

Dataset Integrity Check for Oral
Insulin for Prevention of Diabetes in
Relatives at Risk for Type 1 Diabetes
Mellitus (TN07)

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December 23, 2021

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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

The objective of the study was to determine whether oral insulin delays onset of type 1 diabetes in autoantibody-positive relatives of patients with type 1 diabetes. Between March 2, 2007, and December 21, 2015, relatives with at least 2 autoantibodies, including insulin autoantibodies and normal glucose tolerance, were enrolled in Canada, the United States, Australia, New Zealand, the United Kingdom, Italy, Sweden, Finland, and Germany. The main study group (n = 389) had first-phase insulin release on an intravenous glucose tolerance test that was higher than the threshold. The 55 patients in the secondary stratum 1 had an identical antibody profile as the main study group except they had first-phase insulin release that was lower than the threshold. Secondary strata 2 (n = 114) and strata 3 (n = 3) had different autoantibody profiles and first-phase insulin release threshold combinations. Follow-up continued through December 31, 2016.

3 Archived Datasets

All SAS data files, as provided by the Data Coordinating Center (DCC), are located in the TN07 folder in the data package. For this replication, variables were taken from the “tn07_treatmentstartdate.sas7bdat”, “mastable.sas7bdat”, “tn07_initialvisit.sas7bdat”, “rel.sas7bdat”, “tn07_researchlabs.sas7bdat”, and “hla” datasets.

4 Statistical Methods

Analyses were performed to replicate results for the data published by Krischer et al. [1] for the Effect of Oral Insulin on Prevention of Diabetes in Relatives of Patients With Type 1 Diabetes: A Randomized Clinical Trial. To verify the integrity of the dataset, descriptive statistics were computed.

5 Results

For Table 1 in the publication [1], Distribution of Participant Characteristics by Treatment Group and Strata, Table A lists the variables that were used in the replication, and Table B compares the results calculated from the archived data files to the results published in Table 1. The results of the replication are within expected variation to the published results for the variables able to be replicated. For example, the combination of family members and relatives by degree were not clearly delineated and not able to be replicated in this DSIC.

6 Conclusions

The NIDDK Central Repository is confident that the TN07 data files to be distributed are a true copy of the study data.

7 References

[1] Krischer JP, Schatz DA, Bundy B, Skyler JS, Greenbaum CJ. Effect of Oral Insulin on Prevention of Diabetes in Relatives of Patients With Type 1 Diabetes: A Randomized Clinical Trial. *JAMA*, 318(19), 1891-1902, November 2017. doi: <https://doi.org/10.1001/jama.2017.17070>

Table A: Variables used to replicate Table 1 – Distribution of Participant Characteristics by Treatment Group and Strata

Table Variable	dataset.variable
Age, median (IQR), y	tn07_treatmentstartdate.TreatmentDesc mastable.AgeReg mastable.Stratum2
Boys, No. (%)	tn07_treatmentstartdate.TreatmentDesc mastable.Sex mastable.Stratum2
Race/ethnicity, No. (%)	tn07_treatmentstartdate.TreatmentDesc mastable.race mastable.Stratum2
Non-Hispanic, No. (%)	tn07_treatmentstartdate.TreatmentDesc mastable.Ethnic mastable.Stratum2
BMI, median (IQR)	tn07_initialvisit.HeightinCM tn07_initialvisit.WeighinKg tn07_treatmentstartdate.TreatmentDesc mastable.Stratum2
Family members with type 1 diabetes, No. (%)	tn07_treatmentstartdate.TreatmentDesc rel.relation mastable.Stratum2
Hemoglobin A1c, median (IQR), %	tn07_treatmentstartdate.TreatmentDesc tn07_researchlabs.Test_Name tn07_researchlabs.Result mastable.Stratum2
C-peptide, median (IQR), mmol/L	tn07_treatmentstartdate.TreatmentDesc tn07_researchlabs.Test_Name tn07_researchlabs.Result mastable.Stratum2
Human leukocyte antigen alleles, No. (%)	tn07_treatmentstartdate.TreatmentDesc hla.dr3 hla.dr4 mastable.Stratum2

Table B1: Comparison of values computed in integrity check to reference article Table 1 values (Entire Cohort)

Variable	Oral Insulin Publication (n=283)	Oral Insulin DSIC (n=283)	Diff. (n=0)	Placebo Publication (n=277)	Placebo DSIC (n=277)	Diff. (n=0)
Age, median (IQR), y	8.2 (5.9-12.5)	8.0 (5.0-12.0)	0.2 (0.9-0.5)	8.2 (5.4-11.5)	8.0 (5.0-11.0)	0.2 (0.4-0.5)
Boys, No. (%)	170 (60.1)	170 (60.1)	0 (0)	170 (61.4)	170 (61.4)	0 (0)
Race/ethnicity No. (%)						
White	252 (95.5)	252 (95.5)	0 (0)	249 (94.3)	249 (94.3)	0 (0)
Black	8 (3.0)	8 (3.0)	0 (0)	9 (3.4)	9 (3.4)	0 (0)
Asian/Pacific Islander	4 (1.5)	4 (1.5)	0 (0)	6 (2.3)	6 (2.3)	0 (0)
Non-Hispanic No. (%)	256 (90.5)	256 (90.5)	0 (0)	252 (91.0)	252 (91.0)	0 (0)
BMI, median (IQR)	17.1 (15.3-19.5)	17.1 (15.3-19.7)	0 (0-0.2)	16.9 (15.5-19.2)	17.0 (15.6-19.3)	0.1 (0.1-0.1)
Family members with type 1 diabetes, No. (%)						
Sibling	153 (54.1)	161 (56.9)	8 (2.8)	162 (58.5)	174 (62.8)	12 (4.3)
Identical Twin	6 (2.1)	6 (2.1)	0 (0)	3 (1.1)	3 (1.1)	0 (0)
Offspring	3 (1.1)	6 (2.1)	3 (1.0)	7 (2.5)	7 (2.5)	0 (0)
Parent	71 (25.1)	82 (29.0)	11 (3.9)	57 (20.6)	71 (25.6)	14 (5.0)
Parent and Sibling	10 (3.5)	-	-	13 (4.7)	-	-
Offspring and another first-degree relative	2 (0.7)	-	-	0 (0)	-	-
Second-degree relative	33 (11.7)	-	-	30 (10.8)	-	-
Third-degree or further removed relative	5 (1.8)	-	-	5 (1.8)	-	-
Hemoglobin A, median (IQR)	5.0 (4.8-5.2)	5.1 (4.9-5.3)	0.1 (0.1-0.1)	5.1 (4.8-5.2)	5.1 (4.9-5.3)	0 (0.1-0.1)
C-peptide, median (IQR), mmol/L	1.35 (1.00-1.81)	1.46 (1.06-1.99)	0.11 (0.06-0.18)	1.34 (1.03-1.82)	1.32 (0.99-1.87)	0.02 (0.04-0.05)
Human leukocyte antigen alleles, No. (%)						
DR3	119 (42.2)	119 (42.2)	0 (0)	102 (37.0)	102 (37.0)	0 (0)
DR4	199 (70.6)	199 (70.6)	0 (0)	182 (65.9)	182 (65.9)	0 (0)

Table B2: Comparison of values computed in integrity check to reference article Table 1 values (Primary Stratum)

Variable	Oral Insulin Publication (n=203)	Oral Insulin DSIC (n=202)	Diff. (n=1)	Placebo Publication (n=186)	Placebo DSIC (n=189)	Diff. (n=3)
Age, median (IQR), y	8.6 (6.1-12.8)	8.0 (6.0-12.0)	0.6 (0.1-0.8)	8.2 (5.5-11.8)	8.0 (5.0-11.0)	0.2 (0.5-0.8)
Boys, No. (%)	128 (63.1)	126 (62.4)	2 (0.7)	117 (62.9)	118 (62.4)	1 (0.5)
Race/ethnicity No. (%)						
White	181 (95.3)	180 (95.2)	1 (0.1)	172 (94.5)	175 (94.6)	3 (0.1)
Black	6 (3.2)	6 (3.2)	0 (0)	4 (2.2)	4 (2.2)	0 (0)
Asian/Pacific Islander	3 (1.6)	3 (1.6)	0 (0)	6 (3.3)	6 (3.3)	0 (0)
Non-Hispanic No. (%)	182 (89.7)	181 (89.6)	1 (0.1)	171 (91.9)	173 (91.5)	2 (0.4)
BMI, median (IQR)	17.4 (15.5-20.0)	17.3 (15.5-20.1)	0.1 (0-0.1)	17.1 (15.6-19.6)	17.1 (15.6-19.6)	0 (0-0)
Family members with type 1 diabetes, No. (%)						
Sibling	110 (54.2)	119 (58.9)	9 (4.7)	111 (59.7)	118 (62.4)	7 (2.7)
Identical Twin	3 (1.5)	3 (1.1)	0 (0.4)	2 (1.1)	2 (0.8)	0 (0.3)
Offspring	2 (1.0)	4 (1.5)	2 (0.5)	5 (2.7)	5 (2.0)	0 (0.7)
Parent	45 (22.2)	54 (19.8)	9 (2.4)	40 (21.5)	48 (19.4)	8 (2.1)
Parent and Sibling	9 (4.4)	-	-	6 (3.2)	-	-
Offspring and another first-degree relative	2 (1.0)	-	-	0 (0)	-	-
Second-degree relative	27 (13.3)	-	-	18 (9.7)	-	-
Third-degree or further removed relative	5 (2.5)	-	-	4 (2.2)	-	-
Hemoglobin A, median (IQR)	5.0 (4.8-5.2)	5.1 (4.9-5.3)	0.1 (0.1-0.1)	5.1 (4.8-5.2)	5.1 (4.9-5.3)	0 (0.1-0.1)
C-peptide, median (IQR), mmol/L	1.42 (1.04-1.91)	3.87 (1.98-6.12)	2.45 (0.94-4.21)	1.34 (1.04-1.96)	3.73 (1.80-5.85)	2.39 (0.76-3.89)
Human leukocyte antigen alleles, No. (%)						
DR3	88 (43.3)	88 (43.6)	0 (0.3)	74 (39.8)	77 (40.7)	3 (0.9)
DR4	144 (70.9)	143 (70.8)	1 (0.1)	135 (72.6)	137 (72.5)	2 (0.1)

Table B3: Comparison of values computed in integrity check to reference article Table 1 values (Secondary Stratum 1)

Variable	Oral Insulin Publication (n=28)	Oral Insulin DSIC (n=30)	Diff. (n=2)	Placebo Publication (n=27)	Placebo DSIC (n=26)	Diff. (n=1)
Age, median (IQR), y	9.1 (5.9-13.7)	8.5 (6.0-14.0)	0.6 (0.1-0.3)	8.5 (6.5-10.8)	8.0 (6.0-10.0)	0.5 (0.5-0.8)
Boys, No. (%)	19 (67.9)	21 (70.0)	2 (2.1)	19 (70.4)	18 (69.2)	1 (1.2)
Race/ethnicity No. (%)						
White	25 (96.2)	27 (96.4)	2 (0.2)	25 (100.0)	24 (100.0)	1 (0)
Black	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Asian/Pacific Islander	1 (3.8)	1 (3.6)	0 (0.2)	0 (0)	0 (0)	0 (0)
Non-Hispanic No. (%)	26 (92.9)	28 (93.3)	2 (0.4)	26 (96.3)	25 (96.1)	1 (0.2)
BMI, median (IQR)	16.2 (15-18.1)	16.0 (14.7-18.1)	0.2 (0.3-0)	16.9 (15.5-17.8)	16.9 (15.6-17.7)	0 (0.1-0.1)
Family members with type 1 diabetes, No. (%)						
Sibling	15 (53.6)	16 (53.3)	1 (0.3)	19 (70.4)	21 (80.8)	2 (10.4)
Identical Twin	2 (7.1)	2 (6.7)	0 (0.4)	1 (3.7)	1 (3.8)	0 (0.1)
Offspring	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Parent	7 (25.0)	9 (30.0)	2 (5.0)	3 (11.1)	6 (23.1)	3 (12)
Parent and Sibling	1 (3.6)	-	-	3 (11.1)	-	-
Offspring and another first-degree relative	0 (0)	-	-	0 (0)	-	-
Second-degree relative	3 (10.7)	-	-	1 (3.7)	-	-
Third-degree or further removed relative	0 (0)	-	-	0 (0)	-	-
Hemoglobin A, median (IQR)	5.1 (4.9-5.3)	5.3 (5.0-5.4)	0.2 (0.1-0.1)	5.2 (5.0-5.5)	5.3 (5.1-5.6)	0.1 (0.1-0.1)
C-peptide, median (IQR), mmol/L	1.02 (0.93-1.3)	2.46 (1.3-4.2)	1.44 (0.37-2.9)	1.1 (0.76-1.52)	2.65 (1.2-4.3)	1.55 (0.44-2.78)
Human leukocyte antigen alleles, No. (%)						
DR3	9 (32.1)	10 (33.3)	1 (1.2)	9 (33.3)	9 (34.6)	0 (1.3)
DR4	22 (78.6)	23 (76.7)	1 (1.9)	18 (66.7)	17 (65.4)	1 (1.3)

Table B4: Comparison of values computed in integrity check to reference article Table 1 values (Secondary Strata 2 and 3)

Variable	Oral Insulin Publication (n=52)	Oral Insulin DSIC (n=51)	Diff. (n=1)	Placebo Publication (n=64)	Placebo DSIC (n=62)	Diff. (n=2)
Age, median (IQR), y	7.3 (5.1-10.3)	7.0 (4.0-10.0)	0.3 (1.1-0.3)	8.3 (5.1-11.5)	8.0 (5.0-11.0)	0.3 (0.1-0.5)
Boys, No. (%)	23 (44.2)	23 (45.1)	0 (0.9)	34 (53.1)	34 (54.8)	0 (1.7)
Race/ethnicity No. (%)						
White	46 (95.8)	45 (95.7)	1 (0.1)	52 (91.2)	50 (90.9)	2 (0.3)
Black	2 (4.2)	2 (4.3)	0 (0.1)	5 (8.8)	5 (9.1)	0 (0.3)
Asian/Pacific Islander	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Non-Hispanic No. (%)	48 (92.3)	47 (92.2)	1 (0.1)	55 (85.9)	54 (87.1)	1 (1.2)
BMI, median (IQR)	16.4 (15.0-18.4)	16.6 (15.3-18.9)	0.2 (0.3-0.5)	16.8 (15.3-19.2)	16.9 (15.5-19.3)	0.1 (0.2-0.1)
Family members with type 1 diabetes, No. (%)						
Sibling	28 (53.8)	26 (50.9)	2 (2.9)	32 (50.0)	35 (56.5)	3 (6.5)
Identical Twin	1 (1.9)	1 (2.0)	0 (0.1)	0 (0)	0 (0)	0 (0)
Offspring	1 (1.9)	1 (2.0)	0 (0.1)	2 (3.1)	2 (3.2)	0 (0.1)
Parent	19 (36.5)	19 (37.3)	0 (0.8)	14 (21.9)	17 (27.4)	3 (5.5)
Parent and Sibling	0 (0)	-	-	4 (6.2)	-	-
Offspring and another first-degree relative	0 (0)	-	-	0 (0)	-	-
Second-degree relative	3 (5.8)	-	-	11 (17.2)	-	-
Third-degree relative or further removed relative	0 (0)	-	-	1 (1.6)	-	-
Hemoglobin A, median (IQR)	5.0 (4.9-5.2)	5.1 (4.9-5.3)	0.1 (0-0.1)	5.0 (4.9-5.1)	5.1 (4.9-5.3)	0.1 (0-0.2)
C-peptide, median (IQR), mmol/L	1.36 (1.06-1.75)	3.6 (1.7-6.1)	2.24 (0.64-4.35)	1.43 (1.11-1.8)	3.8 (1.7-5.9)	2.37 (0.59-4.1)
Human leukocyte antigen alleles, No. (%)						
DR3	22 (43.1)	21 (42.0)	1 (1.1)	19 (30.2)	16 (26.2)	3 (4.0)
DR4	33 (64.7)	33 (66.0)	0 (1.3)	29 (46.0)	28 (45.9)	1 (0.1)

Attachment A: SAS Code

```
libname dsic "X:\NIDDK\niddk-dr_studies6\TrialNet_07\private_created_data\Redacted Datasets";  
libname v1 "X:\NIDDK\niddk-dr_studies6\TrialNet_07\private_created_data\TN07_V1\Data";
```

```
/*  
/* TN07 - DSIC Krischer et al. */  
*/
```

```
/* Datasets */
```

```
*Treatment Startdate;  
data trtstart; set dsic.tn07_treatmentstartdate;  
run;
```

```
proc contents data=trtstart;  
run;
```

```
*Mastable;  
data mastable; set v1.mastable;  
run;
```

```
*Merge mastable and treatment start date datasets;  
proc sort data=trtstart;  
by MaskID;  
run;
```

```
proc sort data=mastable;  
by maskid;  
run;
```

```
data trt1;  
merge  
trtstart (in=a)  
mastable (in=b);  
by maskid;  
if b=1 and a=1;  
run;
```

```
data labs; set dsic.tn07_researchlabs;  
run;
```

```
data diabetes; set dsic.tn07_diabetesonset;  
run;
```

```
data hla; set v1.hla;  
run;
```

```

/*****/
/* Total Cohort */
/*****/

proc freq data=trtstart;
tables TreatmentDesc ; *Treatment assignment, either "active" or "placebo";
run;

*Age;
proc sort data=trt1;
by TreatmentDesc;
run;

proc means data=trt1 median q1 q3;
var agereg;
by TreatmentDesc;
run;

*Boys;
proc freq data=trt1;
tables sex*TreatmentDesc/norow nopercnt missing;
run;

*Race/ethnicity;
proc freq data=trt1;
tables race*TreatmentDesc/norow nopercnt missing;
where race = "White" or Race = "Black" or Race = "Asian" or Race = "Pacific Is";
run;

*Non-hispanic;
proc freq data=trt1;
tables ethnic*TreatmentDesc/norow nopercnt missing;
run;

*BMI;
data initial; set dsic.tn07_initialvisit;
run;

proc sort data=initial;
by maskid;
run;

proc sort data=trt1;
by MaskID;
run;

data trt2;

```

```

merge
initial (in=a)
trt1 ( in=b);
by maskid;
if b=1;
run;

*calculate BMI;
data trt2_1; set trt2;

heightinM = HeightinCM/100;

run;

data trt2_2; set trt2_1;
heightsq = heightinM**2;
run;

data trt2_3; set trt2_2;

BMI = weighinKg/heightsq;
run;

proc sort data=trt2_3;
by TreatmentDesc;
run;

proc means data=trt2_3 median q1 q3;
var bmi;
by TreatmentDesc;
run;

*Family members with type 1 diabetes;
data rel; set v1.rel;
run;

proc sort data=rel;
by maskid;
run;

proc sort data=trt1 nodup;
by maskid;

*Brother/Sister;
data trt3;
merge
rel (in=a)
trt1 (in=b);

```

```

by maskid;
if b=1;
if relation = "FS=Brother/Sister";
run;

proc sort data=trt3 nodupkey;
by maskid;
run;

proc freq data=trt3;
tables relation*TreatmentDesc/norow nopercnt;
run;

*Twins;
data trt4;
merge
rel (in=a)
trt1 (in=b);
by maskid;
if b=1;
run;

proc freq data=trt4;
tables relation*TreatmentDesc/norow nopercnt;
run;

*HbA1c;
proc contents data=labs;
run;

proc freq data=labs;
tables Test_Name;
run;

proc sort data=labs;
by MaskID;
run;

data labs1;
merge
trt1 (in=a)
labs (in=b);
by maskid;
if a=1;
run;

data labs2; set labs1;
where Test_Name = "HbA1c";

```

```

run;

proc freq data=labs2;
tables Result;
run;

data labs3; set labs2;
result_n = input(result, 8.);
run;

proc sort data=labs3;
by TreatmentDesc;
run;

proc means data=labs3 median q1 q3;
var result_n;
by TreatmentDesc;
run;

*C-peptide;
proc freq data=labs;
tables Test_Name;
run;

*subsetting dataset;
data cpep; set labs1;
where Test_Name = "PEP-10" OR Test_Name = "PEP0" OR Test_Name = "PEP120"
OR Test_Name = "PEP30" OR Test_Name = "PEP60" OR Test_Name = "PEP90";
run;

data cpep1; set cpep;

results_n = input(result, 8.);
run;

proc sort data=cpep1;
by TreatmentDesc;
run;

proc means data=cpep1 median q1 q3;
var results_n;
by TreatmentDesc;
where Test_Name = "PEP0" OR Test_Name = "PEP-10";
run;

*Human Leukocyte antigen alleles;
proc sort data=hla;
by maskid;

```

```

run;

proc sort data=trt1;
by maskid;
run;

data hla1;
merge
trt1 (in=a)
hla (in=b);
by maskid;
if a=1;
run;

proc freq data=hla1;
tables (dr3 dr4)*TreatmentDesc/norow nopercnt;
run;

/*****
/* Primary Stratum */
*****/
proc sort data=trt1;
by stratum2;
run;

proc freq data=trt1;
tables stratum2*TreatmentDesc;
run;

*Age;
proc sort data=trt1;
by TreatmentDesc;
run;

proc means data=trt1 median q1 q3;
var agereg;
by TreatmentDesc;
where stratum2 = "Primary";
run;

*Boys;
proc freq data=trt1;
tables sex*TreatmentDesc/norow nopercnt;
where stratum2 = "Primary";
run;

*Race;
data race; set trt1;

```

```

where stratum2 = "Primary";
run;

proc freq data=race;
tables race*TreatmentDesc/norow nopercnt missing;
where race = "White" or Race = "Black" or Race = "Asian" or Race = "Pacific Is";
run;

*Ethnicity;
proc freq data=race;
tables ethnic*TreatmentDesc/norow nopercnt;
run;

*BMI;
proc sort data=trt2_3;
by TreatmentDesc;
run;

proc means data=trt2_3 median q1 q3;
var bmi;
by TreatmentDesc;
where stratum2 = "Primary";
run;

*Family members with type 1 diabetes;
data rel; set v1.rel;
run;

proc sort data=rel;
by maskid;
run;

proc sort data=trt1 nodup;
by maskid;

*Brother/Sister;
data trt3;
merge
rel (in=a)
trt1 (in=b);
by maskid;
if b=1;
if relation = "FS=Brother/Sister";
run;

proc sort data=trt3 nodupkey;
by maskid;
run;

```



```

proc freq data=trt3;
tables relation*TreatmentDesc/norow nopercnt;
where stratum2 = "Primary";
run;

*Twins;
data trt4;
merge
rel (in=a)
trt1 (in=b);
by maskid;
if b=1;
run;

proc freq data=trt4;
tables relation*TreatmentDesc/norow nopercnt;
where stratum2 = "Primary";
run;

*HbA1c;
proc means data=labs3 median q1 q3;
var result_n;
by TreatmentDesc;
where stratum2 = "Primary";
run;

*c-peptide;
proc means data=cpep1 median q1 q3;
var results_n;
by TreatmentDesc;
where Test_Name = "PEP0" OR Test_Name = "PEP-10";
where stratum2 = "Primary";
run;

*HLA;
proc freq data=hla1;
tables (dr3 dr4)*TreatmentDesc/norow nopercnt;
where stratum2 = "Primary";
run;

/*****/
/* Secondary Stratum 1 */
/*****/

proc sort data=trt1;
by stratum2;
run;

```

```
proc freq data=trt1;
tables stratum2*TreatmentDesc;
run;
```

```
*Age;
proc sort data=trt1;
by TreatmentDesc;
run;
```

```
proc means data=trt1 median q1 q3;
var agereg;
by TreatmentDesc;
where stratum2 = "Secondary 1";
run;
```

```
*Boys;
proc freq data=trt1;
tables sex*TreatmentDesc/norow nopercnt;
where stratum2 = "Secondary 1";
run;
```

```
*Race;
data race; set trt1;
where stratum2 = "Secondary 1";
run;
```

```
proc freq data=race;
tables race*TreatmentDesc/norow nopercnt missing;
where race = "White" or Race = "Black" or Race = "Asian" or Race = "Pacific Is";
run;
```

```
*Ethnicity;
proc freq data=race;
tables ethnic*TreatmentDesc/norow nopercnt;
run;
```

```
*BMI;
proc sort data=trt2_3;
by TreatmentDesc;
run;
```

```
proc means data=trt2_3 median q1 q3;
var bmi;
by TreatmentDesc;
where stratum2 = "Secondary 1";
run;
```

```

*Family members with type 1 diabetes;
data rel; set v1.rel;
run;

proc sort data=rel;
by maskid;
run;

proc sort data=trt1 nodup;
by maskid;

*Brother/Sister;
data trt3;
merge
rel (in=a)
trt1 (in=b);
by maskid;
if b=1;
if relation = "FS=Brother/Sister";
run;

proc sort data=trt3 nodupkey;
by maskid;
run;

proc freq data=trt3;
tables relation*TreatmentDesc/norow nopercnt;
where stratum2 = "Secondary 1";
run;

*Twins;
data trt4;
merge
rel (in=a)
trt1 (in=b);
by maskid;
if b=1;
run;

proc freq data=trt4;
tables relation*TreatmentDesc/norow nopercnt;
where stratum2 = "Secondary 1";
run;

*HbA1c;
proc means data=labs3 median q1 q3;
var result_n;
by TreatmentDesc;

```

```

where stratum2 = "Secondary 1";
run;

*c-peptide;
proc means data=cpep1 median q1 q3;
var results_n;
by TreatmentDesc;
where Test_Name = "PEP0" OR Test_Name = "PEP-10";
where stratum2 = "Secondary 1";
run;

*HLA;
proc freq data=hla1;
tables (dr3 dr4)*TreatmentDesc/norow nopercnt;
where stratum2 = "Secondary 1";
run;

/*****/
/* Secondary Stratum 2 and 3 */
/*****/

proc sort data=trt1;
by stratum2;
run;

proc freq data=trt1;
tables stratum2*TreatmentDesc;
run;

*Age;
proc sort data=trt1;
by TreatmentDesc;
run;

proc means data=trt1 median q1 q3;
var agereg;
by TreatmentDesc;
where stratum2 = "Secondary 2" OR stratum2 = "Secondary 3";
run;

*Boys;
proc freq data=trt1;
tables sex*TreatmentDesc/norow nopercnt;
where stratum2 = "Secondary 2" OR stratum2 = "Secondary 3";
run;

*Race;
data race; set trt1;

```

```

where stratum2 = "Secondary 2" OR stratum2 = "Secondary 3";
run;

proc freq data=race;
tables race*TreatmentDesc/norow nopercnt missing;
where race = "White" or Race = "Black" or Race = "Asian" or Race = "Pacific Is";
run;

*Ethnicity;
proc freq data=race;
tables ethnic*TreatmentDesc/norow nopercnt;
run;

*BMI;
proc sort data=trt2_3;
by TreatmentDesc;
run;

proc means data=trt2_3 median q1 q3;
var bmi;
by TreatmentDesc;
where stratum2 = "Secondary 2" OR stratum2 = "Secondary 3";
run;

*Family members with type 1 diabetes;
data rel; set v1.rel;
run;

proc sort data=rel;
by maskid;
run;

proc sort data=trt1 nodup;
by maskid;

*Brother/Sister;
data trt3;
merge
rel (in=a)
trt1 (in=b);
by maskid;
if b=1;
if relation = "FS=Brother/Sister";
run;

proc sort data=trt3 nodupkey;
by maskid;
run;

```

```
proc freq data=trt3;
tables relation*TreatmentDesc/norow nopercnt;
where stratum2 = "Secondary 2" OR stratum2 = "Secondary 3";
run;
```

```
*Twins;
data trt4;
merge
rel (in=a)
trt1 (in=b);
by maskid;
if b=1;
run;
```

```
proc freq data=trt4;
tables relation*TreatmentDesc/norow nopercnt;
where stratum2 = "Secondary 2" OR stratum2 = "Secondary 3";
run;
```

```
*HbA1c;
proc means data=labs3 median q1 q3;
var result_n;
by TreatmentDesc;
where stratum2 = "Secondary 2" OR stratum2 = "Secondary 3";
run;
```

```
*c-peptide;
proc means data=cpep1 median q1 q3;
var results_n;
by TreatmentDesc;
where Test_Name = "PEP0" OR Test_Name = "PEP-10";
where stratum2 = "Secondary 2" OR stratum2 = "Secondary 3";
run;
```

```
*HLA;
proc freq data=hla1;
tables (dr3 dr4)*TreatmentDesc/norow nopercnt;
where stratum2 = "Secondary 2" OR stratum2 = "Secondary 3";
run;
```