

Electronic Supplemental Materials (ESM)

ESM – methods: Computing DI^{CGM}

DI^{CGM} was derived from CGM data collected during the OGTT and obtained ¹ by integrating the equation of the Oral Glucose Minimal Model²⁻⁵ with the equation of the Oral Insulin and C-peptide Minimal Model⁶.

$$DI^{CGM} = \frac{\left(\frac{D \cdot f}{BW} - GE \int_{t_{meal}}^{t_{end}} \Delta G(t) dt - V_G \int_{t_{meal}}^{t_{end}} \dot{G}(t) dt \right) \left(1 + \lambda \frac{DG}{\int_{t_{meal}}^{t_{end}} G(t) - G_b dt} \right)}{p_2 \frac{V_{cp}}{V_I} \left(\alpha \int_{t_{meal}}^{t_{end}} e^{-p_2} \star e^{-nt} \star [(1 - HE_b + a_G \Delta G)] (e^{-\alpha t} \star \Delta G) G(t) dt + \lambda \int_{t_{meal}}^{t_{end}} e^{-p_2} \star e^{-nt} \star [(1 + HE_b + a_G \Delta G) G'(t) +] G(t) dt \right)}$$

where $\star$ represents the convolution operator, $G(t)$ [mg/dL] (mg/dL = mmol/l X 18.016) is the measured glucose concentration, and $\Delta G(t)$ is the glucose above the basal (G_b), D [mg] is the amount of carbohydrates ingested during the oral glucose tolerance test, $f = 0.9$ [dimensionless] is the amount of carbohydrates that reaches plasma by the end of the experiment, BW [kg] is the body weight, $GE = 0.019$ [dL/kg/min] is the glucose effectiveness, and $V_G = 1.45$ [dL/kg] is the volume of glucose distribution. V_{cp} [L] represents the C-peptide distribution volume, calculated using the Van Cauter population model⁷.

V_I [L] represents the Insulin distribution volumes, and n [min^{-1}] is the fractional rate of insulin clearance. Both these parameters are derived from the Campioni model⁸. $HE_b = 0.54$ [%] is the hepatic insulin extraction, $\alpha = 0.11$ [1/min] represents the rate constant for the provision of new releasable insulin⁸, and $a_G = 0.0052$ [dL/mg] represents the effectiveness of glucose in reducing hepatic insulin extraction⁹. These parameters were identified using the Oral Insulin C-peptide Minimal Model (OICMM) on plasma concentration collected during the OGTT. Finally, $p_2 = 0.018$ [1/min] is the

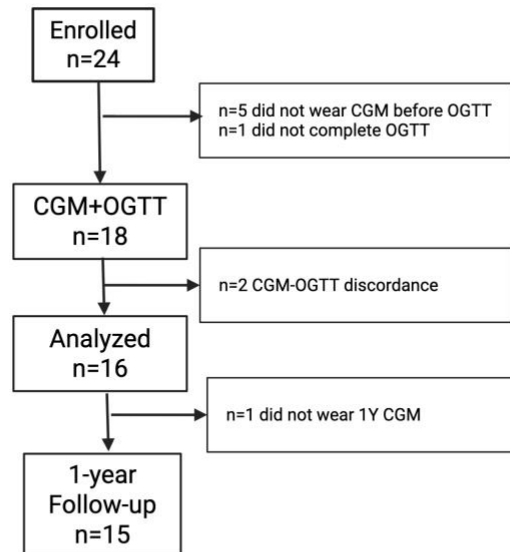
rate constant of insulin action, identified using the OGMM, and $\lambda = \Phi_d/\Phi_s = 12.7$ [min] is the ratio between dynamic and static beta cell responsivity, identified using the OCMM.

Of note, five parameters, that are α , p_2 , HE_b , a_G , and λ , were estimated using the oral minimal model applied to the OGTT plasma glucose, insulin and C-peptide data of this cohort.

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ESM - Table 1. CGM metrics at baseline and follow-up	
	N=15
Mean (mmol/l)	6.1 (5.8, 6.5)
SD (mmol/L)	0.98 (0.90, 1.15)
CV(%)	16.5 (15.2, 18.8)
GMI (%)	5.9 (5.8, 6.1)
TIR 70-180(%)	99.1 (97.8, 99.4)
TIR 70-140 (%)	93.3 (88.9, 96.5)
TB70(%)	0.2 (0.1, 0.7)
TB54(%)	0.0 (0.0, 0.1)
TA140 (%)	5.6 (2.9 – 9.8)
TA180 (%)	0.5 (0.1 - 0.9)
TA250 (%)	0.0 (0.0 - 0.0)

ESM – Figure 1. Participants' Consort flow diagram.



ESM – Figure 2. DI^{CGM} and BMI at baseline.

