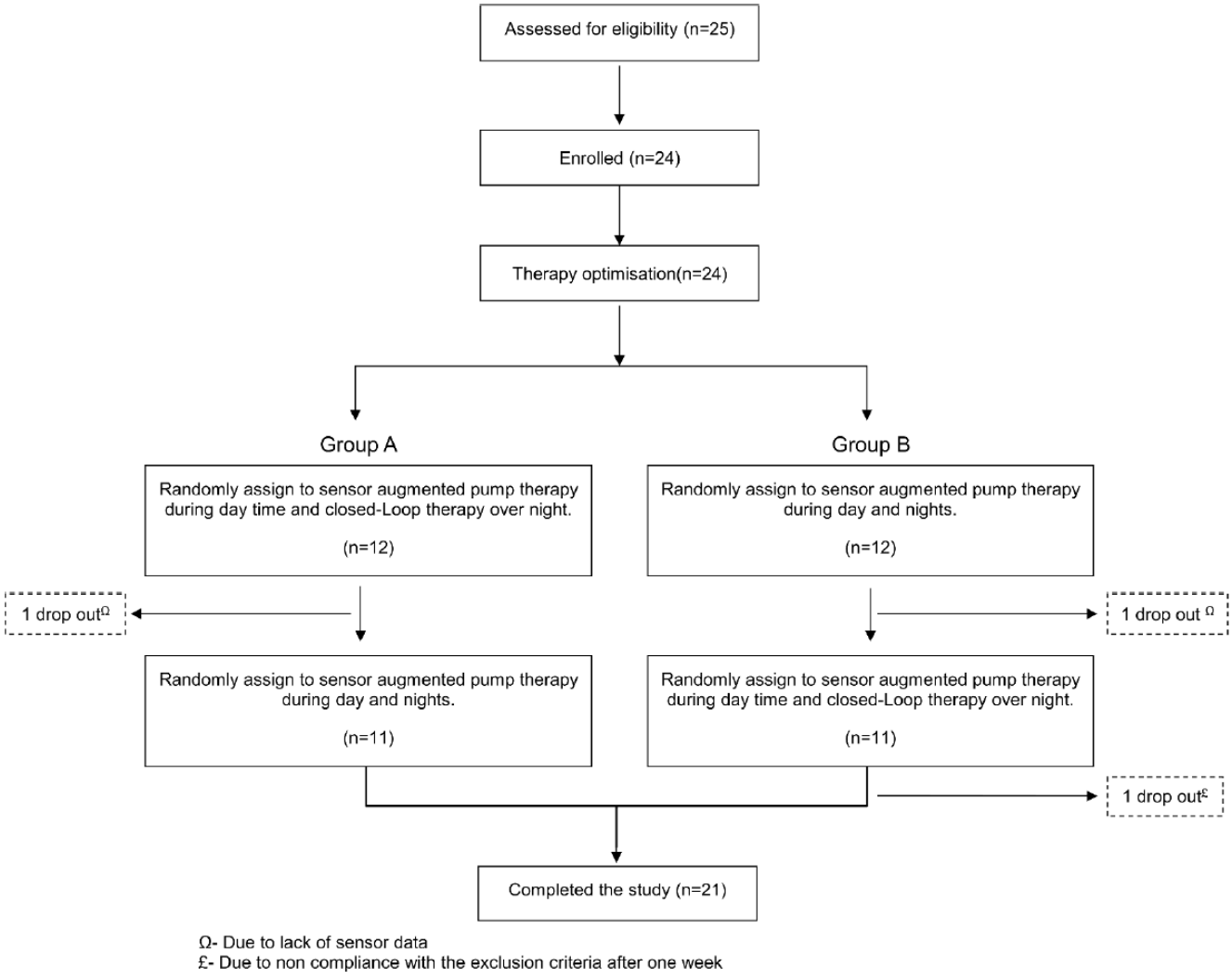
Sensor safety alarms and settings during control nights

During control nights, 9 subjects used the glucose sensor alarms for the whole period of time. Of these 6 modified the pre-defined alarms settings, while 3 also used the low-glucose suspend feature of the pump. Six additional subjects used the sensor alert part of the time; all of them modified the pre-defined settings. Five subjects shut off the alerts for the whole period of time. For one subject no data are available on sensor alert use. During the closed-loop arm patients used the internal safety alerts of the MD-Logic system. These alerts could neither be changed nor shut down, but could be kept silent by turning the computer speaker off.

Supplementary Figure 1. Participant Flow Diagram



Outlined for each group the number of participants who were randomly assigned, received treatment and completed the study. Exclusions and discontinued intervention after randomization are indicated with the reasons for each group.

SUPPLEMENTARY DATA

Supplementary Table 1. Technical fault events during closed- loop operation

Variable (N=19)	Closed-loop ₮
Number of Pump occlusion events	4
Number of PC failure events	4
Number of Internet failure events	2
Average percentage of success communication between the PC and the pump¥	83.8 ± 20.1
Number of communication failure between the PC and the pump	241
Average time of meaningful pump disconnection Φ [min]	63.3 ± 85.7
Number of communication failure between the sensor and the pump	338
Average time of communication failure between the sensor and the pump [min]	41.4 ± 79.0

¥- Percentage of the successful attempts of the system to communicate with the pump from all the attempts.
Φ- Meaningful pump disconnection defined as disconnection of more than 30 minutes.

SUPPLEMENTARY DATA

Supplementary Table 2. Remote monitoring communications with the patients (Total No. of calls = 86)

Reason for Call	Number of Calls	Action taken due to the call
Blood glucose was not measured before bed time	19	Blood glucose measured
Hypoglycemia£	23	In 6 cases patients took carbohydrate due to the call§ In 9 cases patient reported to consumed carbohydrates before the call In 8 cases patients calibrated the sensor or no further action was needed
No data sensor transmitted to the control room¥	28	In 18 cases blood glucose was measured to ensure patient's safety In 4 cases the sensor was lost or needed to be calibrated In 6 cases no further action was taken In 1 case the patient also reported that he gave manual bolus
Hyperglycemia	12	4 cases injected manual bolus¶ 8 cases no further action was needed
Patients were asked to turn on the MDLAP	2	Turn on the MDLAP
Patient decided to close the system in the middle of night	1	System shut off

§ Detailed analysis of these 6 calls shows that: in one event the closed-loop system was off for the whole night, in another event the closed-loop was off for 3.2 hours before the event, in another event the system alert was on but the patient turned the computer speaker off, in another event the call was made one hour after hypoglycemia when blood glucose already started to rise before carb were taken and in another event, the patient was slow to respond to the local alert.

This detailed analysis shows that 2/6 cases of carbohydrate intake were during the time when the closed-loop was not operated (nevertheless entered the ITT analysis).

£ In 11 events the sensor was not accurate and the blood glucose levels were above the hypoglycemic range.

¥ Sensor data was not transmitted to the control due to technical fault with the sensor, disconnection between the pump and the PC or internet disconnection.

¶ In one out of the 4 cases the event happened when the system was off and disconnected (for 1 hour) and in one event it happened due to technical problem in the pump.

SUPPLEMENTARY DATA

Supplementary Table 3. Exploratory Comparisons– Per Protocol

Variable (N=18)	Closed-loop ₮	Control ₮	Paired Difference¥	P Valueɸ
Glucose Control				
Time Within 70-180 mg/dl [%]	78.30 (68.23, 82.48)	59.61 (51.64, 59.14)	16.93 (8.66, 26.52)	<0.001
Mean CGM readings [mg/dl] *	146.22 ± 15.14	160.52 ± 25.64	-14.3 ± 20.2	0.008
Fasting glucose level [mg/dl] *	134.36 ± 17.42	154.27 ± 31.56	-19.63 ± 28.29	0.009
Glucose Variability				
Standard Deviation[mg/dl] *	32.78 ± 5.88	35.85 ± 7.52	-3.07 ± 7.46	0.099
% Coefficient Variable (CV) *	0.22 ± 0.03	0.24 ± 0.05	-0.01 ± 0.05	0.226
Hypoglycemia				
Total Events <70mg/dl	0.15 (0.07, 0.18)	0.19 (0.14, 0.35)	-1.77 (-5.05, 0)	0.107
Total Events <60mg/dl	0.04 (0, 0.08)	0.14 (0.04, 0.19)	-1.25 (-3.37, -0.06)	0.049
Area Below 70mg/dl [mg/dl×min]	89.20 (26.13, 116.35)	193.50 (77.50, 529.81)	-106.75 (-414.52, 4.21)	0.020
Area Below 65mg/dl [mg/dl×min]	46.52 (7.84, 66.69)	121.02 (40.62, 328.75)	-67.07(-264.95, 2.96)	0.022
LBGI‡	0.49 (0.36, 0.66)	0.83(0.64, 1.69)	-0.3 (-1.3, 0)	0.007
Hyperglycemia				
Time > 140mg/dl [%]	48.65 (40.79, 61.18)	57.56 (50.18, 65.73)	-11.69 (-19.92, 1.73)	0.012
Time > 180mg/dl [%]	19.13 (15.07, 29.55)	34.92 (27.51, 42.95)	-11.40 (-23.83, -4.51)	0.001
Area Above 140mg/dl [mg/dl×min]	9443.09 (6784.05, 12879.82)	15228.85 (12972.00, 21406.69)	-5576.85 (-12202.76, -2670.78)	0.001
Area Above 180mg/dl [mg/dl×min]	3046.91 (2441.07, 4505.49)	6608.03 (5523.55, 12284.19)	-3286.06 (-5575.50, -1843.86	0.001
HBGI¶	4.25 (3.05, 5.95)	6.78 (5.68, 9.46)	-2.4 (-5.1, -1.1)	<0.001
Overnight Insulin delivery				
Total Night Dose [Units]	9.06 (7.55, 19.29)	10.70 (8.72, 18.84)	-0.4 (-1.5, 0.35)	0.231
Delivered Basal amount during the night time[Units]	5.29 (4.17, 8.84)	5.65 (4.73, 10.01)	-0.76 (-0.96, -0.49)	<0.001
Delivered Bolus amount during the night time[units]	3.97 (3.01, 9.51)	5.29 (2.83, 6.87)	0.39 (-0.97, 1.03)	0.647

₮-- Median values with the interquartile range in brackets.

**—Average values with the standard deviation.*

ɸ - Comparisons between closed-loop and control nights were performed using the paired non-parametric Wilcoxon Sign Rank Test, unless stated otherwise.

¥ - Closed-loop minus control. A positive value indicates the value was higher on the closed loop compared with control.

‡-- Kovatchev's Low Blood Glucose Index (LBGI) to measure glucose variability (16)

¶-- Kovatchev's High Blood Glucose Index (HBGI) to measure glucose variability (16)

SUPPLEMENTARY DATA

Supplementary Table 4. Numbers of Adverse Events and Serious Adverse Events

Variable (N=19)	Closed-loop	Control
Serious Adverse Events		
Severe Hypoglycemia§	0	1
Diabetes Ketoacidosis	0	0
Adverse Events		
Viral infection	1	1
Gastroenteritis with fever	1	0
Emergency Room	1*	0
Hyperglycemia Intervention	5	4ϕ

§-- An event that required assistance from another person to administer oral carbohydrate, glucagon, or other resuscitative actions

*-- Leg pain

ϕ-- One event with ketonuria

--During washout period: one subject visit the emergency room due to abdominal pain