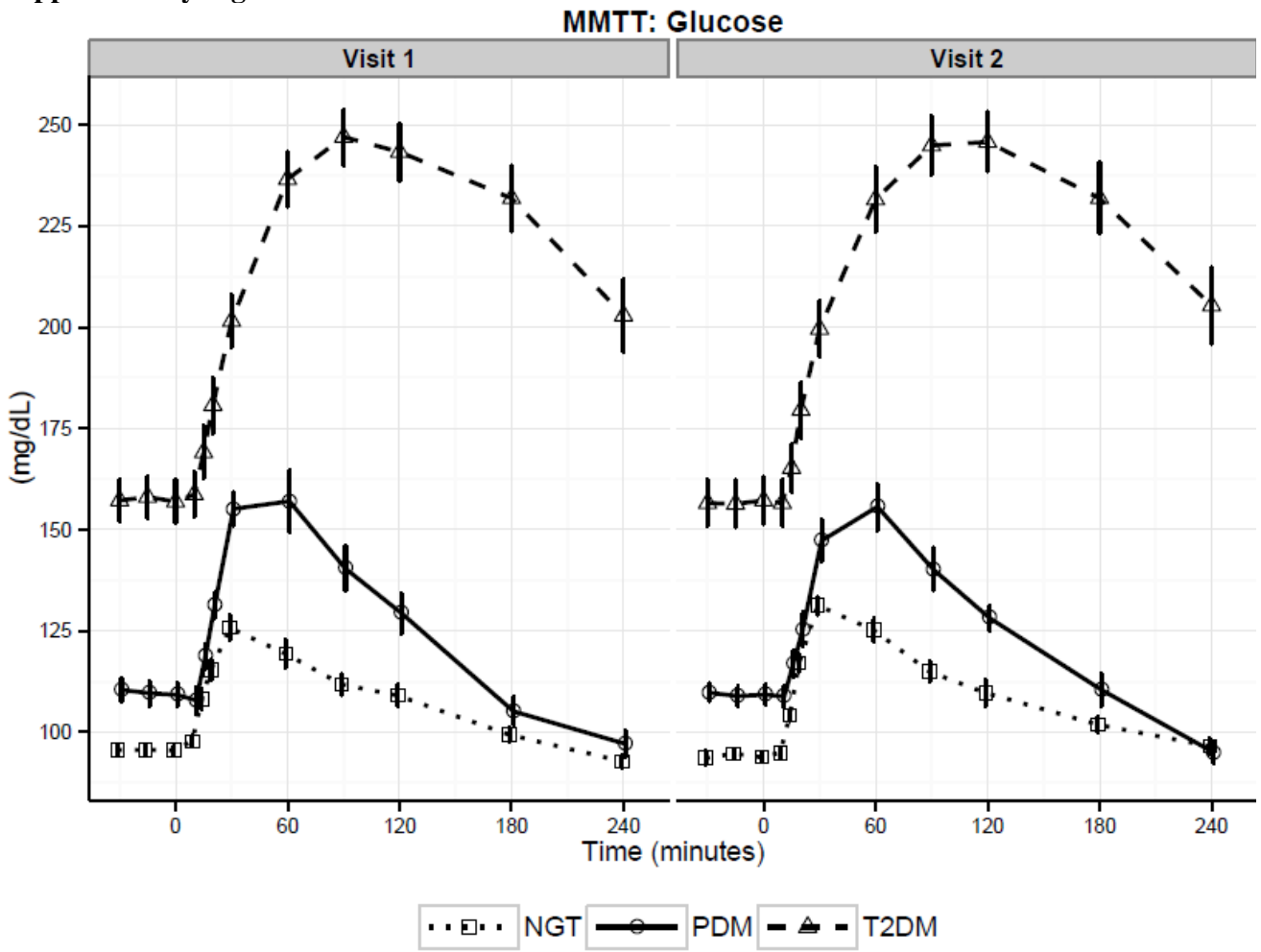


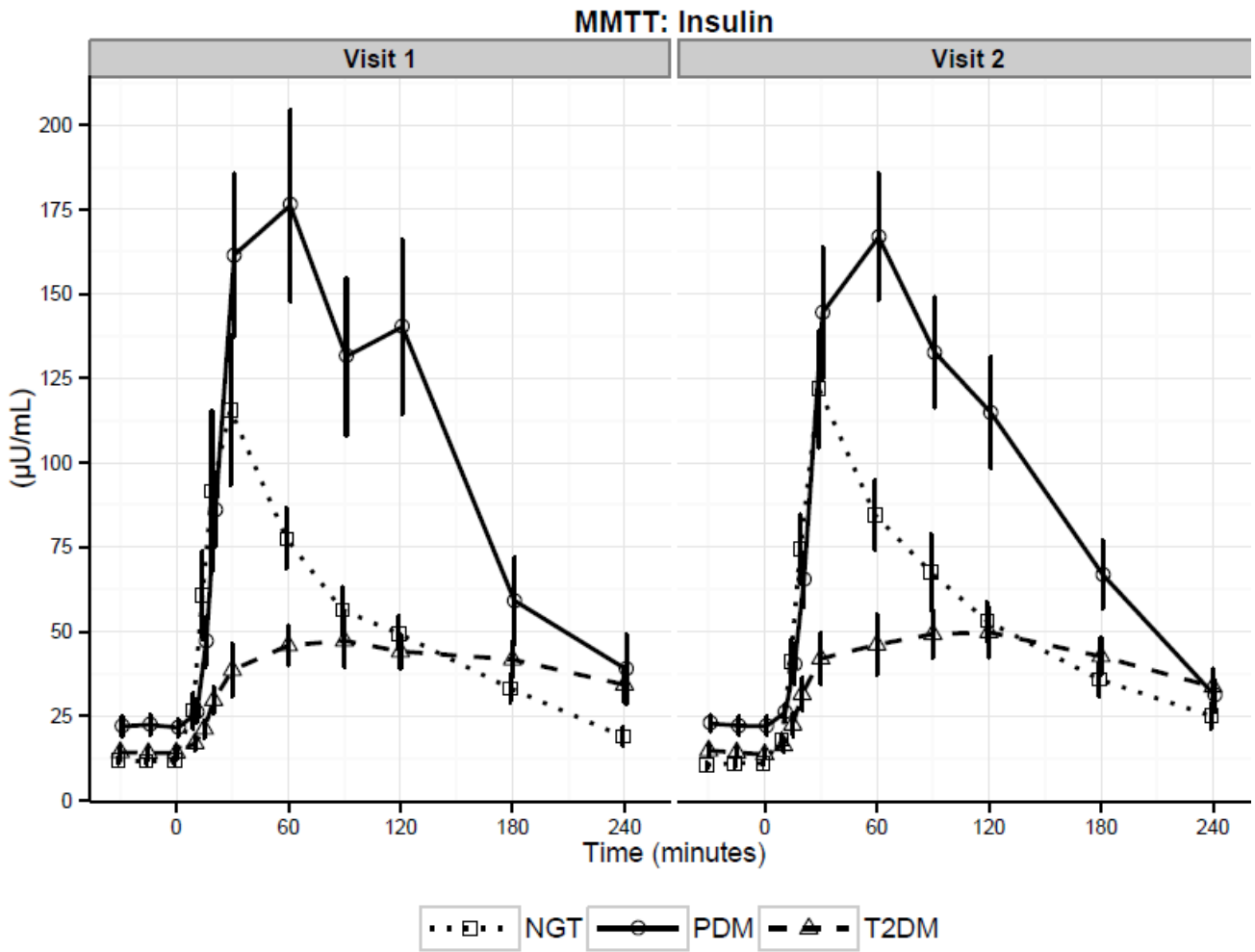
SUPPLEMENTARY DATA

Supplementary Figure 1.1



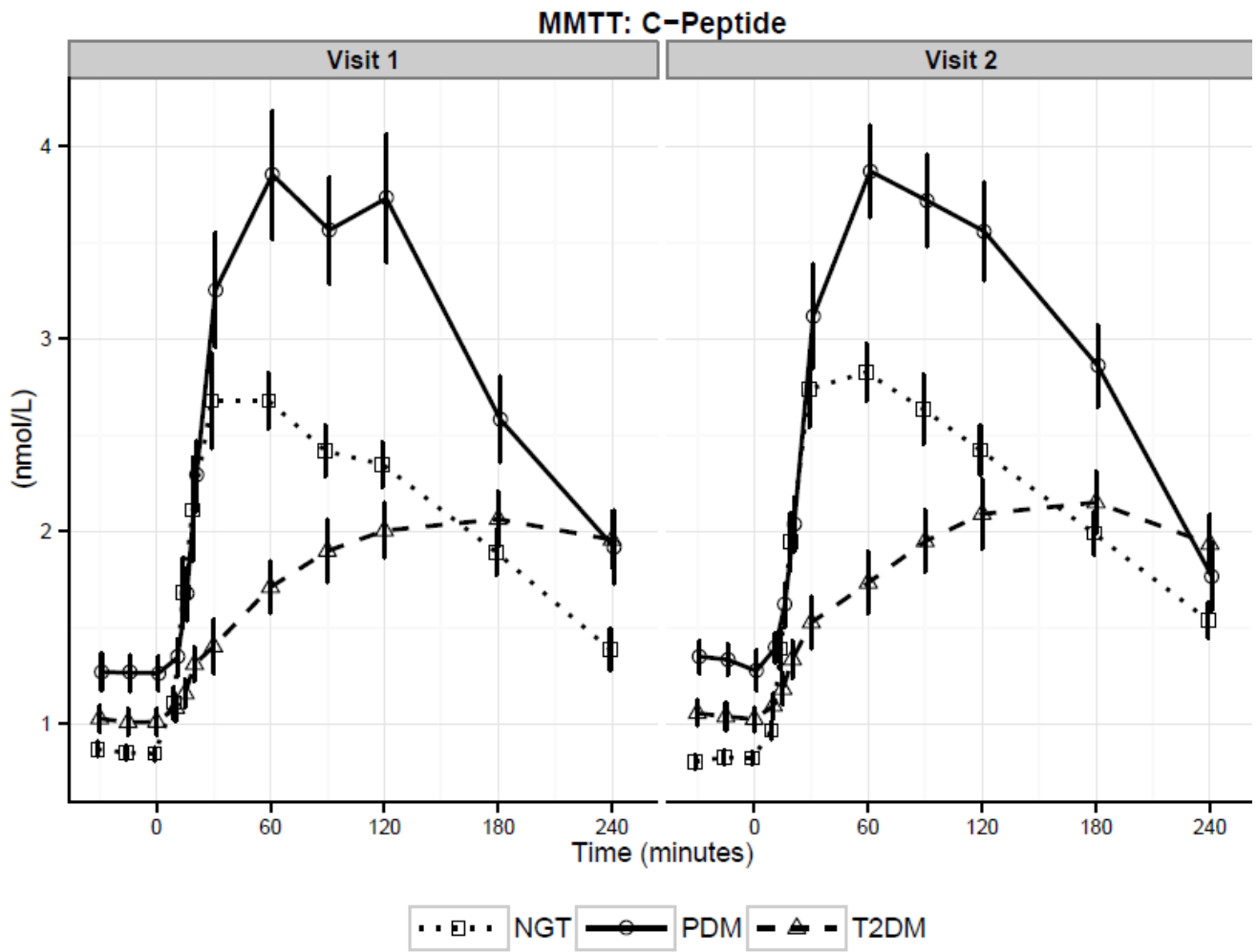
SUPPLEMENTARY DATA

Supplementary Figure 1.2



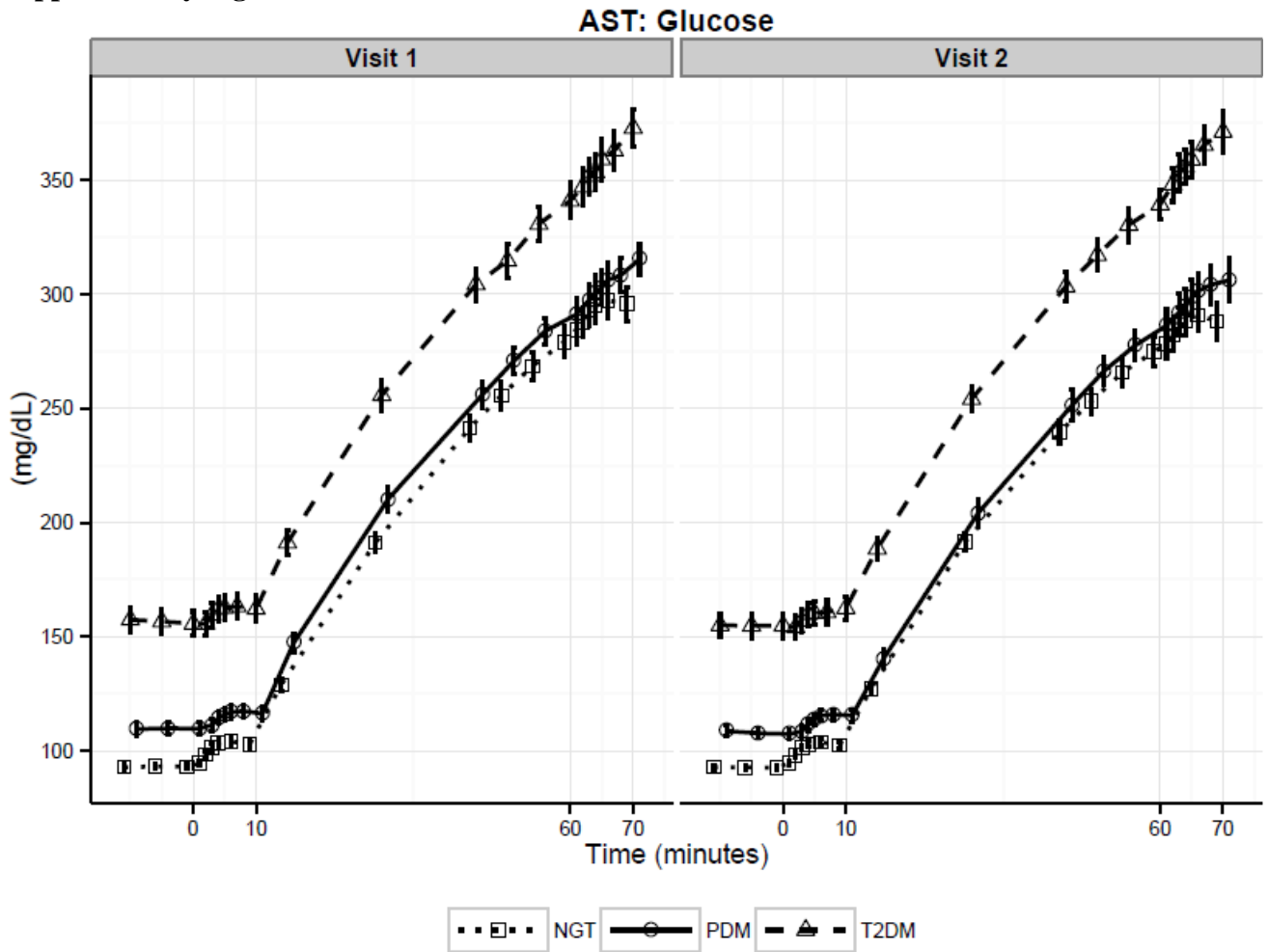
SUPPLEMENTARY DATA

Supplementary Figure 1.3



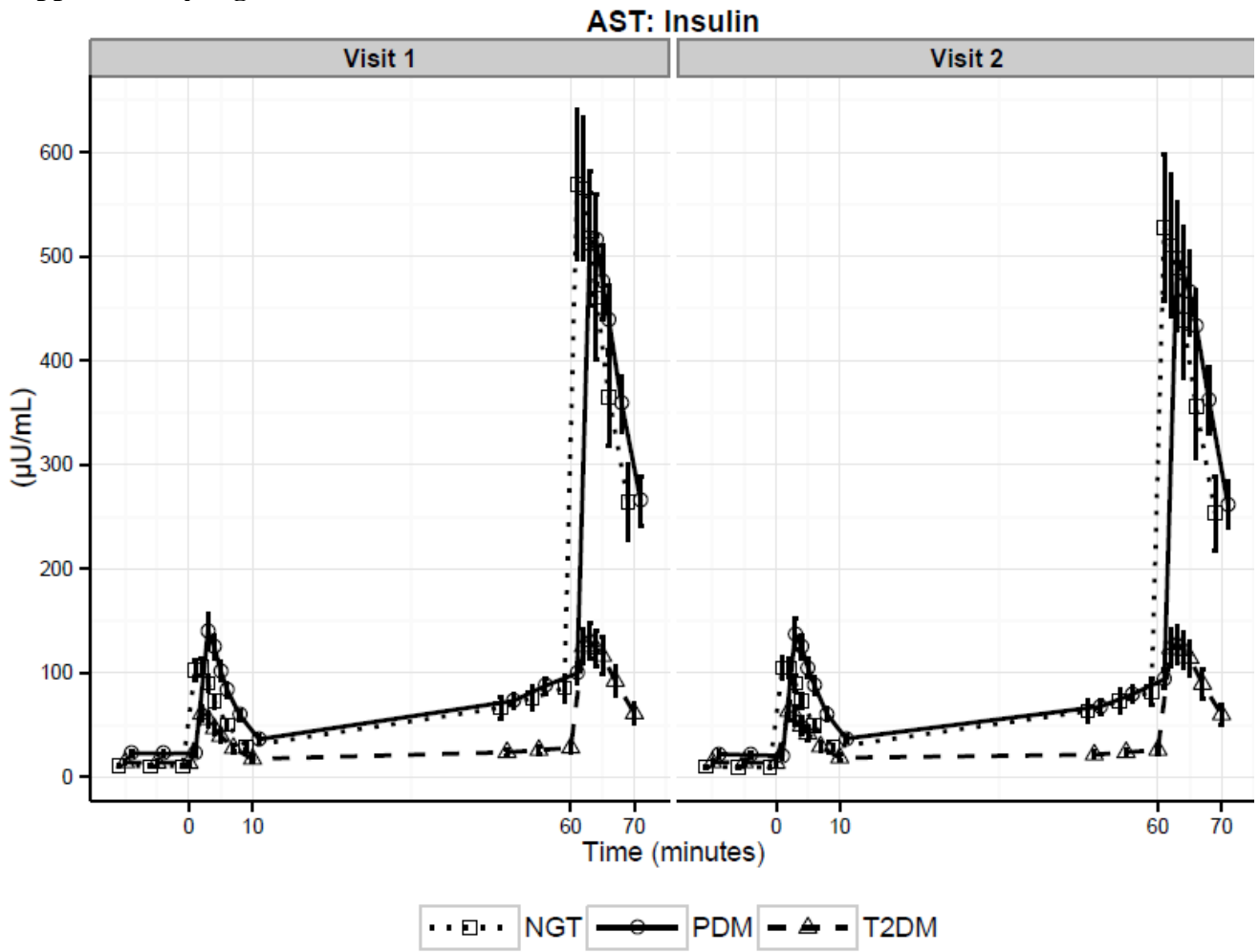
SUPPLEMENTARY DATA

Supplementary Figure 1.4



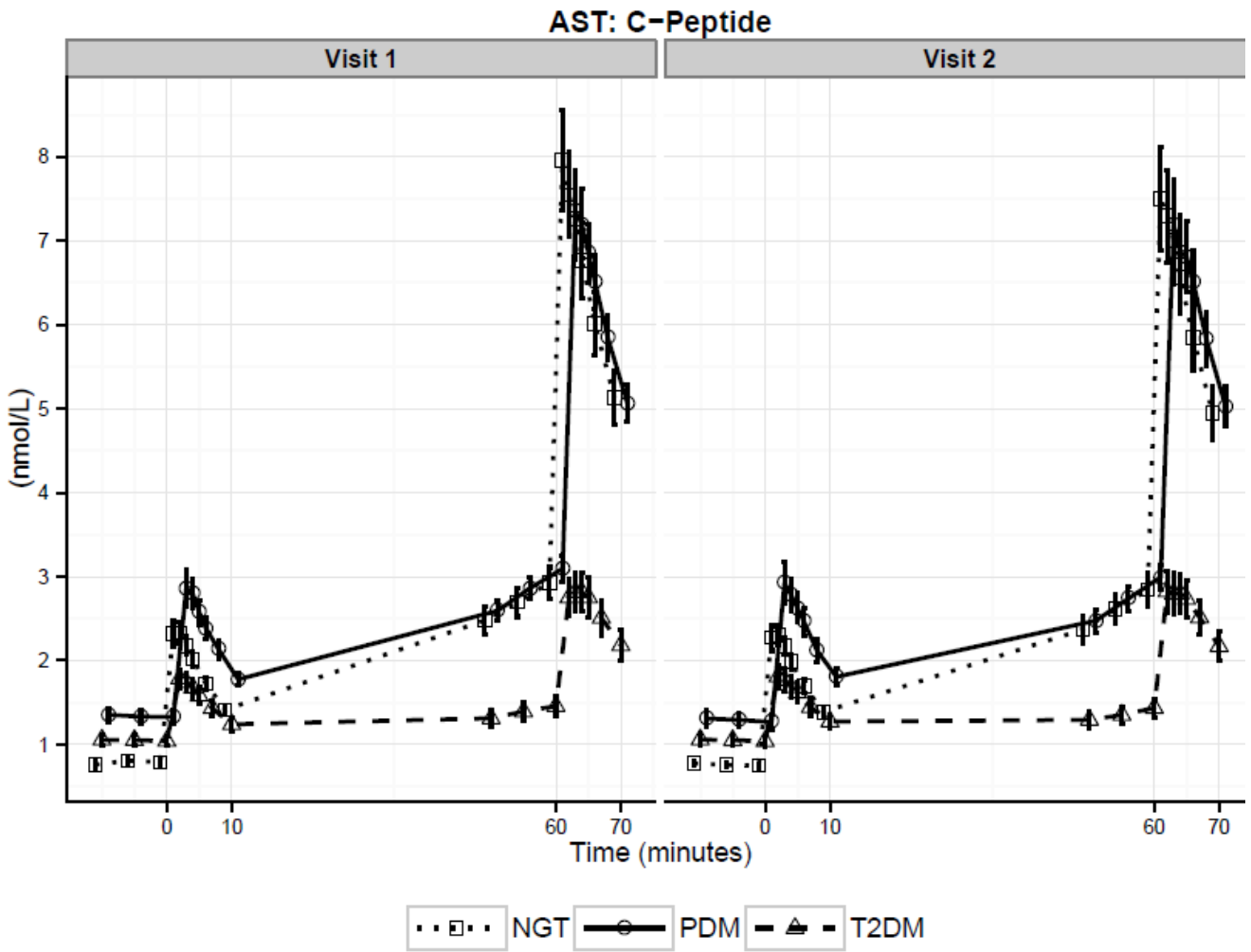
SUPPLEMENTARY DATA

Supplementary Figure 1.5



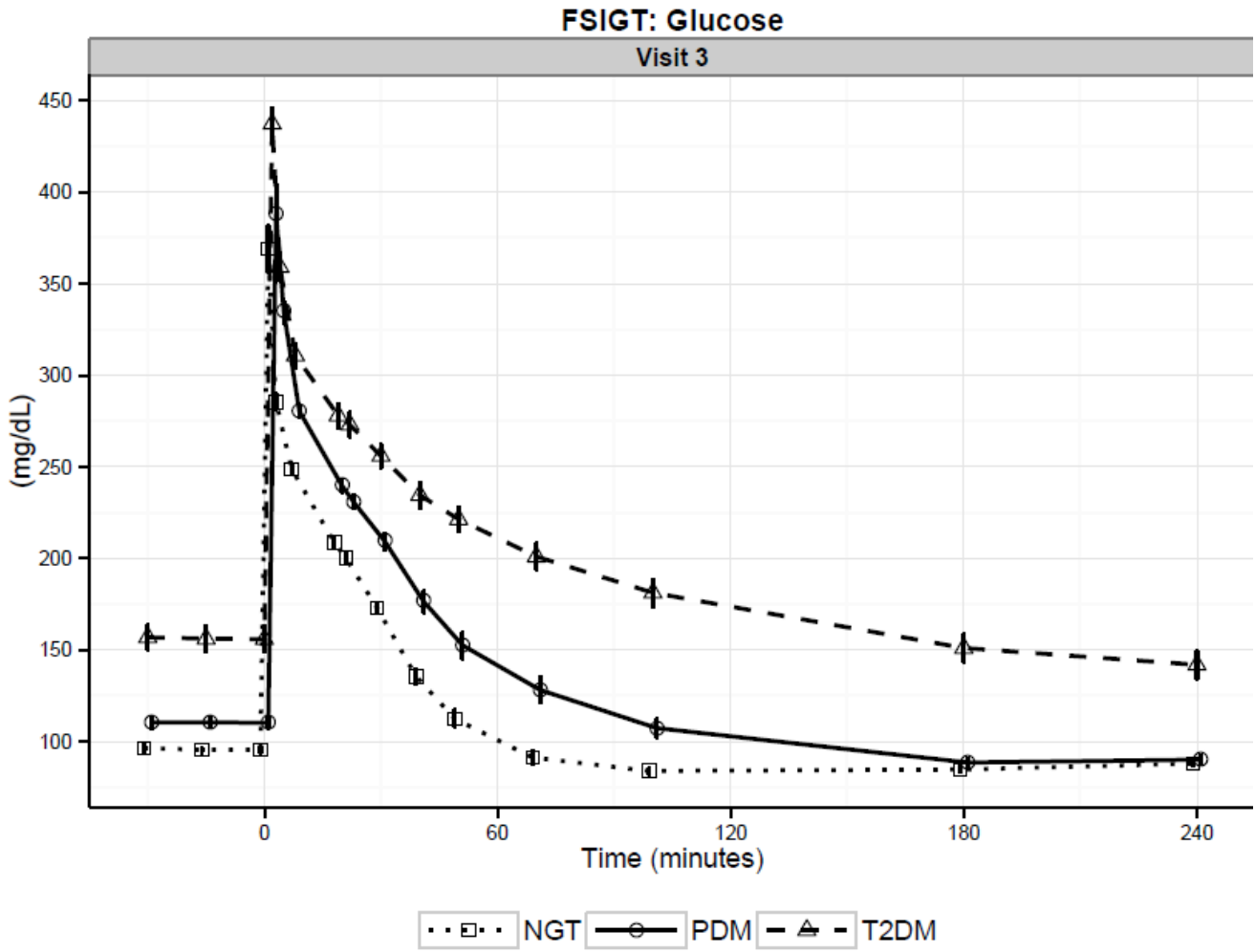
SUPPLEMENTARY DATA

Supplementary Figure 1.6



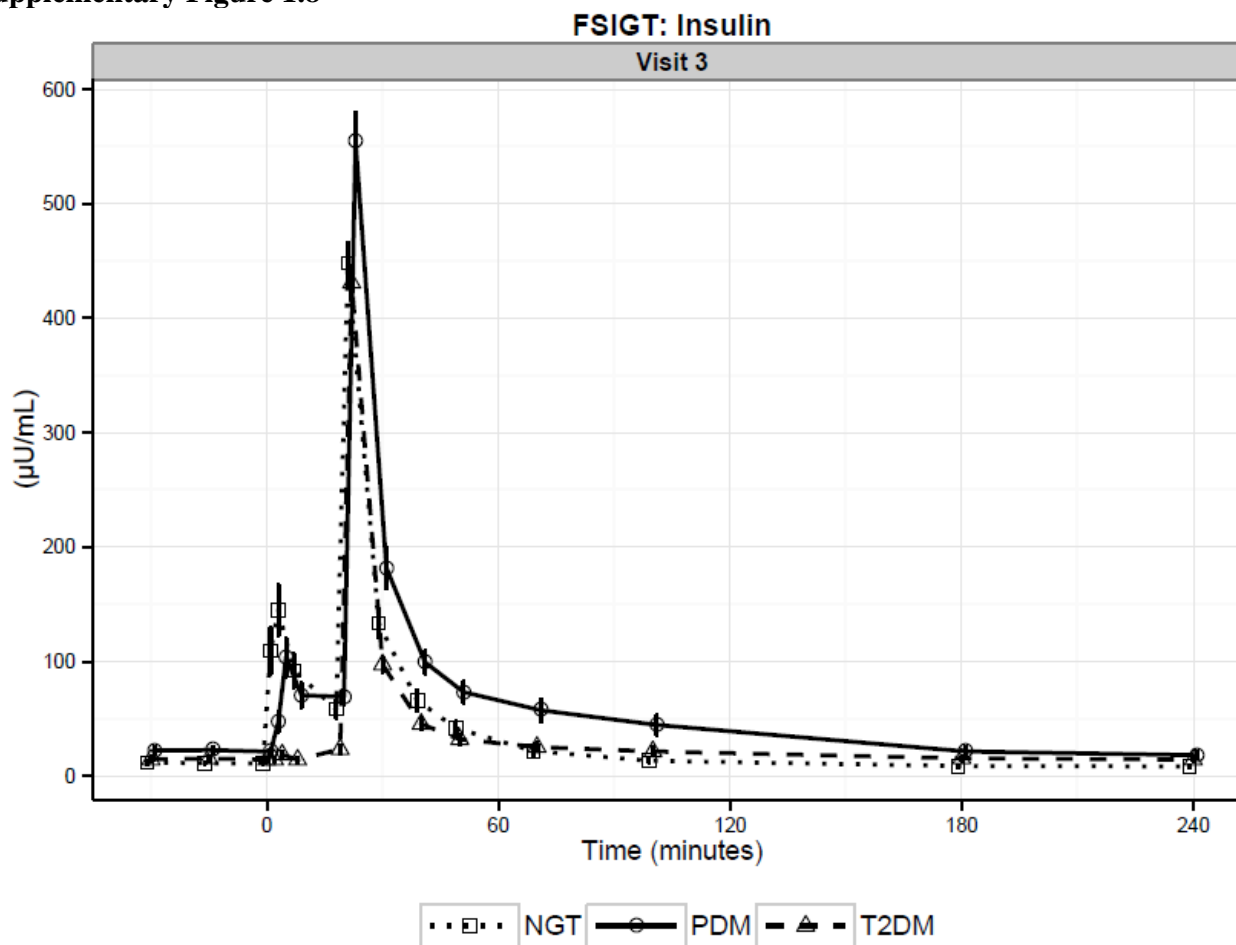
SUPPLEMENTARY DATA

Supplementary Figure 1.7



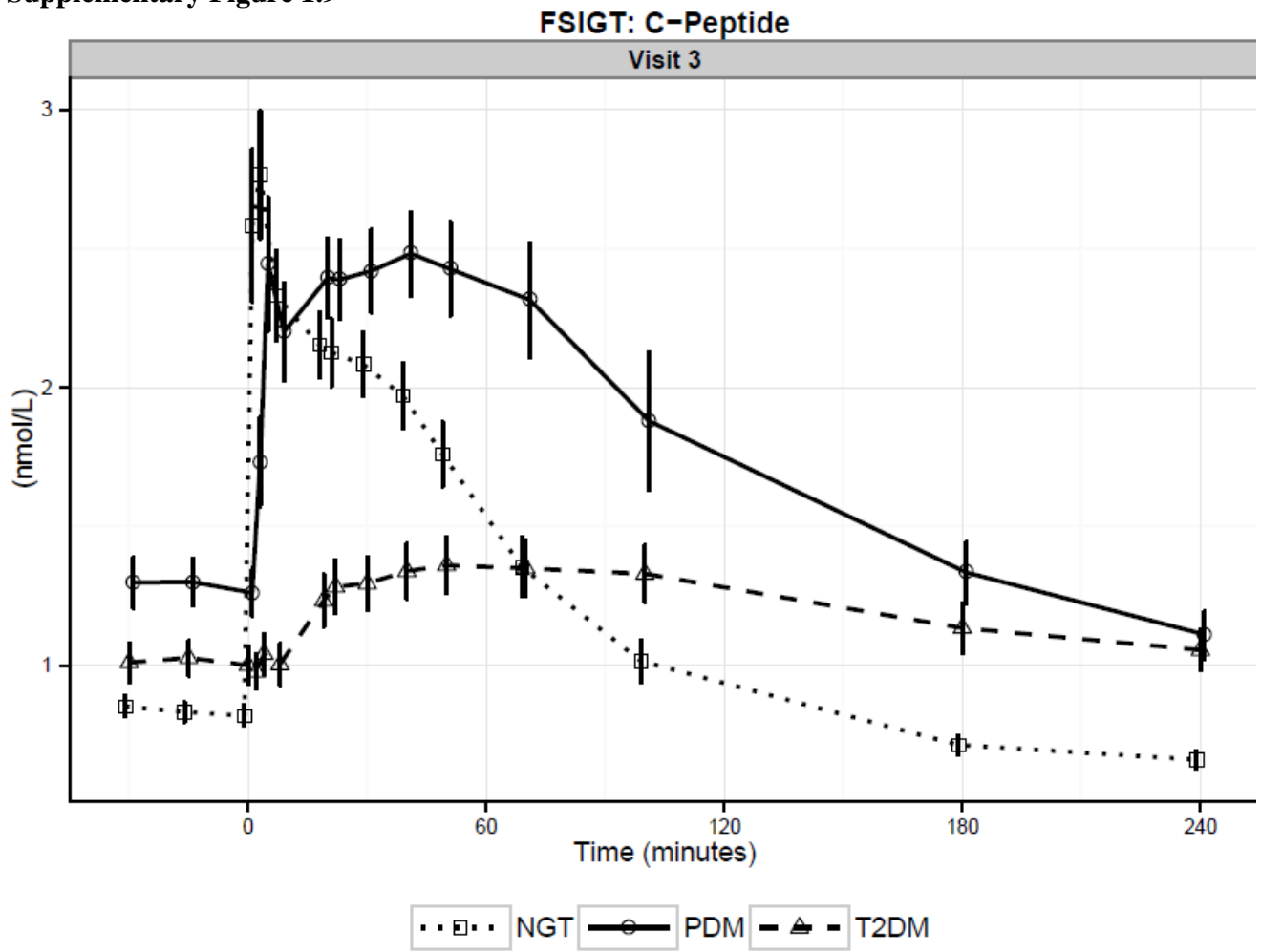
SUPPLEMENTARY DATA

Supplementary Figure 1.8



SUPPLEMENTARY DATA

Supplementary Figure 1.9



SUPPLEMENTARY DATA

Supplementary Table 1.1. Procedure-Emergent Adverse Event Incidence, by Population and Test

	Population	AST	MMTT	FSIGT
Any PEAE	NGT	21 (87.5%) [85]	1 (4.0%) [3]	0
	PDM	15 (88.2%) [51]	8 (47.1%) [11]	3 (18.8%) [6]
	T2DM	14 (63.6%) [44]	10 (41.7%) [13]	2 (9.1%) [3]
Any mild PEAE	NGT	21 (87.5%) [84]	1 (4.0%) [3]	0
	PDM	15 (88.2%) [51]	8 (47.1%) 11]	3 (18.8%) [6]
	T2DM	14 (63.6%) [44]	9 (37.5%) [12]	2 (9.1%) [3]
Any moderate PEAE*	NGT	1 (4.2%) [1]	0	0
	PDM	0	0	0
	T2DM	0	1 (4.2%) [1]	0
Any severe PEAE	All Populations	0	0	0
PEAE related to procedure (PI call)	NGT	21 (87.5%) [78]	1 (4.0%) [3]	0
	PDM	15 (88.2%) [51]	8 (47.1%) 11]	3 (18.8%) [6]
	T2DM	14 (63.6%) [43]	7 (29.2%) [10]	1 (4.5%) [1]

PEAE= Procedure emergent adverse event

*Both moderate adverse events were classed as headaches

Values reflect # subjects with event (per cent of subjects with event) [total # of events]

SUPPLEMENTARY DATA

Supplementary Table 1.2. Selected and Specific Procedure Emergent Adverse Events: All Mild

PEAE	Population	AST	MMTT	FSIGT
Dizziness	NGT	1 (4.2%) [1]	0	0
	PDM	0	0	1 (6.3%) [2]
	T2DM	3 (13.6%) [5]	0	0
Paresthesia (Oral)	NGT	11 (45.8%) [21]	0	0
	PDM	5 (29.4%) [9]	2 (11.8%) [3]	0
	T2DM	0	0	0
Paresthesia (Distal)	NGT	2 (8.3%) [2]	0	0
	PDM	5 (29.4%) [9]	0	0
	T2DM	3 (13.6%) [7]	2 (8.3%) [2]	0
Dysgeusia	NGT	11 (45.8%) [20]	1 (4.0%) [1]	0
	PDM	9 (52.9%) [24]	2 (11.8%) [2]	2 (12.5%) [2]
	T2DM	11 (50.0%) [26]	5 (20.8%) [7]	0
Flushing	NGT	8 (33.3%) [15]	1 (4.0%) [1]	0
	PDM	2 (11.8%) [2]	0	0
	T2DM	2 (9.1%) [2]	1 (4.2%) [1]	0

Values reflect # subjects with event (per cent of subjects with event) [total # of events]

SUPPLEMENTARY DATA

Supplementary Table 2.1. Raw Analyte Data for MMTT

MMTT: Mean ± SEM Baseline and Maximum Observed Post Meal						
Analyte	GT Population	N	Baseline Visit 1	Baseline Visit 2	Maximum Visit 1	Maximum Visit 2
Glucose (mg/dL)	NGT	23	95.6 ± 1.16	94 ± 1.23	134 ± 1.99	135.7 ± 1.91
	PDM	17	109.7 ± 2.92	109.3 ± 2.30	163.8 ± 6.50	160.8 ± 5.00
	T2DM	22	157.4 ± 5.16	156.7 ± 5.84	253.4 ± 6.60	256.9 ± 7.46
Insulin (µU/mL)	NGT	23	11.8 ± 1.03	10.8 ± 1.00	137.9 ± 21.42	130.9 ± 16.58
	PDM	17	22.0 ± 2.72	22.3 ± 2.58	210.6 ± 28.69	198.6 ± 20.98
	T2DM	22	14.1 ± 1.91	14.2 ± 1.76	57.5 ± 8.16	59.8 ± 9.12
C-Peptide (nmol/L)	NGT	23	0.85 ± 0.037	0.82 ± 0.035	3.21 ± 0.192	3.25 ± 0.179
	PDM	17	1.27 ± 0.093	1.32 ± 0.087	4.25 ± 0.338	4.33 ± 0.248
	T2DM	22	1.02 ± 0.068	1.04 ± 0.066	2.21 ± 0.161	2.28 ± 0.183

SUPPLEMENTARY DATA

Supplementary Table 2.2. Derived Non-Compartmental Total AUC (0-4h) from Raw Analyte Data for MMTT, Geometric Means (95% CI), Geometric CVs (between and with) and ICCs

Stimulation Test Parameter	Population (N)	Model Predicted Geometric Mean (95% CI)	Geometric CV% Between Subjects (90% CI)	Geometric CV% Within Subjects (90% CI)	ICC (90% CI)
MMTT: Glucose Total AUC(0-4h) (mg X min / dL)	NGT (N=23)	26165 (24905, 27489)	4 (2.4, 6.6)	5.1 (4, 6.4)	0.385 (0.395, 0.719)
	PDM (N=17)	30044 (28534, 31633)	9.6 (6.9, 13.3)	3.7 (2.8, 4.9)	0.869 (0.837, 0.95)
	T2DM (N=22)	53400 (50817, 56133)	12.5 (9.1, 17.1)	7.5 (5.9, 9.7)	0.731 (0.621, 0.91)
MMTT: Insulin Total AUC(0-4h) (μU X min / mL)	NGT (N=23)	12491 (9887, 15781)	42.9 (32, 58.2)	16.1 (12.6, 20.6)	0.868 (0.792, 0.946)
	PDM (N=17)	22548 (17663, 28783)	42.1 (28.9, 62.7)	23.9 (17.9, 32.1)	0.746 (0.639, 0.898)
	T2DM (N=22)	9028 (7139, 11416)	52.9 (39.3, 72.6)	13.7 (10.7, 17.7)	0.93 (0.907, 0.973)
MMTT: C-Peptide Total AUC(0-4h) (nmol X min / L)	NGT (N=23)	528 (463, 601)	19.5 (14.4, 26.3)	10.7 (8.4, 13.6)	0.767 (0.738, 0.903)
	PDM (N=17)	714 (622, 818)	23.8 (16.9, 33.8)	11.4 (8.6, 15.1)	0.81 (0.698, 0.943)
	T2DM (N=22)	441 (386, 502)	29.5 (22.3, 39.3)	8.1 (6.3, 10.4)	0.927 (0.893, 0.972)

SUPPLEMENTARY DATA

Supplementary Table 2.3. Raw Analyte Data for AST

AST: Mean ± SEM Baseline and Maximum Observed Post Arginine Injection at Basal and Elevated Glucose						
Analyte	GT Population	N	Baseline Visit 1	Baseline Visit 2	Maximum Visit 1	Maximum Visit 2
Glucose (mg/dL) At Basal Glucose	NGT	23	93.1 ± 1.06	92.8 ± 1.01	105.2 ± 1.75	104.8 ± 1.32
	PDM	16	109.8 ± 2.64	107.9 ± 2.17	118.9 ± 2.75	117.2 ± 2.43
	T2DM	22	156.6 ± 5.48	154.9 ± 5.34	165.1 ± 5.29	163.7 ± 5.29
Glucose (mg/dL) At Elevated Glucose	NGT	23	267.7 ± 6.17	263 ± 5.95	300.5 ± 7.52	292.3 ± 7.08
	PDM	16	281.9 ± 6.1	276.6 ± 6.74	315.9 ± 7.11	309.2 ± 8.00
	T2DM	22	328.7 ± 7.25	328.8 ± 6.81	372.9 ± 8.45	371.8 ± 8.67
Insulin (µU/mL) At Basal Glucose	NGT	23	10.6 ± 0.84	9.7 ± 0.65	116.6 ± 9.40	116.8 ± 9.32
	PDM	16	22.8 ± 2.50	21.2 ± 2.52	146.5 ± 15.83	142.7 ± 14.50
	T2DM	22	13.9 ± 1.52	14 ± 1.90	61.9 ± 6.43	64.8 ± 8.73
Insulin (µU/mL) At Elevated Glucose	NGT	23	76.0 ± 1.070	71.5 ± 11.21	597.0 ± 0.07	549.3 ± 67.83
	PDM	16	86.8 ± 7.59	80.4 ± 7.69	535.7 ± 44.04	529.6 ± 48.43
	T2DM	22	26 ± 3.46	23.8 ± 3.30	133.1 ± 16.68	131.4 ± 17.24
C-Peptide (nmol/L) At Basal Glucose	NGT	23	0.79 ± 0.035	0.76 ± 0.029	2.44 ± 0.141	2.43 ± 0.128
	PDM	16	1.34 ± 0.08	1.29 ± 0.09	2.96 ± 0.205	2.99 ± 0.24
	T2DM	22	1.05 ± 0.06	1.05 ± 0.068	1.8 ± 0.113	1.83 ± 0.14
Cpeptide (nmol/L) At Elevated Glucose	NGT	23	2.70 ± 0.173	2.58 ± 0.178	8.13 ± 0.591	7.63 ± 0.600
	PDM	16	2.85 ± 0.134	2.74 ± 0.141	7.51 ± 0.453	7.42 ± 0.489
	T2DM	22	1.39 ± 0.104	1.36 ± 0.104	2.89 ± 0.235	2.91 ± 0.236

SUPPLEMENTARY DATA

Supplementary Table 2.4. Raw Analyte Data for FSIGT

FSIGT: Mean ± SEM Baseline and Maximum Observed (0 to 19 minutes) Post Glucose Injection Insulin at 22 minutes Post Insulin Injection					
Analyte	GT Population	N	Baseline Visit 3	Maximum Visit 3	Insulin AT 22 Minutes Visit 3
Glucose (mg/dL)	NGT	23	95.7 ± 1.29	370.6 ± 11.91	
	PDM	16	110.2 ± 2.65	396.2 ± 13.67	
	T2DM	22	156.3 ± 6.72	437.4 ± 8.49	
Insulin (µU/mL)	NGT	23	11.3 ± 1.02	147.0 ± 22.00	447.9 ± 18.14
	PDM	16	22.0 ± 2.59	109.5 ± 15.47	554.5 ± 25.35
	T2DM	22	14.7 ± 1.81	24.1 ± 3.22	430.9 ± 15.10
C-Peptide (nmol/L)	NGT	23	0.83 ± 0.035	2.90 ± 0.241	
	PDM	16	1.29 ± 0.086	2.66 ± 0.217	
	T2DM	22	1.01 ± 0.065	1.23 ± 0.094	