

Dataset Integrity Check for Metabolic Control Data Files

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1 Standard Disclaimer

The intent of this DSIC is to provide confidence that the data distributed by the NIDDK repository is a true copy of the study data. Our intent is not to assess the integrity of the statistical analyses reported by study investigators. As with all statistical analyses of complex datasets, complete replication of a set of statistical results should not be expected in secondary analysis. This occurs for a number of reasons including differences in the handling of missing data, restrictions on cases included in samples for a particular analysis, software coding used to define complex variables, etc. Experience suggests that most discrepancies can ordinarily be resolved by consultation with the study data coordinating center (DCC), however this process is labor-intensive for both DCC and Repository staff. It is thus not our policy to resolve every discrepancy that is observed in an integrity check. Specifically, we do not attempt to resolve minor or inconsequential discrepancies with published results or discrepancies that involve complex analyses, unless NIDDK Repository staff suspect that the observed discrepancy suggests that the dataset may have been corrupted in storage, transmission, or processing by repository staff. We do, however, document in footnotes to the integrity check those instances in which our secondary analyses produced results that were not fully consistent with those reported in the target publication.

2 Study Background

Sixty-eight individuals (mean age 13.3+/-5.7 years; 35% female, 92% Caucasian) were randomized to HCLC followed by SAP therapy (intensive group; N = 48) or to a usual-care group treated with multiple daily injections or insulin pump therapy (N = 20). Primary outcome was C-peptide concentrations during mixed-meal tolerance tests at 12 months to test the preservation of β -cell function. Enrollment occurred within 6 days of diagnosis. It was found that in new-onset Type 1 diabetes, HCLC followed by SAP therapy did not provide any benefit in preserving β -cell function as compared with conventional care.

3 Archived Datasets

All data files, as provided by the Data Coordinating Center (DCC), are located in the Metabolic Control study data package. For this replication, variables were taken from the raw datasets: "ptroster.sas7bdat", "penrollmenthx.sas7bdat", and "plabresults.sas7bdat", and the analysis datasets: "contacts.sas7bdat", "subjects.sas7bdat", and "gluindices.sas7bdat".

4 Statistical Methods

Analyses were performed to duplicate results for the data published by Buckingham et al. in Diabetes Care, December 2013. To verify the integrity of the datasets, descriptive statistics were computed.

5 Results

For Table 1 in the publication [1], Table 1-Outcome data at 12 months, Table A lists the variables that were used in the replication and Table B compares the results calculated from the archived data file to the results published in Table 1. The results of the replication are an exact match.

For Supplementary Table 1 in the publication [1], Supplementary Table 1-Baseline characteristics, Table C lists the variables that were used in the replication and Table D compares the results calculated from the archived data file to the results published in Supplementary Table 1. The results of the replication are an exact match.

For Supplementary Table 2 in the publication [1], Supplementary Table 2-Study data by visit, Table E lists the variables that were used in the replication and Table F compares the results calculated from the archived data file to the results published in Supplementary Table 2. The results of the replication are an exact match.

For Supplementary Table 3 in the publication [1], Supplementary Table 3-Subgroup analyses, Table G lists the variables that were used in the replication and Table H compares the results calculated from the archived data file to the results published in Supplementary Table 3. The results of the replication are an exact match when available.

6 Conclusions

The NIDDK repository is confident that the Metabolic Control data files to be distributed are a true copy to the manuscript.

7 References

[1] Original Research - Emerging Technologies and Therapeutics: Bruce Buckingham, Roy W. Beck, Katrina J. Ruedy, Peiyao Cheng, Craig Kollman, Stuart A. Weinzimer, Linda A. DiMeglio, Andrew A. Bremer, Robert Slover, William V. Tamborlane, and Diabetes Research in Children Network (DirecNet) and Type 1 Diabetes. TrialNet Study Effectiveness of Early Intensive Therapy on β -Cell Preservation in Type 1 Diabetes Diabetes Care December 2013 36:12 4030-4035

Table A: Variables used to replicate Table 1-Outcome data at 12 months

Characteristic	dataset.variable
C-peptide AUC (pmol/mL)	subjects.log_cpepAvgAUC12
HbA1c (%)	contacts.a1c
HbA1c (mmol/mol)	contacts.a1c_mmol
Mean glucose (mg/dL)	gluindices.gluemean
71-180 mg/dL	gluindices.gluinrange
<70 mg/dL	gluindices.glubelow70
>180 mg/dL	gluindices.gluabove180
CV%	gluindices.gluvcv
TDI (units/kg/day)	contacts.insulinkg
BMI percentile	contacts.bmiperc

Table B: Comparison of values computed in integrity check to reference article Table 1 values

	Intensive Manuscript	Intensive DSIC	Difference	Standard Manuscript	Standard DSIC	Difference
n	47	47	0	20	20	0
C-peptide AUC (pmol/mL), geometric mean (95% CI)	0.43 (0.34-0.52)	0.43 (0.34, 0.52)	0 (0)	0.52 (0.32-0.75)	0.52 (0.32, 0.75)	0 (0)
	N=48	N=48	0	N=20	N=20	0
HbA1c (%), mean \pm SD	7.4 \pm 1.2	7.4 \pm 1.2	0 \pm 0	7.3 \pm 1.1	7.3 \pm 1.1	0 \pm 0
HbA1c (mmol/mol), mean \pm SD	57 \pm 13	57 \pm 13	0 \pm 0	57 \pm 12	57 \pm 12	0 \pm 0
CGM data median	N=31	N=31	0	N=15	N=15	0
Mean glucose (mg/dL)	150	150	0	152	152	0
71-180	69%	69%	0	70%	70%	0
<70	2.50%	2.50%	0	0.70%	0.70%	0
>180	27%	27%	0	22%	22%	0
CV (%)	35	35	0	35	35	0
	N=48	N=48	0	N=20	N=20	0
TDI (units/kg/day)	0.6 \pm 0.2	0.6 \pm 0.2	0 \pm 0	0.6 \pm 0.3	0.6 \pm 0.3	0 \pm 0
	N=46	N=46	0	N=19	N=19	0
BMI percentile	58	58	0	62	62	0

Table C: Variables used to replicate Supplementary Table 1-Baseline characteristics

Characteristic	dataset.variable
Age (years)	subjects.age
Gender	penrollmenthx.gender
Race/Ethnicity	penrollmenthx.ethnicity, penrollmenthx.race
Parent Education	penrollmenthx.educaregvrpedu, penrollmenthx.educaregvrsedu
DKA at Diagnosis	penrollmenthx.dka
BMI Percentile	contacts.bmiperc
C-peptide AUC (pmol/mL)	subjects.cpepAvgAUC0
Initial Glucose (mg/dL) mean \pm SD	penrollmenthx.initgluc
HbA1c (%)	plabresults.labresulttype, plabresults.labanalysisresult
HbA1c (mmol/mol)	(hba1c*10.93)-23.5
Time to Randomization (days)	penrollmenthx.diagdt, ptroster.randdt
Treatment Group	ptroster.txgroup

Table D: Comparison of values computed in integrity check reference article Supplementary Table 1 values

	Intensive Treatment Group Manuscript (N=48)	Intensive Treatment Group DSIC (N=48)	Difference (N=0)	Usual Care Group Manuscript (N=20)	Usual Care Group DSIC (N=20)	Difference (N=0)
Age (years)						
6-<9	5 (10%)	5 (10%)	0 (0)	0	0	0
9-<12	20 (42%)	20 (42%)	0 (0)	6 (30%)	6 (30%)	0 (0)
12-<15	15 (31%)	15 (31%)	0 (0)	8 (40%)	8 (40%)	0 (0)
15-<18	6 (13%)	6 (13%)	0 (0)	5 (25%)	5 (25%)	0 (0)
18-<46	2 (4%)	2 (4%)	0 (0)	1 (5%)	1 (5%)	0 (0)
mean \pm SD	12.7 \pm 4.7	12.7 \pm 4.7	0 \pm 0	14.7 \pm 7.6	14.7 \pm 7.6	0 \pm 0
range	7.8 to 37.7	7.8 to 37.7	0	9.8 to 45.7	9.8 to 45.7	0
Gender: Female N(%)	17 (35%)	17 (35%)	0 (0)	7 (35%)	7 (35%)	0 (0)
Race/Ethnicity N(%)						
White	42 (91%)	42 (91%)	0 (0)	18 (95%)	18 (95%)	0 (0)
Black	1 (2%)	1 (2%)	0 (0)	0	0	0
Hispanic or Latino	2 (4%)	2 (4%)	0 (0)	1 (5%)	1 (5%)	0 (0)
More than one race	1 (2%)	1 (2%)	0 (0)	0	0	0
Parent Education N(%)						
<= 12	4 (9%)	4 (9%)	0 (0)	4 (21%)	4 (21%)	0 (0)
Associate	6 (13%)	6 (13%)	0 (0)	4 (21%)	4 (21%)	0 (0)

	Intensive Treatment Group Manuscript (N=48)	Intensive Treatment Group DSIC (N=48)	Difference (N=0)	Usual Care Group Manuscript (N=20)	Usual Care Group DSIC (N=20)	Difference (N=0)
Bachelors	10 (22%)	10 (22%)	0 (0)	6 (32%)	6 (32%)	0 (0)
Masters	17 (37%)	17 (37%)	0 (0)	3 (16%)	3 (16%)	0 (0)
Professional	9 (20%)	9 (20%)	0 (0)	2 (11%)	2 (11%)	0 (0)
DKA at Diagnosis N(%)	14 (29%)	14 (29%)	0 (0)	6 (30%)	6 (30%)	0 (0)
BMI Percentile						
<20%	15 (33%)	15 (33%)	0 (0)	3 (16%)	3 (16%)	0 (0)
20-<60%	15 (33%)	15 (33%)	0 (0)	9 (47%)	9 (47%)	0 (0)
>=60%	16 (35%)	16 (35%)	0 (0)	7 (37%)	7 (37%)	0 (0)
median (25th, 75th percentiles)	41% (14%, 70%)	41% (14%, 70%)	0 (0)	46% (24%, 74%)	46% (24%, 74%)	0 (0)
C-peptide AUC (pmol/mL)						
<0.15	13 (27%)	13 (27%)	0 (0)	3 (17%)	3 (17%)	0 (0)
0.15-<0.25	13 (27%)	13 (27%)	0 (0)	6 (33%)	6 (33%)	0 (0)
0.25-<0.40	13 (27%)	13 (27%)	0 (0)	4 (22%)	4 (22%)	0 (0)
>=0.40	9 (19%)	9 (19%)	0 (0)	5 (28%)	5 (28%)	0 (0)
median (25th, 75th percentiles)	0.24 (0.15, 0.38)	0.24 (0.15, 0.38)	0 (0)	0.27 (0.20, 0.44)	0.27 (0.20, 0.44)	0 (0)
Initial Glucose (mg/dL) mean ± SD	501 ± 193	501 ± 193	0 ± 0	535 ± 235	535 ± 235	0 ± 0
HbA1c (%)						
5.0-<8.0% (31-<64 mmol/mol)	2 (4%)	2 (4%)	0 (0)	1 (5%)	1 (5%)	0 (0)
8.0-<10.0% (64-<86 mmol/mol)	10 (21%)	10 (21%)	0 (0)	6 (30%)	6 (30%)	0 (0)
10.0-<13.0% (86-<119 mmol/mol)	19 (40%)	19 (40%)	0 (0)	7 (35%)	7 (35%)	0 (0)
>=13.0% (>=119 mmol/mol)	17 (35%)	17 (35%)	0 (0)	6 (30%)	6 (30%)	0 (0)
mean ± SD (%)	11.8 ± 2.4	11.8 ± 2.4	0 ± 0	11.2 ± 2.6	11.2 ± 2.6	0 ± 0
mean ± SD (mmol/mol)	105 ± 27	105 ± 27	0 ± 0	99 ± 28	99 ± 28	0 ± 0
range (%)	6.8 to 16.4	6.8 to 16.4	0	5.8 to 15.9	5.8 to 15.9	0
range (mmol/mol)	51 to 156	51 to 156	0	40 to 150	40 to 150	0
Time to Randomization (days)						
mean ± SD	2.9 ± 1.6	2.9 ± 1.6	0 ± 0	3.0 ± 1.7	3.0 ± 1.7	0 ± 0

	Intensive Treatment Group Manuscript (N=48)	Intensive Treatment Group DSIC (N=48)	Difference (N=0)	Usual Care Group Manuscript (N=20)	Usual Care Group DSIC (N=20)	Difference (N=0)
range	0 to 6	0 to 6	0	1 to 6	1 to 6	0

Table E: Variables used to replicate Supplementary Table 2-Study data by visit

Characteristic	dataset.variable
C-peptide AUC (pmol/mL)	contacts.log_cpepAvgAUC
HbA1c (%)	contacts.a1c
HbA1c (mmol/mol)	contacts.a1c_mmol
Mean glucose (mg/dL)	gluindices.glumean
71-180 mg/dL	gluindices.gluinrange
<70 mg/dL	gluindices.glubelow70
>180 mg/dL	gluindices.gluabove180
CV%	gluindices.gluvc
TDI (units/kg/day)	contacts.insulinkg
BMI percentile	contacts.bmiperc
Treatment group	subjects.txgroup, contacts.txgroup, gluindices.txgroup

Table F: Comparison of values computed in integrity check reference article Supplementary Table 2 values

Baseline

	Intensive Manuscript	Intensive DSIC	Difference	Standard Manuscript	Standard DSIC	Difference
	N=48	N=48	0	N=18	N=18	0
C-peptide AUC (pmol/mL) geometric mean (95% C.I.)	0.29 (0.23, 0.35)	0.29 (0.23, 0.35)	0 (0)	0.35 (0.23, 0.49)	0.35 (0.23, 0.49)	0 (0)
	N=48	N=48	0	N=20	N=20	0
HbA1c (%) mean \pm SD	11.8 \pm 2.4	11.8 \pm 2.4	0 \pm 0	11.2 \pm 2.6	11.2 \pm 2.6	0 \pm 0
HbA1c (mmol/mol) mean \pm SD	105 \pm 27	105 \pm 27	0 \pm 0	99 \pm 28	99 \pm 28	0 \pm 0
CGM Data median	N=26	N=26	0	N=18	N=18	0
Mean Glucose (mg/dL)	208	208	0	167	167	0
71-180 mg/dL	41%	41%	0	63%	63%	0

	Intensive Manuscript	Intensive DSIC	Difference	Standard Manuscript	Standard DSIC	Difference
<70 mg/dL	0.00%	0.00%	0	0.30%	0.30%	0
>180 mg/dL	59%	59%	0	33%	33%	0
CV	31%	31%	0	32%	32%	0
	NA	NA	NA	NA	NA	NA
TDI (U/kg/day)	NA	NA	NA	NA	NA	NA
	N=46	N=46	0	N=19	N=19	0
BMI percentile	41%	41%	0	46%	46%	0

2 weeks

	Intensive Manuscript	Intensive DSIC	Difference	Standard Manuscript	Standard DSIC	Difference
	N=44	N=44	0	N=18	N=18	0
C-peptide AUC (pmol/mL) geometric mean (95% C.I.)	0.49 (0.42, 0.55)	0.49 (0.42, 0.55)	0 (0)	0.60 (0.43, 0.80)	0.60 (0.43, 0.80)	0 (0)
	NA	NA	NA	NA	NA	NA
HbA1c (%) mean \pm SD	NA	NA	NA	NA	NA	NA
HbA1c (mmol/mol) mean \pm SD	NA	NA	NA	NA	NA	NA
CGM Data median	N=47	N=47	0	NA	NA	NA
Mean Glucose (mg/dL)	118	118	0	NA	NA	NA
71-180 mg/dL	89%	89%	0	NA	NA	NA
<70 mg/dL	3.50%	3.50%	0	NA	NA	NA
>180 mg/dL	6%	6%	0	NA	NA	NA
CV	28%	28%	0	NA	NA	NA
	N=48	N=48	0	N=18	N=18	0
TDI (U/kg/day)	0.7 \pm 0.3	0.7 \pm 0.3	0 \pm 0	0.5 \pm 0.3	0.5 \pm 0.3	0 \pm 0
	N=46	N=46	0	N=17	N=17	0
BMI percentile	59%	59%	0	51%	51%	0

6 weeks

	Intensive Manuscript	Intensive DSIC	Difference	Standard Manuscript	Standard DSIC	Difference
	N=47	N=47	0	N=17	N=17	0
C-peptide AUC (pmol/mL) geometric mean (95% C.I.)	0.65 (0.58, 0.73)	0.65 (0.58, 0.73)	0 (0)	0.80 (0.64, 0.99)	0.80 (0.64, 0.99)	0 (0)
	N=48	N=48	0	N=16	N=16	0
HbA1c (%) mean ± SD	7.7 ± 0.9	7.7 ± 0.9	0 ± 0	7.9 ± 1.0	7.9 ± 1.0	0 ± 0
HbA1c (mmol/mol) mean ± SD	60 ± 10	60 ± 10	0 ± 0	63 ± 11	63 ± 11	0 ± 0
CGM Data median	N=47	N=47	0	NA	NA	NA
Mean Glucose (mg/dL)	124	124	0	NA	NA	NA
71-180 mg/dL	87%	87%	0	NA	NA	NA
<70 mg/dL	1.80%	1.80%	0	NA	NA	NA
>180 mg/dL	7%	7%	0	NA	NA	NA
CV	28%	28%	0	NA	NA	NA
	N=48	N=48	0	N=17	N=17	0
TDI (U/kg/day)	0.5 ± 0.2	0.5 ± 0.2	0 ± 0	0.4 ± 0.3	0.4 ± 0.3	0 ± 0
	N=46	N=46	0	N=16	N=16	0
BMI percentile	59%	59%	0	54%	54%	0

3 months

	Intensive Manuscript	Intensive DSIC	Difference	Standard Manuscript	Standard DSIC	Difference
	N=47	N=47	0	N=17	N=17	0
C-peptide AUC (pmol/mL) geometric mean (95% C.I.)	0.67 (0.58, 0.75)	0.67 (0.58, 0.75)	0 (0)	0.83 (0.63, 1.06)	0.83 (0.63, 1.06)	0 (0)
	N=48	N=48	0	N=18	N=18	0
HbA1c (%) mean ± SD	6.0 ± 0.5	6.0 ± 0.5	0 ± 0	6.4 ± 0.7	6.4 ± 0.7	0 ± 0
HbA1c (mmol/mol) mean ± SD	42 ± 6	42 ± 6	0 ± 0	46 ± 8	46 ± 8	0 ± 0
CGM Data median	N=45	N=45	0	N=14	N=14	0

	Intensive Manuscript	Intensive DSIC	Difference	Standard Manuscript	Standard DSIC	Difference
Mean Glucose (mg/dL)	131	131	0	124	124	0
71-180 mg/dL	85%	85%	0	83%	83%	0
<70 mg/dL	2.50%	2.50%	0	0.90%	0.90%	0
>180 mg/dL	12%	12%	0	6%	6%	0
CV	31%	31%	0	31%	31%	0
	N=48	N=48	0	N=18	N=18	0
TDI (U/kg/day)	0.5 ± 0.2	0.5 ± 0.2	0 ± 0	0.4 ± 0.4	0.4 ± 0.4	0 ± 0
	N=46	N=46	0	N=17	N=17	0
BMI percentile	59%	59%	0	59%	59%	0

6 months

	Intensive Manuscript	Intensive DSIC	Difference	Standard Manuscript	Standard DSIC	Difference
	N=47	N=47	0	N=17	N=17	0
C-peptide AUC (pmol/mL) geometric mean (95% C.I.)	0.57 (0.50, 0.65)	0.57 (0.5, 0.65)	0 (0)	0.71 (0.50, 0.95)	0.71 (0.5, 0.95)	0 (0)
	N=48	N=48	0	N=17	N=17	0
HbA1c (%) mean ± SD	6.4 ± 0.8	6.4 ± 0.8	0 ± 0	6.6 ± 0.9	6.6 ± 0.9	0 ± 0
HbA1c (mmol/mol) mean ± SD	46 ± 9	46 ± 9	0 ± 0	48 ± 10	48 ± 10	0 ± 0
CGM Data median	N=44	N=44	0	N=15	N=15	0
Mean Glucose (mg/dL)	141	141	0	126	126	0
71-180 mg/dL	78%	78%	0	88%	88%	0
<70 mg/dL	2.10%	2.10%	0	2.80%	2.80%	0
>180 mg/dL	16%	16%	0	9%	9%	0
CV	32%	32%	0	30%	30%	0
	N=48	N=48	0	N=17	N=17	0
TDI (U/kg/day)	0.5 ± 0.2	0.5 ± 0.2	0 ± 0	0.4 ± 0.3	0.4 ± 0.3	0 ± 0
	N=46	N=46	0	N=16	N=16	0
BMI percentile	57%	57%	0	49%	49%	0

9 months

	Intensive Manuscript	Intensive DSIC	Difference	Standard Manuscript	Standard DSIC	Difference
	N=46	N=46	0	N=17	N=17	0
C-peptide AUC (pmol/mL) geometric mean (95% C.I.)	0.50 (0.42, 0.59)	0.50 (0.42, 0.59)	0 (0)	0.61 (0.41, 0.84)	0.61 (0.41, 0.84)	0 (0)
	N=47	N=47	0	N=17	N=17	0
HbA1c (%) mean ± SD	7 ± 1.2	7 ± 1.2	0 ± 0	6.8 ± 0.9	6.8 ± 0.9	0 ± 0
HbA1c (mmol/mol) mean ± SD	53 ± 13	53 ± 13	0 ± 0	51 ± 10	51 ± 10	0 ± 0
CGM Data median	N=45	N=45	0	N=15	N=15	0
Mean Glucose (mg/dL)	161	161	0	165	165	0
71-180 mg/dL	68%	68%	0	64%	64%	0
<70 mg/dL	1.30%	1.30%	0	1.20%	1.20%	0
>180 mg/dL	29%	29%	0	28%	28%	0
CV	33%	33%	0	31%	31%	0
	N=48	N=48	0	N=17	N=17	0
TDI (U/kg/day)	0.6 ± 0.2	0.6 ± 0.2	0 ± 0	0.4 ± 0.3	0.4 ± 0.3	0 ± 0
	N=46	N=46	0	N=16	N=16	0
BMI percentile	56%	56%	0	49%	49%	0

12 months

	Intensive Manuscript	Intensive DSIC	Difference	Standard Manuscript	Standard DSIC	Difference
n	47	47	0	20	20	0
C-peptide AUC (pmol/mL) geometric mean (95% C.I.)	0.43 (0.34-0.52)	0.43 (0.34, 0.52)	0 (0)	0.52 (0.32-0.75)	0.52 (0.32, 0.75)	0 (0)
	N=48	N=48	0	N=20	N=20	0
HbA1c (%), mean ± SD	7.4 ± 1.2	7.4 ± 1.2	0 ± 0	7.3 ± 1.1	7.3 ± 1.1	0 ± 0
HbA1c (mmol/mol), mean ± SD	57 ± 13	57 ± 13	0 ± 0	57 ± 12	57 ± 12	0 ± 0
CGM data median	N=31	N=31	0	N=15	N=15	0

	Intensive Manuscript	Intensive DSIC	Difference	Standard Manuscript	Standard DSIC	Difference
Mean glucose (mg/dL)	150	150	0	152	152	0
71-180 mg/dL	69%	69%	0	70%	70%	0
<70 mg/dL	2.50%	2.50%	0	0.70%	0.70%	0
>180 mg/dL	27%	27%	0	22%	22%	0
CV	35	35	0	35	35	0
	N=48	N=48	0	N=20	N=20	0
TDI (U/kg/day)	0.6 ± 0.2	0.6 ± 0.2	0 ± 0	0.6 ± 0.3	0.6 ± 0.3	0 ± 0
	N=46	N=46	0	N=19	N=19	0
BMI percentile	58	58	0	62	62	0

Table G: Variables used to replicate Supplementary Table 3-Subgroup analyses

Characteristic	dataset.variable
Overall Intent to Treat Analysis	All subjects where log_cpepAvgAUC0 or log_cpepAvgAUC12 is not missing
Per Protocol Analysis	subjects.perprotflg
Age	subjects.age
Gender	subjects.gender
DKA at diagnosis	subjects.dka
Baseline lab HbA1c	subjects.a1c0
Baseline C-peptide at 90 min (pmol/mol)	plabresults.labanalysisresult, where labresulttype = 'PEP90'
Baseline C-peptide AUC	subjects.log_cpepAvgAUC0
12 month C-peptide AUC	subjects.log_cpepAvgAUC12
Treatment group	subjects.txgroup

Table H: Comparison of values computed in integrity check reference article Supplementary Table 3 values

Baseline C-peptide AUC

	N Manuscript	N DSIC	Difference	Intensive Mean (95% CI) Manuscript	Intensive Mean (95% CI) DSIC	Difference	Standard Mean (95% CI) Manuscript	Standard Mean (95% CI) DSIC	Difference
Overall Intent to Treat Analysis	48/18	48/18	0	0.29 (0.23, 0.35)	0.29 (0.23, 0.35)	0 (0)	0.35 (0.23, 0.49)	0.35 (0.23, 0.49)	0 (0)

	N Manuscript	N DSIC	Difference	Intensive Mean (95% CI) Manuscript	Intensive Mean (95% CI) DSIC	Difference	Standard Mean (95% CI) Manuscript	Standard Mean (95% CI) DSIC	Difference
Per Protocol Analysis	22/13	22/13	0	0.32 (0.23, 0.42)	0.32 (0.23, 0.42)	0 (0)	0.34 (0.21, 0.47)	0.34 (0.21, 0.47)	0 (0)
Age									
7-<12 Years	25/4	25/4	0	0.27 (0.18, 0.37)	0.27 (0.18, 0.37)	0	0.21 (0.12, 0.32)	0.21 (0.12, 0.32)	0
>= 12 Years	23/14	23/14	0	0.31 (0.23, 0.38)	0.31 (0.23, 0.38)	0	0.39 (0.23, 0.57)	0.39 (0.23, 0.57)	0
Gender									
Female	17/6	17/6	0	0.35 (0.23, 0.49)	0.35 (0.23, 0.49)	0	0.49 (0.11, 1.02)	0.49 (0.11, 1.02)	0
Male	31/12	31/12	0		0.25 (0.20, 0.31)			0.28 (0.20, 0.37)	
DKA at diagnosis									
Yes	14/5	14/5	0	0.21 (0.17, 0.26)	0.21 (0.17, 0.26)	0	0.20 (0.09, 0.31)	0.20 (0.09, 0.31)	0
No	34/13	34/13	0	0.32 (0.24, 0.40)	0.32 (0.24, 0.40)	0	0.41 (0.25, 0.60)	0.41 (0.25, 0.60)	0
Baseline lab HbA1c									
<10.0 % (<86 mmol/mol)	12/7	12/7	0	0.50 (0.32, 0.71)	0.50 (0.32, 0.71)	0	0.56 (0.25, 0.94)	0.56 (0.25, 0.94)	0
>= 10.0% (>=86 mmol/mol)	36/11	36/11	0	0.22 (0.19, 0.26)	0.22 (0.19, 0.26)	0	0.23 (0.17, 0.29)	0.23 (0.17, 0.29)	0
Baseline C- peptide at 90 min (pmol/mol)									
<0.30	26/9	26/9	0	0.16 (0.14, 0.18)	0.16 (0.14, 0.18)	0 (0)	0.19 (0.15, 0.23)	0.19 (0.15, 0.23)	0 (0)
>= 0.30	22/9	22/9	0	0.46 (0.37, 0.56)	0.46 (0.37, 0.56)	0 (0)	0.54 (0.32, 0.79)	0.54 (0.32, 0.79)	0 (0)

12 month C-peptide AUC

	N Manuscript	N DSIC	Difference	Intensive Mean (95% CI) Manuscript	Intensive Mean (95% CI) DSIC	Difference	Standard Mean (95% CI) Manuscript	Standard Mean (95% CI) DSIC	Difference
Overall Intent to Treat Analysis	47/20	47/20	0	0.43 (0.34, 0.52)	0.43 (0.34, 0.52)	0 (0)	0.52 (0.32, 0.75)	0.52 (0.32, 0.75)	0 (0)
Per Protocol Analysis	22/15	22/15	0	0.54 (0.39, 0.71)	0.54 (0.39, 0.71)	0 (0)	0.43 (0.23, 0.66)	0.43 (0.23, 0.66)	0 (0)
Age									
7-<12 Years	24/6	24/6	0	0.32 (0.22, 0.43)	0.32 (0.22, 0.43)	0	0.33 (0.08, 0.63)	0.33 (0.08, 0.63)	0
>= 12 Years	23/14	23/14	0	0.55 (0.41, 0.71)	0.55 (0.41, 0.71)	0	0.61 (0.33, 0.94)	0.61 (0.33, 0.94)	0
Gender									
Female	17/7	17/7	0	0.52 (0.33, 0.74)	0.52 (0.33, 0.74)	0	0.74 (0.18, 1.56)	0.74 (0.18, 1.56)	0
Male	30/13	30/13	0		0.38 (0.28, 0.48)			0.41 (0.25, 0.59)	
DKA at diagnosis									
Yes	14/6	14/6	0	0.34 (0.19, 0.51)	0.34 (0.19, 0.51)	0	0.52 (0.18, 0.95)	0.52 (0.18, 0.95)	0
No	33/14	33/14	0	0.47 (0.36, 0.59)	0.47 (0.36, 0.59)	0	0.47 (0.36, 0.59)	0.47 (0.36, 0.59)	0
Baseline lab HbA1c									
<10.0 % (<86 mmol/mol)	12/7	12/7	0	0.57 (0.33, 0.86)	0.57 (0.33, 0.86)	0	0.66 (0.17, 1.36)	0.66 (0.17, 1.36)	0
>= 10.0% (>=86 mmol/mol)	35/13	35/13	0	0.38 (0.29, 0.48)	0.38 (0.29, 0.48)	0	0.44 (0.24, 0.69)	0.44 (0.24, 0.69)	0
Baseline C- peptide at 90 min (pmol/mol)									
<0.30	25/9	25/9	0	0.31 (0.22, 0.41)	0.31 (0.22, 0.41)	0 (0)	0.37 (0.16, 0.61)	0.37 (0.16, 0.61)	0 (0)
>= 0.30	22/9	22/9	0	0.57 (0.42, 0.74)	0.57 (0.42, 0.74)	0 (0)	0.72 (0.31, 1.25)	0.72 (0.31, 1.25)	0 (0)

Attachment A: SAS Code

```
title1 "%sysfunc(getoption(sysin))";
title2 " ";

*** File containing macro for examining each dataset ***;
%include '/prj/niddk/ims_analysis/sas_macros/redaction_data_summary.sas';

filename trans '/prj/niddk/ims_analysis/Metabolic_Control_Data/private_orig_data/MetabolicControl/MC_primary.trns';
libname new '/prj/niddk/ims_analysis/Metabolic_Control_Data/private_orig_data/MetabolicControl';
proc cimport library=new infile=trans;
run;

libname analysis '/prj/niddk/ims_analysis/Metabolic_Control_Data/private_orig_data/MetabolicControl/';

libname sasver '/prj/niddk/ims_analysis/Metabolic_Control_Data/private_created_data/';

proc format;
  value agef 6-8 = '6-<9'
           9-11 = '9-<12'
           12-14 = '12-<15'
           15-17 = '15-<18'
           18-45 = '18-<46';

  value hbalcf 5-<8 = '5-<8'
            8-<10 = '8-<10'
            10-<13 = '10-<13'
            13 - HIGH = '>= 13';

  value bmif 0-<20 = '<20%'
            20-<60 = '20-<60%'
            60 - HIGH = '> 60%';

  value aucf 0-<0.15 = '<0.15'
            0.15-<0.25 = '0.15-<0.25'
            0.25-<0.4 = '0.25-<0.4'
            0.4 - HIGH = '>=0.4';

  value glucosef 0-<70 = '<70'
                71-180 = '71-180'
                181 - HIGH = '>180';

  value eduf 1 = '<=12'
            2 = 'Associate'
            3 = 'Bachelors'
            4 = 'Masters'
            5 = 'Professional';

data ptroster;
  set sasver.ptroster;

data plabresults;
  set sasver.plabresults;
  length lrn 8.;
```



```

if Labanalysisresult ne "<0.05" then lrn=input(Labanalysisresult,8.);
if visit in ("12 month", "Enrollment");

proc freq data=sasver.plabresults;
    tables visit;

data penrollmenthx;
    set sasver.penrollmenthx;

data pinsmanage;
    set sasver.pinsmanage;

data pfollowuphx;
    set sasver.pfollowuphx;
    if visit = '12 month';

proc sort data=penrollmenthx;
    by PTID;

proc sort data=pinsmanage;
    by PTID;

proc sort data=ptroster;
    by PTID;

proc sort data=plabresults;
    by PTID;

proc sort data=pfollowuphx;
    by ptid;

data subjects;
    set analysis.subjects;

proc sort data=subjects;
    by txgroup;

data contacts;
    set analysis.contacts;
    bmiperc = 100*bmiperc;

proc freq data=contacts;
    tables visit;

proc sort data=contacts;
    by txgroup;

data gluindices;
    set analysis.gluindices;
    glucv= glucv*100;
    gluInRange=gluinrange*100;
    gluBelow70=glubelow70*100;
    gluAbove180=gluabove180*100;

proc sort data=gluindices;
    by txgroup;

```

```

proc freq data=gluindices;
    table visit;

proc contents data=gluindices;

data analysis_insulin;
    merge penrollmenthx(keep=PTID WEIGHT race) pinsmanage(keep=PTID Visit DINSULIN) ptroster(keep=PTID TxGroup ABStatus);
    by PTID;
    DINSULIN_PER_KG=DINSULIN/WEIGHT;
    if ABStatus="Positive" and VISIT="12 month";

data analysis_lab;
    merge ptroster(keep=PTID TxGroup ABStatus) plabresults;
    by PTID;
    if ABStatus="Positive";

data analysis_lab;
    set analysis_lab;
    output;
    if LabResultType in ("HBA1C", "HbA1c") then do;
        LabResultType="HBA1C_CONV";
        lrn=(lrn*10.93)-23.5;
    output;
    end;

data baseline_c_pep_90min;
    set analysis_lab;
    lrn = lrn * 0.333;
    if visit = 'Enrollment' and LabResultType = 'PEP90';

data subjects;
    set subjects;
    id = input(ptid, 8.);

*** Supplementary Table 1;

data baseline_info;
    merge ptroster
        penrollmenthx;
    by ptid;
    age_in_months = ageatranddt*12;
    randdt = datepart(randdt);
    time_to_rand = randdt-diagdt;
    if EduCareGvrPEdu in ('11', '12') then p_parent_edu = 1;
    if EduCareGvrPEdu = 'Associates' then p_parent_edu = 2;
    if EduCareGvrPEdu = 'Bachelors' then p_parent_edu = 3;
    if EduCareGvrPEdu = 'Masters' then p_parent_edu = 4;
    if EduCareGvrPEdu = 'Professional' then p_parent_edu = 5;
    if EduCareGvrsEdu in ('11', '12') then s_parent_edu = 1;
    if EduCareGvrSEdu = 'Associates' then s_parent_edu = 2;
    if EduCareGvrSEdu = 'Bachelors' then s_parent_edu = 3;
    if EduCareGvrSEdu = 'Masters' then s_parent_edu = 4;
    if EduCareGvrSEdu = 'Professional' then s_parent_edu = 5;
    if p_parent_edu > s_parent_edu then parent_edu = p_parent_edu;
    else if s_parent_edu > p_parent_edu then parent_edu = s_parent_edu;

```

```

else parent_edu = p_parent_edu;
if abstatus = 'Positive';

proc contents data=baseline_info;

proc sort data=baseline_info;
  by txgroup;

proc freq data=baseline_info;
  tables ageatranddt /list missing;
  by txgroup;
  format ageatranddt agef.;
  title3 'Supplementary Table 1 - Baseline Age';

proc means data=subjects n mean std min max;
  var age;
  class txgroup;

proc freq data=baseline_info;
  tables gender /list missing;
  by txgroup;
  title3 'Supplementary Table 1 - Baseline Gender';

proc freq data=baseline_info;
  tables race*ethnicity /list;
  where race ne 'Unknown/not reported' or ethnicity not in ('Not Hispanic or Latino', 'Unknown/not reported');
  by txgroup;
  title3 'Supplementary Table 1- Baseline Race/Ethnicity';

proc freq data=baseline_info;
  tables parent_edu /list missing;
  where EduCareGvrP ne 'Subject';
  by txgroup;
  format parent_edu eduf.;
  title3 'Supplementary Table 1 - Baseline Parent education';

proc freq data=baseline_info;
  tables dka /list missing;
  by txgroup;
  title3 'Supplementary Table 1 - Baseline DKA at Diagnosis';

proc freq data=contacts;
  where visit = 'A)Enrollment';
  tables bmiperc;
  format bmiperc bmif.;
  by txgroup;
  title3 'Supplementary Table 1 - Baseline BMI Percentile';

proc means data=contacts median p25 p75;
  where visit = 'A)Enrollment';
  var bmiperc;
  class txgroup;

proc freq data=subjects;
  tables cpepAvgAUC0;
  by txgroup;

```

```

format cpepAvgAUC0 aucf.;
title3 'Supplementary Table 1 - Baseline C-peptide AUC';

proc means data=subjects median p25 p75;
var cpepAvgAUC0;
class txgroup;

proc means data=baseline_info n mean std min max;
where ABstatus = 'Positive';
var initgluc;
class txgroup;
title3 'Supplementary Table 1 - Baseline Initial Glucose';

proc sort data=analysis_lab;
by ptid;

data analysis_lab_enroll;
set analysis_lab;
if visit = 'Enrollment' then output analysis_lab_enroll;

data hbalc;
set sasver.pdcahbalc;

proc sort data=hbalc;
by ptid;

data hbalc_enroll;
merge hbalc ptooster;
by ptid;
if visit = 'Baseline Tests' and abstatus = 'Positive' then output hbalc_enroll;

proc sort data=analysis_lab_enroll;
by ptid txgroup;

proc sort data=hbalc_enroll;
by ptid txgroup;

data analysis_lab_enroll;
merge analysis_lab_enroll (in=val1)
      hbalc_enroll (in=val2 keep=ptid DCAHbAlc txgroup);
by ptid txgroup;

data analysis_lab_enroll;
set analysis_lab_enroll;
by ptid;
retain hemoglobin_alc hemoglobin_alc_conv .;
if first.ptid then do;
  hemoglobin_alc = .;
  hemoglobin_alc_conv = .;
end;
if labresultttype in ('HBA1C', 'HbA1c') then hemoglobin_alc = lrn;
if labresultttype = 'HBA1C_CONV' then hemoglobin_alc_conv = lrn;
if last.ptid then output;

data analysis_lab_enroll;
set analysis_lab_enroll;

```

```

if hemoglobin_alc = . then hemoglobin_alc = DCAHbA1c;
if hemoglobin_alc_conv = . then hemoglobin_alc_conv = (DCAHbA1c*10.93)-23.5;

proc sort data=analysis_lab_enroll;
  by txgroup;

proc freq data=analysis_lab_enroll;
  tables hemoglobin_alc;
  format hemoglobin_alc hbalcf.;
  by txgroup;
  title3 'Supplementary Table 1 - Baseline HbA1C';

proc means data=analysis_lab_enroll;
  var hemoglobin_alc hemoglobin_alc_conv;
  class TxGroup;

proc means data=baseline_info n mean std min max;
  where ABstatus = 'Positive';
  var time_to_rand;
  class txgroup;
  title3 'Supplementary Table 1 - Baseline Time to Randomization';

*** Manuscript Table 1;

proc means data=subjects;
  var log_cpepAvgAUC12;
  class txgroup;
  output out=log_auc mean = mean;
  title3 'Table 1 C-Peptide AUC';

data log_auc;
  set log_auc;
  mean = exp(mean)-1;

proc print data=log_auc;

proc means data=subjects alpha = 0.05 clm;
  var log_cpepAvgAUC12;
  output out = log_auc lclm = lclm uclm = uclm;
  class txgroup;

data log_auc;
  set log_auc;
  lclm = exp(lclm)-1;
  uclm = exp(uclm)-1;

proc print data=log_auc;

proc means data = contacts n mean std;
  where visit = 'I)12 month';
  var alc alc_mmol;
  class txgroup;
  title3 'Table 1 - HbA1C';

proc means data=gluindices n median;
  where visit = 'I)12 month';

```

```

var glumean;
class txgroup;
title3 'Table 1 CGM Mean Glucose';

proc means data = gluindices median;
  where visit = 'I)12 month';
  var gluInRange gluBelow70 gluAbove180;
  class txgroup;

proc means data=gluindices median;
  where visit = 'I)12 month';
  var gluCV;
  class txgroup;

proc means data = contacts n mean std;
  where visit = 'I)12 month';
  var insulinkg;
  class txgroup;
  title3 'Table 1 - TDI';

proc means data = contacts n median;
  where visit = 'I)12 month';
  var bmiperc;
  class txgroup;
  title3 'Table 1 - BMI percentile';

*** Supplementary Table 2;

proc means data=subjects;
  var log_cpepAvgAUC0;
  class txgroup;
  output out=log_auc mean = mean;
  title3 'Supplementary Table 2 Baseline C-Peptide AUC';

data log_auc;
  set log_auc;
  mean = exp(mean)-1;

proc print data=log_auc;

proc means data=subjects alpha = 0.05 clm;
  var log_cpepAvgAUC0;
  output out = log_auc lclm = lclm uclm = uclm;
  class txgroup;

data log_auc;
  set log_auc;
  lclm = exp(lclm)-1;
  uclm = exp(uclm)-1;

proc print data=log_auc;

proc means data = contacts n mean std;
  where visit = 'A)Enrollment';
  var a1c a1c_mmol;
  class txgroup;

```

```

title3 'Supplementary Table 2 - Baseline HbA1C';

proc means data=gluindices n median;
  where visit = 'A)Enrollment';
  var glumean;
  class txgroup;
  title3 'Supplementary Table 2 Baseline CGM Mean Glucose';

proc means data = gluindices median;
  where visit = 'A)Enrollment';
  var gluInRange gluBelow70 gluAbove180;
  class txgroup;

proc means data=gluindices median;
  where visit = 'A)Enrollment';
  var gluCV;
  class txgroup;

proc means data = contacts n mean std;
  where visit = 'A)Enrollment';
  var insulinkg;
  class txgroup;
  title3 'Supplementary Table 2 - Baseline TDI';

proc means data = contacts n median;
  where visit = 'A)Enrollment';
  var bmiperc;
  class txgroup;
  title3 'Supplementary Table 2 - Baseline BMI percentile';

proc means data=contacts;
  where visit = 'D)2 week';
  var log_cpepAvgAUC;
  class txgroup;
  output out=log_auc mean = mean;
  title3 'Supplementary Table 2 - 2 week C-Peptide AUC';

data log_auc;
  set log_auc;
  mean = exp(mean)-1;

proc print data=log_auc;

proc means data=contacts alpha = 0.05 clm;
  where visit = 'D)2 week';
  var log_cpepAvgAUC;
  output out = log_auc lclm = lclm uclm = uclm;
  class txgroup;

data log_auc;
  set log_auc;
  lclm = exp(lclm)-1;
  uclm = exp(uclm)-1;

proc print data=log_auc;

```

```

proc means data = contacts n mean std;
  where visit = 'D)2 week';
  var alc alc_mmol;
  class txgroup;
  title3 'Supplementary Table 2 - 2 week HbA1C';

proc means data=gluindices n median;
  where visit = 'D)2 week';
  var glumean;
  class txgroup;
  title3 'Supplementary Table 2 - 2 wekk CGM Mean Glucose';

proc means data = gluindices median;
  where visit = 'D)2 week';
  var gluInRange gluBelow70 gluAbove180;
  class txgroup;

proc means data=gluindices median;
  where visit = 'D)2 week';
  var gluCV;
  class txgroup;

proc means data = contacts n mean std;
  where visit = 'D)2 week';
  var insulinkg;
  class txgroup;
  title3 'Supplementary Table 2 - 2 week TDI';

proc means data = contacts n median;
  where visit = 'D)2 week';
  var bmiperc;
  class txgroup;
  title3 'Supplementary Table 2 - 2 week BMI percentile';

proc means data=contacts;
  where visit = 'E)6 week';
  var log_cpepAvgAUC;
  class txgroup;
  output out=log_auc mean = mean;
  title3 'Supplementary Table 2 - 6 week C-Peptide AUC';

data log_auc;
  set log_auc;
  mean = exp(mean)-1;

proc print data=log_auc;

proc means data=contacts alpha = 0.05 clm;
  where visit = 'E)6 week';
  var log_cpepAvgAUC;
  output out = log_auc lclm = lclm uclm = uclm;
  class txgroup;

data log_auc;
  set log_auc;
  lclm = exp(lclm)-1;

```



```

uclm = exp(uclm)-1;

proc print data=log_auc;

proc means data = contacts n mean std;
  where visit = 'E)6 week';
  var alc alc_mmol;
  class txgroup;
  title3 'Supplementary Table 2 - 6 week HbA1c';

proc means data=gluindices n median;
  where visit = 'E)6 week';
  var glumean;
  class txgroup;
  title3 'Supplementary Table 2 - 6 week CGM Mean Glucose';

proc means data = gluindices median;
  where visit = 'E)6 week';
  var gluInRange gluBelow70 gluAbove180;
  class txgroup;

proc means data=gluindices median;
  where visit = 'E)6 week';
  var gluCV;
  class txgroup;

proc means data = contacts n mean std;
  where visit = 'E)6 week';
  var insulinkg;
  class txgroup;
  title3 'Supplementary Table 2 - 6 week TDI';

proc means data = contacts n median;
  where visit = 'E)6 week';
  var bmiperc;
  class txgroup;
  title3 'Supplementary Table 2 - 6 week BMI percentile';

proc means data=contacts;
  where visit = 'F)3 month';
  var log_cpepAvgAUC;
  class txgroup;
  output out=log_auc mean = mean;
  title3 'Supplementary Table 2 - 3 month C-Peptide AUC';

data log_auc;
  set log_auc;
  mean = exp(mean)-1;

proc print data=log_auc;

proc means data=contacts alpha = 0.05 clm;
  where visit = 'F)3 month';
  var log_cpepAvgAUC;
  output out = log_auc lclm = lclm uclm = uclm;
  class txgroup;

```

```

data log_auc;
  set log_auc;
  lclm = exp(lclm)-1;
  uclm = exp(uclm)-1;

proc print data=log_auc;

proc means data = contacts n mean std;
  where visit = 'F)3 month';
  var alc alc_mmol;
  class txgroup;
  title3 'Supplementary Table 2 - 3 month HbA1C';

proc means data=gluindices n median;
  where visit = 'F)3 month';
  var glumean;
  class txgroup;
  title3 'Supplementary Table 2 - 3 month CGM Mean Glucose';

proc means data = gluindices median;
  where visit = 'F)3 month';
  var gluInRange gluBelow70 gluAbove180;
  class txgroup;

proc means data=gluindices median;
  where visit = 'F)3 month';
  var gluCV;
  class txgroup;

proc means data = contacts n mean std;
  where visit = 'F)3 month';
  var insulinkg;
  class txgroup;
  title3 'Supplementary Table 2 - 3 month TDI';

proc means data = contacts n median;
  where visit = 'F)3 month';
  var bmiperc;
  class txgroup;
  title3 'Supplementary Table 2 - 3 month BMI percentile';

proc means data=contacts;
  where visit = 'G)6 month';
  var log_cpepAvgAUC;
  class txgroup;
  output out=log_auc mean = mean;
  title3 'Supplementary Table 2 - 6 month C-Peptide AUC';

data log_auc;
  set log_auc;
  mean = exp(mean)-1;

proc print data=log_auc;

proc means data=contacts alpha = 0.05 clm;

```

```

    where visit = 'G)6 month';
    var log_cpepAvgAUC;
    output out = log_auc lclm = lclm uclm = uclm;
    class txgroup;

data log_auc;
    set log_auc;
    lclm = exp(lclm)-1;
    uclm = exp(uclm)-1;

proc print data=log_auc;

proc means data = contacts n mean std;
    where visit = 'G)6 month';
    var alc alc_mmol;
    class txgroup;
    title3 'Supplementary Table 2 - 6 month HbA1C';

proc means data=gluindices n median;
    where visit = 'G)6 month';
    var glumean;
    class txgroup;
    title3 'Supplementary Table 2 - 6 month CGM Mean Glucose';

proc means data = gluindices median;
    where visit = 'G)6 month';
    var gluInRange gluBelow70 gluAbove180;
    class txgroup;

proc means data=gluindices median;
    where visit = 'G)6 month';
    var gluCV;
    class txgroup;

proc means data = contacts n mean std;
    where visit = 'G)6 month';
    var insulinkg;
    class txgroup;
    title3 'Supplementary Table 2 - 6 month TDI';

proc means data = contacts n median;
    where visit = 'G)6 month';
    var bmiperc;
    class txgroup;
    title3 'Supplementary Table 2 - 6 month BMI percentile';

proc means data=contacts;
    where visit = 'H)9 month';
    var log_cpepAvgAUC;
    class txgroup;
    output out=log_auc mean = mean;
    title3 'Supplementary Table 2 - 9 month C-Peptide AUC';

data log_auc;
    set log_auc;
    mean = exp(mean)-1;

```

```

proc print data=log_auc;

proc means data=contacts alpha = 0.05 clm;
  where visit = 'H)9 month';
  var log_cpepAvgAUC;
  output out = log_auc lclm = lclm uclm = uclm;
  class txgroup;

data log_auc;
  set log_auc;
  lclm = exp(lclm)-1;
  uclm = exp(uclm)-1;

proc print data=log_auc;

proc means data = contacts n mean std;
  where visit = 'H)9 month';
  var a1c a1c_mmol;
  class txgroup;
  title3 'Supplementary Table 2 - 9 month HbA1C';

proc means data=gluindices n median;
  where visit = 'H)9 month';
  var glumean;
  class txgroup;
  title3 'Supplementary Table 2 - 9 month CGM Mean Glucose';

proc means data = gluindices median;
  where visit = 'H)9 month';
  var gluInRange gluBelow70 gluAbove180;
  class txgroup;

proc means data=gluindices median;
  where visit = 'H)9 month';
  var gluCV;
  class txgroup;

proc means data = contacts n mean std;
  where visit = 'H)9 month';
  var insulinkg;
  class txgroup;
  title3 'Supplementary Table 2 - 9 month TDI';

proc means data = contacts n median;
  where visit = 'H)9 month';
  var bmiperc;
  class txgroup;
  title3 'Supplementary Table 2 - 9 month BMI percentile';

*** Supplementary Table 3;

proc sort data=subjects;
  by id;

proc sort data=baseline_c_pep_90min;

```

```

    by ptid;

data subjects_c_pep_90min;
  merge subjects          (in=val1)
        baseline_c_pep_90min (in=val2 keep=ptid lrn rename = (ptid=id));
  by id;
  if val1 and val2 then output subjects_c_pep_90min;

proc means data=subjects;
  var log_cpepAvgAUC0;
  class txgroup;
  output out=log_auc mean = mean;
  title3 'Supplementary Table 3 - Overall Intent to Treat Analysis';

data log_auc;
  set log_auc;
  mean = exp(mean)-1;

proc print data=log_auc;

proc means data=subjects alpha = 0.05 clm;
  var log_cpepAvgAUC0;
  output out = log_auc lclm = lclm uclm = uclm;
  class txgroup;

data log_auc;
  set log_auc;
  lclm = exp(lclm)-1;
  uclm = exp(uclm)-1;

proc print data=log_auc;

proc means data=subjects;
  where perprotflg = 1 ;
  var log_cpepAvgAUC0;
  class txgroup;
  output out=log_auc mean = mean;
  title3 'Supplementary Table 3 - Per Protocol Analysis';

data log_auc;
  set log_auc;
  mean = exp(mean)-1;

proc print data=log_auc;

proc means data=subjects alpha = 0.05 clm;
  where perprotflg = 1;
  var log_cpepAvgAUC0;
  output out = log_auc lclm = lclm uclm = uclm;
  class txgroup;

data log_auc;
  set log_auc;
  lclm = exp(lclm)-1;
  uclm = exp(uclm)-1;

```

```

proc print data=log_auc;

proc means data=subjects;
  where age < 12 ;
  var log_cpepAvgAUC0;
  class txgroup;
  output out=log_auc mean = mean;
  title3 'Supplementary Table 3 - Baseline C-Peptide AUC 7-<12 years';

data log_auc;
  set log_auc;
  mean = exp(mean)-1;

proc print data=log_auc;

proc means data=subjects alpha = 0.05 clm;
  where age < 12;
  var log_cpepAvgAUC0;
  output out = log_auc lclm = lclm uclm = uclm;
  class txgroup;

data log_auc;
  set log_auc;
  lclm = exp(lclm)-1;
  uclm = exp(uclm)-1;

proc print data=log_auc;

proc means data=subjects;
  where age >= 12 ;
  var log_cpepAvgAUC0;
  class txgroup;
  output out=log_auc mean = mean;
  title3 'Supplementary Table 3 - Baseline C-Peptide AUC >= 12 years';

data log_auc;
  set log_auc;
  mean = exp(mean)-1;

proc print data=log_auc;

proc means data=subjects alpha = 0.05 clm;
  where age >= 12;
  var log_cpepAvgAUC0;
  output out = log_auc lclm = lclm uclm = uclm;
  class txgroup;

data log_auc;
  set log_auc;
  lclm = exp(lclm)-1;
  uclm = exp(uclm)-1;

proc print data=log_auc;

proc means data=subjects;
  where gender = 'F' ;

```

```

var log_cpepAvgAUC0;
class txgroup;
output out=log_auc mean = mean;
title3 'Supplementary Table 3 - Baseline C-Peptide AUC Female';

data log_auc;
set log_auc;
mean = exp(mean)-1;

proc print data=log_auc;

proc means data=subjects alpha = 0.05 clm;
where gender = 'F';
var log_cpepAvgAUC0;
output out = log_auc lclm = lclm uclm = uclm;
class txgroup;

data log_auc;
set log_auc;
lclm = exp(lclm)-1;
uclm = exp(uclm)-1;

proc print data=log_auc;

proc means data=subjects;
where gender = 'M' ;
var log_cpepAvgAUC0;
class txgroup;
output out=log_auc mean = mean;
title3 'Supplementary Table 3 - Baseline C-Peptide AUC Male';

data log_auc;
set log_auc;
mean = exp(mean)-1;

proc print data=log_auc;

proc means data=subjects alpha = 0.05 clm;
where gender = 'M';
var log_cpepAvgAUC0;
output out = log_auc lclm = lclm uclm = uclm;
class txgroup;

data log_auc;
set log_auc;
lclm = exp(lclm)-1;
uclm = exp(uclm)-1;

proc print data=log_auc;

proc means data=subjects;
where DKA = 'Yes' ;
var log_cpepAvgAUC0;
class txgroup;
output out=log_auc mean = mean;
title3 'Supplementary Table 3 - Baseline C-Peptide AUC DKA=Yes';

```

```

data log_auc;
  set log_auc;
  mean = exp(mean)-1;

proc print data=log_auc;

proc means data=subjects alpha = 0.05 clm;
  where DKA = 'Yes';
  var log_cpepAvgAUC0;
  output out = log_auc lclm = lclm uclm = uclm;
  class txgroup;

data log_auc;
  set log_auc;
  lclm = exp(lclm)-1;
  uclm = exp(uclm)-1;

proc print data=log_auc;

proc means data=subjects;
  where DKA = 'No' ;
  var log_cpepAvgAUC0;
  class txgroup;
  output out=log_auc mean = mean;
  title3 'Supplementary Table 3 - Baseline C-Peptide AUC DKA=No';

data log_auc;
  set log_auc;
  mean = exp(mean)-1;

proc print data=log_auc;

proc means data=subjects alpha = 0.05 clm;
  where DKA = 'No';
  var log_cpepAvgAUC0;
  output out = log_auc lclm = lclm uclm = uclm;
  class txgroup;

data log_auc;
  set log_auc;
  lclm = exp(lclm)-1;
  uclm = exp(uclm)-1;

proc print data=log_auc;

proc means data=subjects;
  where alc0 <10 ;
  var log_cpepAvgAUC0;
  class txgroup;
  output out=log_auc mean = mean;
  title3 'Supplementary Table 3 - Baseline C-Peptide AUC HbA1c < 10%';

data log_auc;
  set log_auc;
  mean = exp(mean)-1;

```



```

proc print data=log_auc;

proc means data=subjects alpha = 0.05 clm;
  where alc0 < 10;
  var log_cpepAvgAUC0;
  output out = log_auc lclm = lclm uclm = uclm;
  class txgroup;

data log_auc;
  set log_auc;
  lclm = exp(lclm)-1;
  uclm = exp(uclm)-1;

proc print data=log_auc;

proc means data=subjects;
  where alc0 >= 10 ;
  var log_cpepAvgAUC0;
  class txgroup;
  output out=log_auc mean = mean;
  title3 'Supplementary Table 3 - Baseline C-Peptide AUC HbA1c >= 10%';

data log_auc;
  set log_auc;
  mean = exp(mean)-1;

proc print data=log_auc;

proc means data=subjects alpha = 0.05 clm;
  where alc0 >= 10;
  var log_cpepAvgAUC0;
  output out = log_auc lclm = lclm uclm = uclm;
  class txgroup;

data log_auc;
  set log_auc;
  lclm = exp(lclm)-1;
  uclm = exp(uclm)-1;

proc print data=log_auc;

proc means data=subjects_c_pep_90min;
  where lrn < 0.3 ;
  var log_cpepAvgAUC0;
  class txgroup;
  output out=log_auc mean = mean;
  title3 'Supplementary Table 3 - Baseline C-Peptide at 90 Min < 0.30';

data log_auc;
  set log_auc;
  mean = exp(mean)-1;

proc print data=log_auc;

proc means data=subjects_c_pep_90min alpha = 0.05 clm;

```

```

where lrn < 0.3;
var log_cpepAvgAUC0;
output out = log_auc lclm = lclm uclm = uclm;
class txgroup;

data log_auc;
set log_auc;
lclm = exp(lclm)-1;
uclm = exp(uclm)-1;

proc print data=log_auc;

proc means data=subjects_c_pep_90min;
where lrn >= 0.3 ;
var log_cpepAvgAUC0;
class txgroup;
output out=log_auc mean = mean;
title3 'Supplementary Table 3 - Baseline C-Peptide at 90 Min >= 0.30';

data log_auc;
set log_auc;
mean = exp(mean)-1;

proc print data=log_auc;

proc means data=subjects_c_pep_90min alpha = 0.05 clm;
where lrn >= 0.3;
var log_cpepAvgAUC0;
output out = log_auc lclm = lclm uclm = uclm;
class txgroup;

data log_auc;
set log_auc;
lclm = exp(lclm)-1;
uclm = exp(uclm)-1;

proc print data=log_auc;

proc means data=subjects;
var log_cpepAvgAUC12;
class txgroup;
output out=log_auc mean = mean;
title3 'Supplementary Table 3 - Overall Intent to Treat Analysis';

data log_auc;
set log_auc;
mean = exp(mean)-1;

proc print data=log_auc;

proc means data=subjects alpha = 0.05 clm;
var log_cpepAvgAUC12;
output out = log_auc lclm = lclm uclm = uclm;
class txgroup;

data log_auc;

```

```

    set log_auc;
    lclm = exp(lclm)-1;
    uclm = exp(uclm)-1;

proc print data=log_auc;

proc means data=subjects;
  where perprotflg = 1 ;
  var log_cpepAvgAUC12;
  class txgroup;
  output out=log_auc mean = mean;
  title3 'Supplementary Table 3 - Per Protocol Analysis';

data log_auc;
  set log_auc;
  mean = exp(mean)-1;

proc print data=log_auc;

proc means data=subjects alpha = 0.05 clm;
  where perprotflg = 1;
  var log_cpepAvgAUC12;
  output out = log_auc lclm = lclm uclm = uclm;
  class txgroup;

data log_auc;
  set log_auc;
  lclm = exp(lclm)-1;
  uclm = exp(uclm)-1;

proc print data=log_auc;

proc means data=subjects;
  where age < 12 ;
  var log_cpepAvgAUC12;
  class txgroup;
  output out=log_auc mean = mean;
  title3 'Supplementary Table 3 - 12 month C-Peptide AUC 7-<12 years';

data log_auc;
  set log_auc;
  mean = exp(mean)-1;

proc print data=log_auc;

proc means data=subjects alpha = 0.05 clm;
  where age < 12;
  var log_cpepAvgAUC12;
  output out = log_auc lclm = lclm uclm = uclm;
  class txgroup;

data log_auc;
  set log_auc;
  lclm = exp(lclm)-1;
  uclm = exp(uclm)-1;

```

```

proc print data=log_auc;

proc means data=subjects;
  where age >= 12 ;
  var log_cpepAvgAUC12;
  class txgroup;
  output out=log_auc mean = mean;
  title3 'Supplementary Table 3 - 12 month C-Peptide AUC >= 12 years';

data log_auc;
  set log_auc;
  mean = exp(mean)-1;

proc print data=log_auc;

proc means data=subjects alpha = 0.05 clm;
  where age >= 12;
  var log_cpepAvgAUC12;
  output out = log_auc lclm = lclm uclm = uclm;
  class txgroup;

data log_auc;
  set log_auc;
  lclm = exp(lclm)-1;
  uclm = exp(uclm)-1;

proc print data=log_auc;

proc means data=subjects;
  where gender = 'F' ;
  var log_cpepAvgAUC12;
  class txgroup;
  output out=log_auc mean = mean;
  title3 'Supplementary Table 3 - 12 month C-Peptide AUC Female';

data log_auc;
  set log_auc;
  mean = exp(mean)-1;

proc print data=log_auc;

proc means data=subjects alpha = 0.05 clm;
  where gender = 'F';
  var log_cpepAvgAUC12;
  output out = log_auc lclm = lclm uclm = uclm;
  class txgroup;

data log_auc;
  set log_auc;
  lclm = exp(lclm)-1;
  uclm = exp(uclm)-1;

proc print data=log_auc;

proc means data=subjects;

```

```

where gender = 'M' ;
var log_cpepAvgAUC12;
class txgroup;
output out=log_auc mean = mean;
title3 'Supplementary Table 3 - 12 month C-Peptide AUC Male';

data log_auc;
  set log_auc;
  mean = exp(mean)-1;

proc print data=log_auc;

proc means data=subjects alpha = 0.05 clm;
  where gender = 'M';
  var log_cpepAvgAUC12;
  output out = log_auc lclm = lclm uclm = uclm;
  class txgroup;

data log_auc;
  set log_auc;
  lclm = exp(lclm)-1;
  uclm = exp(uclm)-1;

proc print data=log_auc;

proc means data=subjects;
  where DKA = 'Yes' ;
  var log_cpepAvgAUC12;
  class txgroup;
  output out=log_auc mean = mean;
  title3 'Supplementary Table 3 - 12 month C-Peptide AUC DKA=Yes';

data log_auc;
  set log_auc;
  mean = exp(mean)-1;

proc print data=log_auc;

proc means data=subjects alpha = 0.05 clm;
  where DKA = 'Yes';
  var log_cpepAvgAUC12;
  output out = log_auc lclm = lclm uclm = uclm;
  class txgroup;

data log_auc;
  set log_auc;
  lclm = exp(lclm)-1;
  uclm = exp(uclm)-1;

proc print data=log_auc;

proc means data=subjects;
  where DKA = 'No' ;
  var log_cpepAvgAUC12;
  class txgroup;
  output out=log_auc mean = mean;

```

```

title3 'Supplementary Table 3 - 12 month C-Peptide AUC DKA=No';

data log_auc;
  set log_auc;
  mean = exp(mean)-1;

proc print data=log_auc;

proc means data=subjects alpha = 0.05 clm;
  where DKA = 'No';
  var log_cpepAvgAUC12;
  output out = log_auc lclm = lclm uclm = uclm;
  class txgroup;

data log_auc;
  set log_auc;
  lclm = exp(lclm)-1;
  uclm = exp(uclm)-1;

proc print data=log_auc;

proc means data=subjects;
  where alc0 <10 ;
  var log_cpepAvgAUC12;
  class txgroup;
  output out=log_auc mean = mean;
  title3 'Supplementary Table 3 - 12 month C-Peptide AUC HbA1c < 10%';

data log_auc;
  set log_auc;
  mean = exp(mean)-1;

proc print data=log_auc;

proc means data=subjects alpha = 0.05 clm;
  where alc0 < 10;
  var log_cpepAvgAUC12;
  output out = log_auc lclm = lclm uclm = uclm;
  class txgroup;

data log_auc;
  set log_auc;
  lclm = exp(lclm)-1;
  uclm = exp(uclm)-1;

proc print data=log_auc;

proc means data=subjects;
  where alc0 >= 10 ;
  var log_cpepAvgAUC12;
  class txgroup;
  output out=log_auc mean = mean;
  title3 'Supplementary Table 3 - 12 month C-Peptide AUC HbA1c >= 10%';

data log_auc;
  set log_auc;

```

```

mean = exp(mean)-1;
proc print data=log_auc;
proc means data=subjects alpha = 0.05 clm;
  where alc0 >= 10;
  var log_cpepAvgAUC12;
  output out = log_auc lclm = lclm uclm = uclm;
  class txgroup;
data log_auc;
  set log_auc;
  lclm = exp(lclm)-1;
  uclm = exp(uclm)-1;
proc print data=log_auc;
proc means data=subjects_c_pep_90min;
  where lrn < 0.3 ;
  var log_cpepAvgAUC12;
  class txgroup;
  output out=log_auc mean = mean;
  title3 'Supplementary Table 3 - 12 month C-Peptide at 90 Min < 0.30';
data log_auc;
  set log_auc;
  mean = exp(mean)-1;
proc print data=log_auc;
proc means data=subjects_c_pep_90min alpha = 0.05 clm;
  where lrn < 0.3;
  var log_cpepAvgAUC12;
  output out = log_auc lclm = lclm uclm = uclm;
  class txgroup;
data log_auc;
  set log_auc;
  lclm = exp(lclm)-1;
  uclm = exp(uclm)-1;
proc print data=log_auc;
proc means data=subjects_c_pep_90min;
  where lrn >= 0.3 ;
  var log_cpepAvgAUC12;
  class txgroup;
  output out=log_auc mean = mean;
  title3 'Supplementary Table 3 - 12 month C-Peptide at 90 Min >= 0.30';
data log_auc;
  set log_auc;
  mean = exp(mean)-1;
proc print data=log_auc;

```

```
proc means data=subjects_c_pep_90min alpha = 0.05 clm;
  where lrn >= 0.3;
  var log_cpepAvgAUC12;
  output out = log_auc lclm = lclm uclm = uclm;
  class txgroup;

data log_auc;
  set log_auc;
  lclm = exp(lclm)-1;
  uclm = exp(uclm)-1;

proc print data=log_auc;
```