

## **Supplemental Material**

**Supplemental Table S1: Participant Characteristics**

<b>Parameter</b>	<b>Value (mean <math>\pm</math> _SD) / Number (%)</b>
Age (years)	27.3 $\pm$ 8
Gender (Male/Female)	10 (59%) / 7 (41%)
Education status (Secondary/Bachelor)	2 (12%) / 15 (88%)
Duration of Diabetes (years)	10.97 $\pm$ 6.01
Smoker	3 (17%)
Recent DKA in the last 12 months	1 (5%)
Severe hypoglycemia in the last 12 months	2 (12%)
Participants using MDI therapy	14 (82%)
Participants using CSII therapy	3 (17%)
Participants using sensor-augmented pump therapy	2 (12%)
Previous CGM use	4 (23%)
Body Mass Index (kg/m <sup>2</sup> )	25.07 $\pm$ 5.32
body fat (%)	27.49 $\pm$ 12.90
HbA1c (%)	7.34 $\pm$ 0.92
HbA1c (mmol/mol)	57 $\pm$ 7.7
LDL cholesterol (mmol/L)	2.62 $\pm$ 0.80

**Supplemental Table S2: Comparison of study outcomes by Treatment Arm After Each Hypoglycaemic Event occurred after 8 hours of fast:**

Outcome	OG Mean $\pm$ SD N (10)	MDG Mean $\pm$ SD N(23)	Difference (*) Mean (95% CI)	P- value
Change in glucose at Time 0 <sup>(†)</sup> –15 minutes, mg/dL <sup>(‡)</sup>	29.6 $\pm$ 28.5	40.7 $\pm$ 19.9	11.0 (-4.7, 26.7)	0.17
Change in glucose at Time 0–30 min, mg/dL, $\Delta^{t30}$ <sup>(‡)</sup>	41.5 $\pm$ 16.7	60.8 $\pm$ 22.1	17.5 (3.5, 31.4)	0.01
Change in glucose at Time 0–45 min, mg/dL	40.0 $\pm$ 20.5	50.0 $\pm$ 48.0	3.9 (-25.2, 33.0)	0.79
Change in glucose at Time 0–60 min, mg/dL, $\Delta^{t60}$	47.1 $\pm$ 25.5	61.9 $\pm$ 42.1	12.8 (-18.1, 43.7)	0.42
Change in glucose at Time 0–120 min, mg/dL	57.3 $\pm$ 31.2	47.7 $\pm$ 32.8	-9.4 (-33.9, 15.0)	0.45
Minimum glucose in 60 min, mg/dL	47.0 $\pm$ 12.0	54.6 $\pm$ 10.9	6.9 (-0.5, 14.2)	0.07
Maximum glucose in 60 min, mg/dL	85.0 $\pm$ 25.6	102.6 $\pm$ 31.1	8.2 (-11.9, 28.3)	0.42
Mean glucose in 60 min, mg/dL	57.3 $\pm$ 15.7	70.9 $\pm$ 16.4	9.7 (-1.0, 20.3)	0.07
Time >180 mg/dL in 60 min, (%)	0 $\pm$ 0	0 $\pm$ 0	-	-
Time 70-180 mg/dL in 60 min, (%)	19.8 $\pm$ 34.5	36.7 $\pm$ 28.6	10.4 (-8.1, 28.9)	0.27
Time <70 mg/dL in 60 min, (%)	80.3 $\pm$ 34.5	63.3 $\pm$ 28.7	-10.4 (-28.9, 8.1)	0.27
Minimum glucose in 120 min, mg/dL	51.0 $\pm$ 16.5	54.6 $\pm$ 10.9	1.6 (-6.9, 10.2)	0.71
Maximum glucose in 120 min, mg/dL	110.5 $\pm$ 29.7	132.5 $\pm$ 51.6	18.6 (-16.9, 54.1)	0.31
Mean glucose in 120 min, mg/dL	76.6 $\pm$ 15.7	93.9 $\pm$ 27.3	13.1 (-5.2, 31.4)	0.16
Time >180 mg/dL in 120 min, (%)	3.13 $\pm$ 10.7	2.6 $\pm$ 10.2	0.03 (0.08, 0.16)	0.75
Time 70-180 mg/dL in 120 min, (%)	49.4 $\pm$ 11.9	56.4 $\pm$ 22.3	5.8 (-10.5, 22.1)	0.49
Time <70 mg/dL in 120 min, (%)	44.8 $\pm$ 21.6	36.7 $\pm$ 21.0	-3.9 (-16.4, 8.6)	0.54
Glucose $\geq$ 100 mg/dL or increased by 30 mg/dL 1-hour after treatment, n (%) <sup>(§)</sup>	4 (50.0%)	15 (83.3%)	4.57 (0.67, 31.3)	0.12

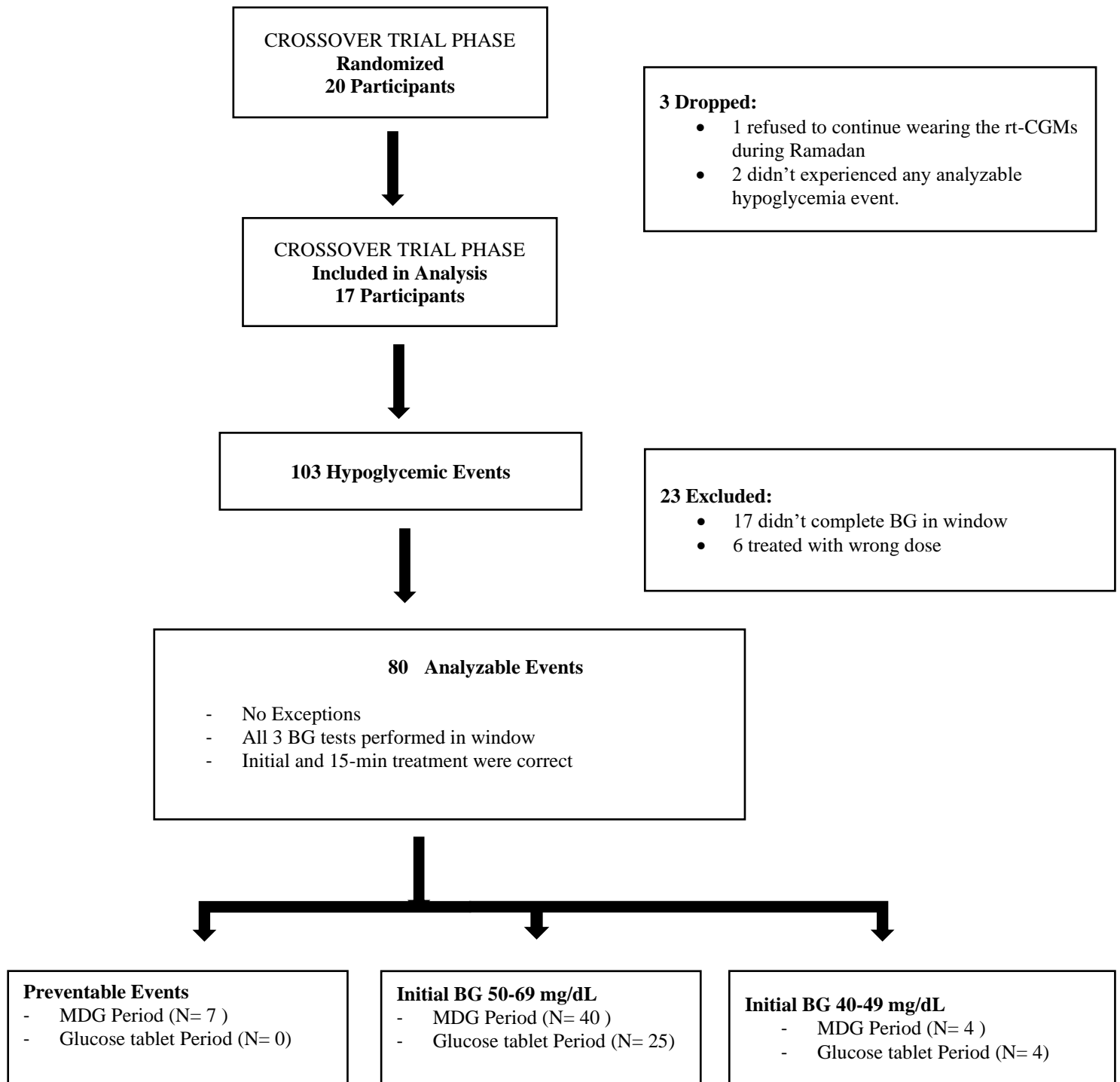
(\*) Differences reported as values for MDG minus values for oral glucose

(†) Time point was set as “Time 0” when the participant experienced hypoglycemia

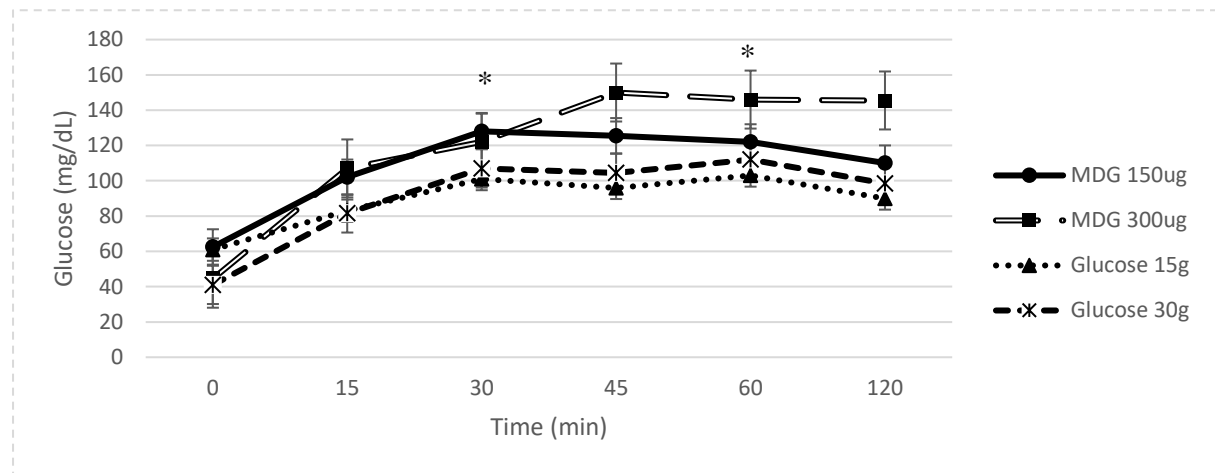
(‡) Data derived from blood glucose meter.

(§) Differences reported as values for MDG relative to values for oral glucose

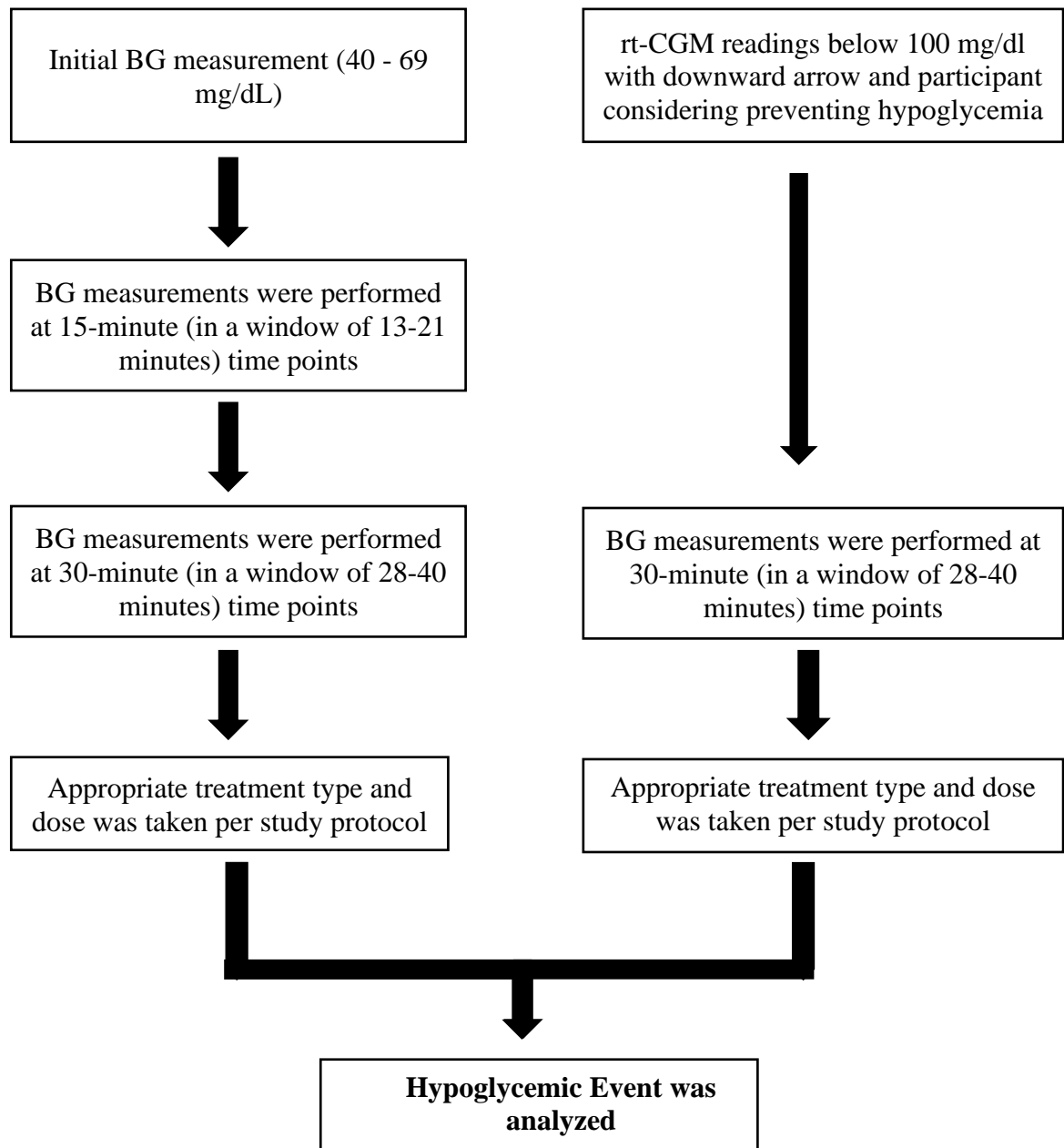
**Supplemental Figure S1. Crossover Flow Chart Accounting for Participants and hypoglycemic events**



**Supplemental Figure S2. Interstitial glucose responses from rt-CGM by treatment arm after hypoglycemic event treatment in 17 individuals. The circles and square represent the mean for events during the MDG period using 150 and 300 ug, the triangle and star signs represent the mean for events during OG period using 15 and 30 g. Data are mean  $\pm$ SE.\*P < 0.05**



**Supplemental Figure S3: Hypoglycemic Event Analysis Flow Chart. Two blinded (M.G, T.M) independent investigators reviewed all glucose values, along with corresponding time elapsed since treatment, to assess the outcomes.**



## Supplemental Figure S4: Mini-Dose Glucagon Protocol

***Don't use the following protocol and break your fast using any preferred oral carbohydrate in case of any of the following situation:***

- 1- If you are doing exercise
- 2- If hypoglycemia occur during sleep or 30 minutes before going to the bed.
- 3- Severe hypoglycemia necessitating third-party assistance or blood glucose concentrations  $<40$  mg/dL should be treated as needed with carbohydrates or commercially available rescue glucagon preparations.

**You will need:**

**Glucagon Hypokit**



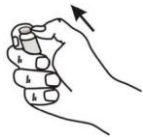
**An Insulin syringe**



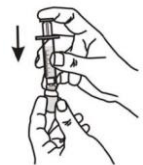
**Blood glucose meter and strips**



### Instructions for the preparation of mini-dose glucagon



**Remove the cap from the vial**



**Insert the needle and inject all the liquid from the syringe into the vial then **discard this needle****



**Swirl the vial gently until the liquid become clear**



**Turn the vial upside down and insert the **insulin syringe**. Draw up the required amount according to the chart below\***

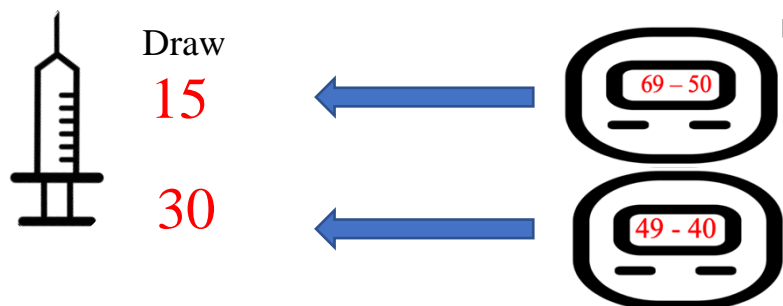
\*Each mark on the syringe, equivalent to 10 $\mu$ g, subsequently referred to as “units”

## Instructions for taking the mini-dose glucagon:

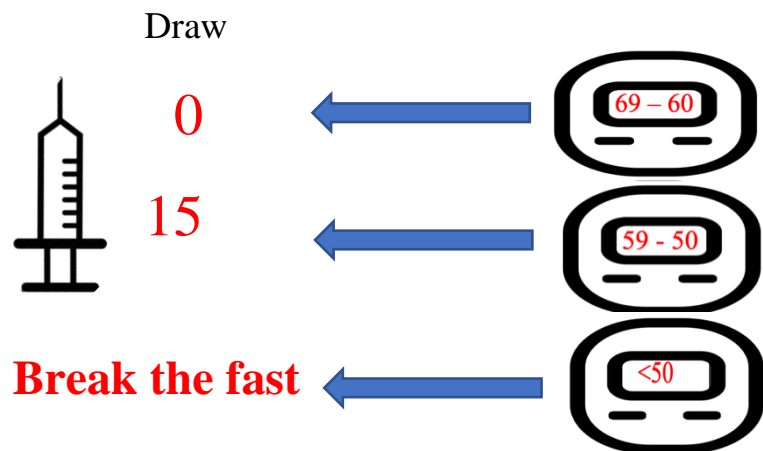
*Check your blood glucose with study meter in any of the following situations:*

- 1- Developed hypoglycemia symptoms
- 2- Rt-CGM reads below 70 mg/dl
- 3- When the rt-CGM glucose was below 100 with downward arrow and you intended to treat to prevent hypoglycemia.

**Inject the mini-dose glucagon exactly in the same way you take insulin (subcutaneously) according to the following diagram:**



**After 15 minutes check your blood glucose and take the mini-dose glucagon according to your blood glucose reading:**



**After 30 minutes check your blood glucose and follow the diagram below:**

