Supplemental Tables and Figures:

Supplemental Table 1: Unadjusted and adjusted Hazard Ratios (HRs) for the association between risk of developing type 1 diabetes and time to peak C-peptide/peak glucose at baseline in the PTP cohort stratified by age less than 18 and those 18 years or older.

PTP (Age < 18 years); N =2758)						
	Unadjusted			*Adjusted**		
	HR	**95% CI**	***p*-value**	**HR**	**95% CI**	***p*-value**
Time to Peak C-peptide (> 60 vs ≤ 60 mins)	2.85	2.40, 3.37	<0.001	2.87	2.37, 3.47	<0.001
Time to Peak Glucose (> 30 vs at 30 mins)	3.45	2.90, 4.10	<0.001	2.14	1.74, 2.64	<0.001
PTP (Age ≥ 18 years); N =959**)						
	HR	**95% CI**	***p*-value**	**HR**	**95% CI**	***p*-value**
Time to Peak C-peptide (> 60 vs ≤ 60 mins)	3.46	2.12, 5.65	<0.001	3.69	2.07, 6.58	<0.001
Time to Peak Glucose (> 30 vs at 30 mins)	5.10	2.92, 8.91	<0.001	2.51	1.27, 4.95	0.004
* C-peptide adjusted for peak C-peptide level, age, sex, race, BMI z-score and HOMA-IR. Glucose adjusted for peak glucose level, age, sex, race, BMI z-score and HOMA-IR. **Age was missing in 3.						

Supplemental Table 2: Unadjusted and adjusted HRs for association between risk of developing type 1 diabetes and time to peak C-peptide/peak glucose at baseline in the PTP cohort stratified by number of antibody status (single versus multiple).

PTP (Single Ab+; N=1481)						
	Unadjusted			*Adjusted**		
	HR	**95% CI**	***p*-value**	**HR**	**95% CI**	***p*-value**
Time to Peak C-peptide (> 60 vs ≤ 60 min)	2.67	1.82, 3.92	<0.001	2.91	1.86, 4.54	<0.001
Time to Peak Glucose (> 30 vs at 30 min)	3.024	2.19, 4.81	<0.001	2.11	1.31, 3.39	0.002
PTP (Multiple Ab+; N=2239)						
	HR	**95% CI**	***p*-value**	**HR**	**95% CI**	***p*-value**
Time to Peak C-peptide (> 60 vs ≤ 60 min)	2.44	2.05, 2.91	<0.001	2.57	2.11, 3.14	<0.001
Time to Peak Glucose (> 30 vs at 30 min)	2.97	2.48, 3.57	<0.001	1.87	1.50, 2.34	<0.001
* C-peptide adjusted for peak C-peptide level, age, gender, race, BMI-z-score and HOMA-IR. Glucose adjusted for peak glucose level, age, gender, race, BMI-z-score and HOMA-IR.						

Supplemental Table 3: Change in HOMA-IR and BMI-z from first to last OGTT by progressor status as well as by timing of peak status:

Change from 1st to (Last OGTT)	Non-Progressors	Progressors	P-Value
By Progression Status			
HOMA-IR	0.204 (1.737)	0.310 (1.533)	0.110
BMI Z-Score	0.081 (0.673)	0.061 (0.556)	0.395
By Glucose Peak and Progression Status			
Glucose Peak =30 mins			
HOMA-IR	0.193 (1.607)	0.259 (2.003)	0.663
BMI Z-Score	0.062 (0.710)	0.149 (0.702)	0.089
Glucose Peak >30 mins			
HOMA-IR	0.217 (1.875)	0.327 (1.335)	0.161
BMI Z-Score	0.102 (0.629)	0.028 (0.487)	0.006
By C-Peptide Peak and Progression Status			
C-peptide Peak ≤60 mins			
HOMA-IR:	0.243 (1.602)	0.297 (1.384)	0.612
BMI Z-Score	0.071 (0.630)	0.138 (0.721)	0.187
C-peptide Peak > 60 mins			
HOMA-IR	0.163 (1.870)	0.315 (1.588)	0.081
BMI Z-Score	0.091 (0.717)	0.030 (0.471)	0.029

HOMA IR = [Fasting Insulin (µU/L) * Fasting Glucose (mg/dL)] / 405
Values represent mean (±SD)

Supplemental Table 4: Comparison of measures of β-cell function and insulin resistance

	Glucose Peak =30 mins	Glucose Peak >30 mins	p-value
HOMA-IR	1.739 (1.589)	1.798 (1.728)	0.305
C-peptide Index	0.092 (0.096)	0.068 (0.212)	<0.001

	C-peptide Peak ≤60 mins	C-peptide Peak >60 mins	p-value
HOMA-IR	1.729 (1.418)	1.805 (1.849)	0.180
C-peptide Index	0.097 (0.228)	0.065 (0.090)	<0.001

C-peptide Index = (Change in C-peptide 30 – 0 minutes (ng/mL))/(Change in Glucose 30 – 0 minutes (mg/dL))
Values represent the mean (±SD)

Supplemental Figure Legends:

Supplemental Figure 1: PTP Sample selection
Supplemental Figure 2: Type 1 Diabetes Free curve by timing of peak glucose in the DPT-1 cohort.

Supplemental Figure 3: Type 1 Diabetes Free curve by timing of peak C-peptide in the DPT-1 cohort.

Supplemental Figure 4: Evaluation of the relationship between 1/fasting insulin and C-peptide index

Supplemental Figure 4:
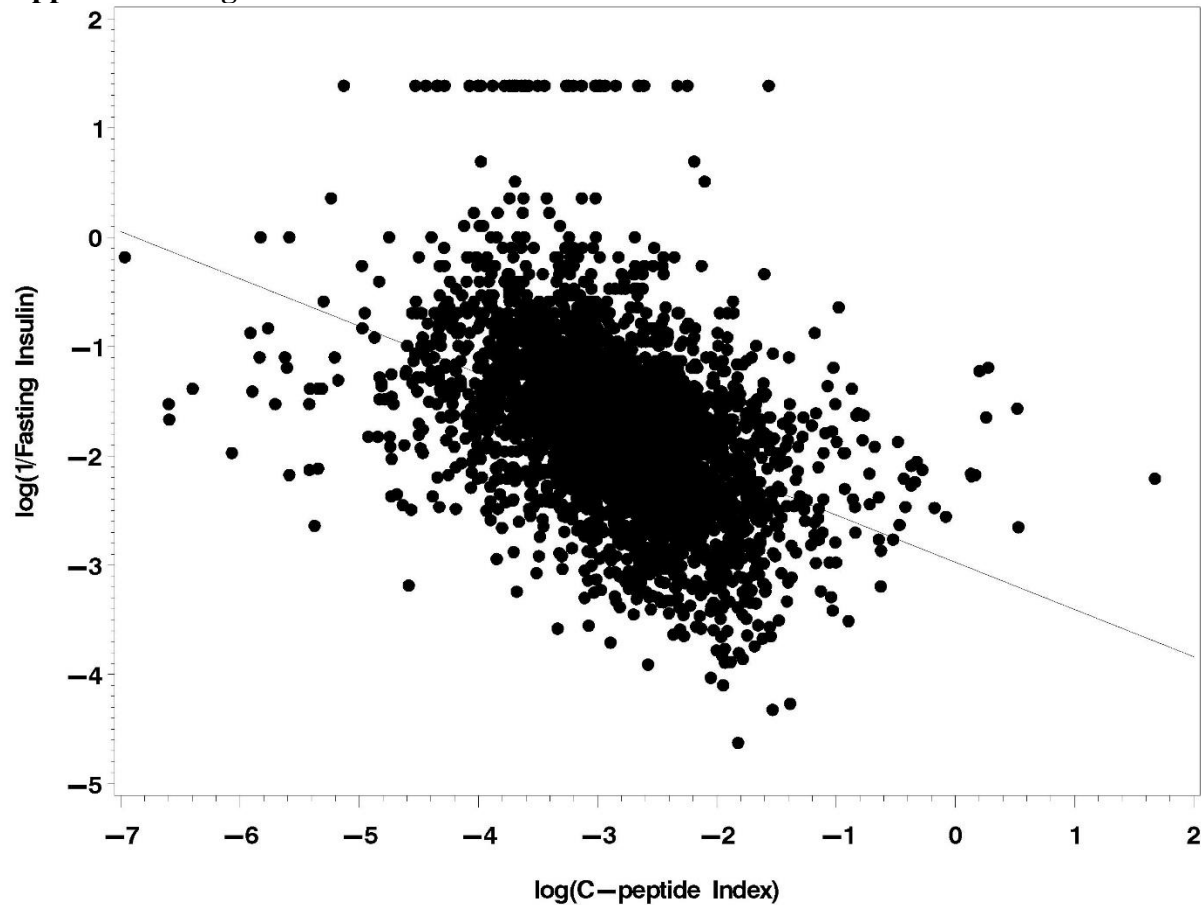
In order to evaluate the relationship between 1/fasting insulin and C-peptide index, the log of these of parameters were calculated, and plotted against each other. We used data from a total of 3277 participants (from those with insulin levels from IVGTTs in DPT-1 and OGTTs in PTP). The source for the procedures to test for the hyperbolic relationship is referenced in Retnakaran et. al, Obesity, 2008.

Using a regression model of log(1/fasting) vs. log (C-peptide index), a hyperbolic relationship can be confirmed if the parameter estimate for log (C-peptide index) is -1 with a 95% confidence interval that excludes 0. In supplemental figure 4, the parameter estimate for log (C-peptide index) is -0.43 with a 95% CI of (-0.46, -40). It was, thus, concluded that the relationship was not hyperbolic.

Similarly, when using log HOMA-IR in place of log 1/fasting insulin in the regression model, the results of the analysis were that, like the oDI calculated using 1/fasting Insulin – the relationship is not hyperbolic. The parameter estimate for log(C-peptide index) was 0.44 with a 95% CI of (0.40, 0.47), which is not -1.

Retnakaran R, Shen S, Hanley AJ, Vuksan V, Hamilton JK, Zinman B. Hyperbolic relationship between insulin secretion and sensitivity on oral glucose tolerance test. Obesity (Silver Spring). 2008 Aug;16(8):1901-7. doi: 10.1038/oby.2008.307. Epub 2008 Jun 12. PMID: 18551118. (https://pubmed.ncbi.nlm.nih.gov/18551118/)