

Dataset Integrity Check for The Environmental Determinants of Diabetes in the Young (TEDDY) M221 Krischer

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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 TEDDY study was designed to follow children with and without a family history of type 1 diabetes (T1D) to understand the environmental factors that contribute to the disease. Newborn children younger than 4 months were screened for high-risk HLA alleles, and those with qualifying haplotypes were eligible for follow-up. Information is collected on medical information (infections, medication, immunizations), exposure to dietary and other environmental factors, negative life events, family history, tap water, and measurements of psychological stress. Biospecimens, including blood, stool, urine, and nail clippings, are taken at baseline and follow-up study visits. The primary outcome measures include two endpoints—the first appearance of one or more islet cell autoantibodies (GADA, IAA, or IA-2A), confirmed at two consecutive visits, and development of T1D. The cohort will be followed for 15 years, or until the occurrence of one of the primary endpoints.

The M221 study sought to assess the predictive power of TEDDY-identified risk factors for islet autoimmunity (IA), the type of autoantibody appearing first, and T1D.

3 Archived Datasets

All data files, as provided by the Data Coordinating Center (DCC), are located in the TEDDY M221 folder in the data package. For this replication, variables were taken from the “m_221_krischer_niddk_31jul2017_1.sas7bdat” and “m_221_krischer_niddk_31jul2017_2.sas7bdat” datasets.

4 Statistical Methods

Analyses were performed to replicate results for the data in the publication by Krischer et al. [1]. To verify the integrity of the data, only descriptive statistics were computed.

5 Results

For Table 1 in the publication [1], Characteristics of the TEDDY study population, Table A lists the variables that were used in the replication, and Tables B1-B3 compare the results calculated from the archived data files to the results in Table 1. The results of the replication are an exact match to the published results.

6 Conclusions

The NIDDK Central Repository is confident that the TEDDY M221 data files to be distributed are a true copy of the study data.

7 References

[1] Krischer JP, Liu X, Vehik K, Akolkar B, Hagopian WA, Rewers MJ, She JX, Toppari J, Ziegler AG, Lernmark Å. Predicting Islet Cell Autoimmunity and Type 1 Diabetes: An 8-Year TEDDY Study Progress Report. *Diabetes Care*, 42(6), 1051-1060, June 2019. doi: <https://doi.org/10.2337/dc18-2282>

Table A: Variables used to replicate Table 1 – Characteristics of the TEDDY study population

Table Variable	dataset.variable
Country	m_221_krischer_niddk_31jul2017_1.country m_221_krischer_niddk_31jul2017_2.country
Family history	m_221_krischer_niddk_31jul2017_1.family m_221_krischer_niddk_31jul2017_2.family
Sex	m_221_krischer_niddk_31jul2017_1.female m_221_krischer_niddk_31jul2017_2.female
HLA genotype	m_221_krischer_niddk_31jul2017_1.hla_5grps m_221_krischer_niddk_31jul2017_2.hla_5grps
Probiotics introduction age	m_221_krischer_niddk_31jul2017_1.prob_expose
Weight z-score at 12 months	m_221_krischer_niddk_31jul2017_1.wtz_12m
First infant formula type during the first 7 days of life	m_221_krischer_niddk_31jul2017_1.formula_cat_1w
First infant formula type during the first 3 months of life	m_221_krischer_niddk_31jul2017_1.formula_cat_3mo
Age at multiple persistent confirmed autoantibodies	m_221_krischer_niddk_31jul2017_2.age_mab_mos
Type of first autoantibody	m_221_krischer_niddk_31jul2017_1.first_autoantibody m_221_krischer_niddk_31jul2017_2.first_autoantibody
rs1004446 (INS)	m_221_krischer_niddk_31jul2017_1.rs1004446_A
rs10517086	m_221_krischer_niddk_31jul2017_1.rs10517086_A
rs1534422	m_221_krischer_niddk_31jul2017_2.rs1534422_G
rs2327832 (TNFAIP3)	m_221_krischer_niddk_31jul2017_2.rs2327832_G
rs1143678 (ITGAM)	m_221_krischer_niddk_31jul2017_1.rs1143678_A
rs12708716 (CLEC16A)	m_221_krischer_niddk_31jul2017_1.rs12708716_G
rs2292239 (ERBB3)	m_221_krischer_niddk_31jul2017_1.rs2292239_A
rs2476601 (PTPN22)	m_221_krischer_niddk_31jul2017_1.rs2476601_A
rs2816316 (RGS1)	m_221_krischer_niddk_31jul2017_1.rs2816316_C
rs3184504 (SH2B3)	m_221_krischer_niddk_31jul2017_1.rs3184504_A
rs4597342 (ITGAM)	m_221_krischer_niddk_31jul2017_1.rs4597342_A
rs4948088 (COBL)	m_221_krischer_niddk_31jul2017_1.rs4948088_A

Table B1: Comparison of values computed in integrity check to reference article Table 1 (IA negative and Any IA)

Characteristics	Pub: IA negative (n=7041)	DSIC: IA negative (n=7041)	Diff. (n=0)	Pub: Any IA (n=736)	DSIC: Any IA (n=736)	Diff. (n=0)
Country						
U.S.	2972 (42.2)	2972 (42.2)	0 (0)	246 (33.4)	246 (33.4)	0 (0)
Finland	1525 (21.7)	1525 (21.7)	0 (0)	187 (25.4)	187 (25.4)	0 (0)
Germany	475 (6.7)	475 (6.7)	0 (0)	53 (7.2)	53 (7.2)	0 (0)
Sweden	2069 (29.4)	2069 (29.4)	0 (0)	250 (34.0)	250 (34.0)	0 (0)
Family history						
FDR: Mother	284 (4.0)	284 (4.0)	0 (0)	35 (4.8)	35 (4.8)	0 (0)
FDR: Father	346 (4.9)	346 (4.9)	0 (0)	74 (10.1)	74 (10.1)	0 (0)
FDR: Sibling	103 (1.5)	103 (1.5)	0 (0)	33 (4.5)	33 (4.5)	0 (0)
GP	6308 (89.6)	6308 (89.6)	0 (0)	594 (80.7)	594 (80.7)	0 (0)
Sex						
Male	3562 (50.6)	3562 (50.6)	0 (0)	404 (54.9)	404 (54.9)	0 (0)
Female	3479 (49.4)	3479 (49.4)	0 (0)	332 (45.1)	332 (45.1)	0 (0)
HLA genotype						
DR3/4	2668 (37.9)	2668 (37.9)	0 (0)	362 (49.2)	362 (49.2)	0 (0)
DR4/4	1396 (19.8)	1396 (19.8)	0 (0)	139 (18.9)	139 (18.9)	0 (0)
DR4/8	1226 (17.4)	1226 (17.4)	0 (0)	113 (15.4)	113 (15.4)	0 (0)
DR3/3	1523 (21.6)	1523 (21.6)	0 (0)	96 (13.0)	96 (13.0)	0 (0)
FDR specific	228 (3.2)	228 (3.2)	0 (0)	26 (3.5)	26 (3.5)	0 (0)
Probiotics introduction age						
≥ 28 days	6522 (92.6)	6522 (92.6)	0 (0)	694 (94.3)	694 (94.3)	0 (0)
< 28 days	519 (7.4)	519 (7.4)	0 (0)	42 (5.7)	42 (5.7)	0 (0)
Weight z-score at 12 months, mean (SD)	-0.132 (1.022)	-0.132 (1.022)	0 (0)	-0.008 (1.033)	-0.008 (1.033)	0 (0)
First infant formula type during the first 7 days of life						
No formula no cow's milk	4442 (63.1)	4442 (63.1)	0 (0)	473 (64.3)	473 (64.3)	0 (0)
No formula only cow's milk	1 (0.0)	1 (0.0)	0 (0)	0 (0.0)	0 (0.0)	0 (0)
Nonhydrolyzed formula	2237 (31.8)	2237 (31.8)	0 (0)	211 (28.7)	211 (28.7)	0 (0)
Partially hydrolyzed formula	89 (1.3)	89 (1.3)	0 (0)	10 (1.4)	10 (1.4)	0 (0)
Extensively hydrolyzed formula	169 (2.4)	169 (2.4)	0 (0)	32 (4.3)	32 (4.3)	0 (0)
Other formula	103 (1.5)	103 (1.5)	0 (0)	10 (1.4)	10 (1.4)	0 (0)

Characteristics	Pub: IA negative (n=7041)	DSIC: IA negative (n=7041)	Diff. (n=0)	Pub: Any IA (n=736)	DSIC: Any IA (n=736)	Diff. (n=0)
First infant formula type during the first 3 months of life						
No formula no cow's milk	1880 (26.7)	1880 (26.7)	0 (0)	213 (28.9)	213 (28.9)	0 (0)
No formula only cow's milk	17 (0.2)	17 (0.2)	0 (0)	5 (0.7)	5 (0.7)	0 (0)
Nonhydrolyzed formula	4523 (64.2)	4523 (64.2)	0 (0)	450 (61.1)	450 (61.1)	0 (0)
Partially hydrolyzed formula	220 (3.1)	220 (3.1)	0 (0)	18 (2.4)	18 (2.4)	0 (0)
Extensively hydrolyzed formula	218 (3.1)	218 (3.1)	0 (0)	36 (4.9)	36 (4.9)	0 (0)
Other formula	183 (2.6)	183 (2.6)	0 (0)	14 (1.9)	14 (1.9)	0 (0)
rs1004446 (INS)						
GG	2771 (39.4)	2771 (39.4)	0 (0)	332 (45.1)	332 (45.1)	0 (0)
AG	3287 (46.7)	3287 (46.7)	0 (0)	331 (45.0)	331 (45.0)	0 (0)
AA	983 (14.0)	983 (14.0)	0 (0)	73 (9.9)	73 (9.9)	0 (0)
rs10517086						
GG	3612 (51.3)	3612 (51.3)	0 (0)	363 (49.3)	363 (49.3)	0 (0)
AG	2878 (40.9)	2878 (40.9)	0 (0)	308 (41.8)	308 (41.8)	0 (0)
AA	551 (7.8)	551 (7.8)	0 (0)	65 (8.8)	65 (8.8)	0 (0)
rs1143678 (ITGAM)						
CC	5162 (73.3)	5162 (73.3)	0 (0)	545 (74.0)	545 (74.0)	0 (0)
CT	1708 (24.3)	1708 (24.3)	0 (0)	174 (23.6)	174 (23.6)	0 (0)
TT	171 (2.4)	171 (2.4)	0 (0)	17 (2.3)	17 (2.3)	0 (0)
rs12708716 (CLEC16A)						
AA	3086 (43.9)	3086 (43.9)	0 (0)	352 (47.9)	352 (47.9)	0 (0)
AG	3100 (44.1)	3100 (44.1)	0 (0)	322 (43.8)	322 (43.8)	0 (0)
GG	837 (11.9)	837 (11.9)	0 (0)	61 (8.3)	61 (8.3)	0 (0)
rs2292239 (ERBB3)						
GG	3266 (46.4)	3266 (46.4)	0 (0)	291 (39.5)	291 (39.5)	0 (0)
TG	3070 (43.6)	3070 (43.6)	0 (0)	359 (48.8)	359 (48.8)	0 (0)
TT	704 (10.0)	704 (10.0)	0 (0)	86 (11.7)	86 (11.7)	0 (0)
rs2476601 (PTPN22)						
GG	5665 (80.5)	5665 (80.5)	0 (0)	518 (70.4)	518 (70.4)	0 (0)
AG	1292 (18.3)	1292 (18.3)	0 (0)	205 (27.9)	205 (27.9)	0 (0)
AA	84 (1.2)	84 (1.2)	0 (0)	13 (1.8)	13 (1.8)	0 (0)

Characteristics	Pub: IA negative (n=7041)	DSIC: IA negative (n=7041)	Diff. (n=0)	Pub: Any IA (n=736)	DSIC: Any IA (n=736)	Diff. (n=0)
rs2816316 (RGS1)						
AA	4693 (66.7)	4693 (66.7)	0 (0)	485 (65.9)	485 (65.9)	0 (0)
AC	2111 (30.0)	2111 (30.0)	0 (0)	223 (30.3)	223 (30.3)	0 (0)
CC	237 (3.4)	237 (3.4)	0 (0)	28 (3.8)	28 (3.8)	0 (0)
rs3184504 (SH2B3)						
CC	2224 (31.6)	2224 (31.6)	0 (0)	175 (23.8)	175 (23.8)	0 (0)
CT	3446 (48.9)	3446 (48.9)	0 (0)	365 (49.6)	365 (49.6)	0 (0)
TT	1371 (19.5)	1371 (19.5)	0 (0)	196 (26.6)	196 (26.6)	0 (0)
rs4597342 (ITGAM)						
CC	3135 (44.5)	3135 (44.5)	0 (0)	311 (42.3)	311 (42.3)	0 (0)
CT	3091 (43.9)	3091 (43.9)	0 (0)	341 (46.3)	341 (46.3)	0 (0)
TT	812 (11.5)	812 (11.5)	0 (0)	84 (11.4)	84 (11.4)	0 (0)
rs4948088 (COBL)						
CC	6401 (90.9)	6401 (90.9)	0 (0)	689 (93.6)	689 (93.6)	0 (0)
AC	619 (8.8)	619 (8.8)	0 (0)	45 (6.1)	45 (6.1)	0 (0)
AA	21 (0.3)	21 (0.3)	0 (0)	2 (0.3)	2 (0.3)	0 (0)

Table B2: Comparison of values computed in integrity check to reference article Table 1 (IAA-first and GADA-first)

Characteristics	Pub: IAA-first (n=281)	DSIC: IAA-first (n=281)	Diff. (n=0)	Pub: GADA-first (n=316)	DSIC: GADA-first (n=316)	Diff. (n=0)
Country						
U.S.	83 (29.5)	83 (29.5)	0 (0)	123 (38.9)	123 (38.9)	0 (0)
Finland	92 (32.7)	92 (32.7)	0 (0)	62 (19.6)	62 (19.6)	0 (0)
Germany	20 (7.1)	20 (7.1)	0 (0)	14 (4.4)	14 (4.4)	0 (0)
Sweden	86 (30.6)	86 (30.6)	0 (0)	117 (37.0)	117 (37.0)	0 (0)
Family history						
FDR: Mother	11 (3.9)	11 (3.9)	0 (0)	14 (4.4)	14 (4.4)	0 (0)
FDR: Father	29 (10.3)	29 (10.3)	0 (0)	32 (10.1)	32 (10.1)	0 (0)
FDR: Sibling	20 (7.1)	20 (7.1)	0 (0)	7 (2.2)	7 (2.2)	0 (0)
GP	221 (78.6)	221 (78.6)	0 (0)	263 (83.2)	263 (83.2)	0 (0)
Sex						
Male	160 (56.9)	160 (56.9)	0 (0)	167 (52.8)	167 (52.8)	0 (0)
Female	121 (43.1)	121 (43.1)	0 (0)	149 (47.2)	149 (47.2)	0 (0)
HLA genotype						
DR3/4	137 (48.8)	137 (48.8)	0 (0)	155 (49.1)	155 (49.1)	0 (0)
DR4/4	51 (18.1)	51 (18.1)	0 (0)	52 (16.5)	52 (16.5)	0 (0)
DR4/8	59 (21.0)	59 (21.0)	0 (0)	38 (12.0)	38 (12.0)	0 (0)
DR3/3	21 (7.5)	21 (7.5)	0 (0)	68 (21.5)	68 (21.5)	0 (0)
FDR specific	13 (4.6)	13 (4.6)	0 (0)	3 (0.9)	3 (0.9)	0 (0)
Probiotics introduction age						
≥ 28 days	267 (95.0)	267 (95.0)	0 (0)	300 (94.9)	300 (94.9)	0 (0)
< 28 days	14 (5.0)	14 (5.0)	0 (0)	16 (5.1)	16 (5.1)	0 (0)
Weight z-score at 12 months, mean (SD)	-0.033 (1.055)	-0.033 (1.055)	0 (0)	0.045 (1.038)	0.045 (1.038)	0 (0)
First infant formula type during the first 7 days of life						
No formula, no cow's milk	177 (63.0)	177 (63.0)	0 (0)	205 (64.9)	205 (64.9)	0 (0)
No formula, only cow's milk	0 (0.0)	0 (0.0)	0 (0)	0 (0.0)	0 (0.0)	0 (0)
Nonhydrolyzed formula	79 (28.1)	79 (28.1)	0 (0)	94 (29.7)	94 (29.7)	0 (0)
Partially hydrolyzed formula	3 (1.1)	3 (1.1)	0 (0)	4 (1.3)	4 (1.3)	0 (0)
Extensively hydrolyzed formula	16 (5.7)	16 (5.7)	0 (0)	11 (3.5)	11 (3.5)	0 (0)
Other formula	6 (2.1)	6 (2.1)	0 (0)	2 (0.6)	2 (0.6)	0 (0)

Characteristics	Pub: IAA-first (n=281)	DSIC: IAA-first (n=281)	Diff. (n=0)	Pub: GADA-first (n=316)	DSIC: GADA-first (n=316)	Diff. (n=0)
First infant formula type during the first 3 months of life						
No formula, no cow's milk	87 (31.0)	87 (31.0)	0 (0)	88 (27.8)	88 (27.8)	0 (0)
No formula, only cow's milk	0 (0.0)	0 (0.0)	0 (0)	3 (0.9)	3 (0.9)	0 (0)
Nonhydrolyzed formula	163 (58.0)	163 (58.0)	0 (0)	202 (63.9)	202 (63.9)	0 (0)
Partially hydrolyzed formula	6 (2.1)	6 (2.1)	0 (0)	7 (2.2)	7 (2.2)	0 (0)
Extensively hydrolyzed formula	17 (6.0)	17 (6.0)	0 (0)	12 (3.8)	12 (3.8)	0 (0)
Other formula	8 (2.8)	8 (2.8)	0 (0)	4 (1.3)	4 (1.3)	0 (0)
rs1004446 (INS)						
GG	135 (48.0)	135 (48.0)	0 (0)	130 (41.1)	130 (41.1)	0 (0)
AG	118 (42.0)	118 (42.0)	0 (0)	152 (48.1)	152 (48.1)	0 (0)
AA	28 (10.0)	28 (10.0)	0 (0)	34 (10.8)	34 (10.8)	0 (0)
rs10517086						
GG	137 (48.8)	137 (48.8)	0 (0)	164 (51.9)	164 (51.9)	0 (0)
AG	114 (40.6)	114 (40.6)	0 (0)	128 (40.5)	128 (40.5)	0 (0)
AA	30 (10.7)	30 (10.7)	0 (0)	24 (7.6)	24 (7.6)	0 (0)
rs1143678 (ITGAM)						
CC	206 (73.3)	206 (73.3)	0 (0)	234 (74.1)	234 (74.1)	0 (0)
CT	69 (24.6)	69 (24.6)	0 (0)	72 (22.8)	72 (22.8)	0 (0)
TT	6 (2.1)	6 (2.1)	0 (0)	10 (3.2)	10 (3.2)	0 (0)
rs12708716 (CLEC16A)						
AA	125 (44.5)	125 (44.5)	0 (0)	157 (49.8)	157 (49.8)	0 (0)
AG	130 (46.3)	130 (46.3)	0 (0)	136 (43.2)	136 (43.2)	0 (0)
GG	26 (9.3)	26 (9.3)	0 (0)	22 (7.0)	22 (7.0)	0 (0)
rs2292239 (ERBB3)						
GG	112 (39.9)	112 (39.9)	0 (0)	125 (39.6)	125 (39.6)	0 (0)
TG	141 (50.2)	141 (50.2)	0 (0)	152 (48.1)	152 (48.1)	0 (0)
TT	28 (10.0)	28 (10.0)	0 (0)	39 (12.3)	39 (12.3)	0 (0)
rs2476601 (PTPN22)						
GG	194 (69.0)	194 (69.0)	0 (0)	225 (71.2)	225 (71.2)	0 (0)
AG	79 (28.1)	79 (28.1)	0 (0)	87 (27.5)	87 (27.5)	0 (0)
AA	8 (2.8)	8 (2.8)	0 (0)	4 (1.3)	4 (1.3)	0 (0)

Characteristics	Pub: IAA-first (n=281)	DSIC: IAA-first (n=281)	Diff. (n=0)	Pub: GADA-first (n=316)	DSIC: GADA-first (n=316)	Diff. (n=0)
rs2816316 (RGS1)						
AA	188 (66.9)	188 (66.9)	0 (0)	210 (66.5)	210 (66.5)	0 (0)
AC	81 (28.8)	81 (28.8)	0 (0)	95 (30.1)	95 (30.1)	0 (0)
CC	12 (4.3)	12 (4.3)	0 (0)	11 (3.5)	11 (3.5)	0 (0)
rs3184504 (SH2B3)						
CC	71 (25.3)	71 (25.3)	0 (0)	70 (22.2)	70 (22.2)	0 (0)
CT	133 (47.3)	133 (47.3)	0 (0)	158 (50.0)	158 (50.0)	0 (0)
TT	77 (27.4)	77 (27.4)	0 (0)	88 (27.8)	88 (27.8)	0 (0)
rs4597342 (ITGAM)						
CC	132 (47.0)	132 (47.0)	0 (0)	128 (40.5)	128 (40.5)	0 (0)
CT	116 (41.3)	116 (41.3)	0 (0)	153 (48.4)	153 (48.4)	0 (0)
TT	33 (11.7)	33 (11.7)	0 (0)	35 (11.1)	35 (11.1)	0 (0)
rs4948088 (COBL)						
CC	265 (94.3)	265 (94.3)	0 (0)	293 (92.7)	293 (92.7)	0 (0)
AC	16 (5.7)	16 (5.7)	0 (0)	22 (7.0)	22 (7.0)	0 (0)
AA	0 (0.0)	0 (0.0)	0 (0)	1 (0.3)	1 (0.3)	0 (0)

Table B3: Comparison of values computed in integrity check to reference article Table 1 (Multiple IAs without Progression to T1D and Multiple IAs with Progression to T1D)

Characteristics	Pub: Multiple IAs without Progression to T1D (n=215)	DSIC: Multiple IAs without Progression to T1D (n=215)	Diff. (n=0)	Pub: Multiple IAs with Progression to T1D (n=219)	DSIC: Multiple IAs with Progression to T1D (n=219)	Diff. (n=0)
Country						
U.S.	80 (37.2)	80 (37.2)	0 (0)	65 (29.7)	65 (29.7)	0 (0)
Finland	47 (21.9)	47 (21.9)	0 (0)	67 (30.6)	67 (30.6)	0 (0)
Germany	16 (7.4)	16 (7.4)	0 (0)	21 (9.6)	21 (9.6)	0 (0)
Sweden	72 (33.5)	72 (33.5)	0 (0)	66 (30.1)	66 (30.1)	0 (0)
Family history						
FDR: Mother	13 (6.0)	13 (6.0)	0 (0)	12 (5.5)	12 (5.5)	0 (0)
FDR: Father	26 (12.1)	26 (12.1)	0 (0)	30 (13.7)	30 (13.7)	0 (0)
FDR: Sibling	10 (4.7)	10 (4.7)	0 (0)	14 (6.4)	14 (6.4)	0 (0)
GP	166 (77.2)	166 (77.2)	0 (0)	163 (74.4)	163 (74.4)	0 (0)
Sex						
Male	136 (63.3)	136 (63.3)	0 (0)	109 (49.8)	109 (49.8)	0 (0)
Female	79 (36.7)	79 (36.7)	0 (0)	110 (50.2)	110 (50.2)	0 (0)
HLA genotype						
DR3/4	116 (54.0)	116 (54.0)	0 (0)	123 (56.2)	123 (56.2)	0 (0)
DR4/4	49 (22.8)	49 (22.8)	0 (0)	37 (16.9)	37 (16.9)	0 (0)
DR4/8	27 (12.6)	27 (12.6)	0 (0)	30 (13.7)	30 (13.7)	0 (0)
DR3/3	15 (7.0)	15 (7.0)	0 (0)	17 (7.8)	17 (7.8)	0 (0)
FDR specific	8 (3.7)	8 (3.7)	0 (0)	12 (5.5)	12 (5.5)	0 (0)
Age at multiple persistent confirmed autoantibodies (months), mean (SD)	60.4 (31.5)	60.4 (21.5)	0 (0)	30.2 (21.3)	30.2 (21.3)	0 (0)
Type of first autoantibody						
GADA only	87 (40.5)	87 (40.5)	0 (0)	53 (24.2)	53 (24.2)	0 (0)
IAA only	80 (37.2)	80 (37.2)	0 (0)	85 (38.8)	85 (38.8)	0 (0)
IA-2A only	3 (1.4)	3 (1.4)	0 (0)	4 (1.8)	4 (1.8)	0 (0)
Two or more autoantibodies	45 (20.9)	45 (20.9)	0 (0)	77 (35.2)	77 (35.2)	0 (0)

Characteristics	Pub: Multiple IAs without Progression to T1D (n=215)	DSIC: Multiple IAs without Progression to T1D (n=215)	Diff. (n=0)	Pub: Multiple IAs with Progression to T1D (n=219)	DSIC: Multiple IAs with Progression to T1D (n=219)	Diff. (n=0)
rs1004446 (INS)						
GG	100 (46.5)	100 (46.5)	0 (0)	110 (50.2)	110 (50.2)	0 (0)
AG	95 (44.2)	95 (44.2)	0 (0)	88 (40.2)	88 (40.2)	0 (0)
AA	20 (9.3)	20 (9.3)	0 (0)	21 (9.6)	21 (9.6)	0 (0)
rs10517086						
GG	101 (47.0)	101 (47.0)	0 (0)	97 (44.3)	97 (44.3)	0 (0)
AG	96 (44.7)	96 (44.7)	0 (0)	99 (45.2)	99 (45.2)	0 (0)
AA	18 (8.4)	18 (8.4)	0 (0)	23 (10.5)	23 (10.5)	0 (0)
rs1534422						
AA	76 (35.3)	76 (35.3)	0 (0)	50 (22.8)	50 (22.8)	0 (0)
AG	106 (49.3)	106 (49.3)	0 (0)	115 (52.5)	115 (52.5)	0 (0)
GG	33 (15.3)	33 (15.3)	0 (0)	54 (24.7)	54 (24.7)	0 (0)
rs2327832 (TNFAIP3)						
AA	144 (67.0)	144 (67.0)	0 (0)	134 (61.2)	134 (61.2)	0 (0)
AG	66 (30.7)	66 (30.7)	0 (0)	70 (32.0)	70 (32.0)	0 (0)
GG	5 (2.3)	5 (2.3)	0 (0)	15 (6.8)	15 (6.8)	0 (0)

Attachment A: SAS Code

```
libname m221 "X:\NIDDK\niddk-dr_studies6\TEDDY\private_created_data\M221";
```

```
/******  
/* TEDDY M221 DSIC */  
/******
```

```
proc contents data=m221.m_221_krischer_niddk_31jul2017_1;  
run;
```

```
proc contents data=m221.m_221_krischer_niddk_31jul2017_2;  
run;
```

```
*Table B1;
```

```
proc freq data=m221.m_221_krischer_niddk_31jul2017_1;  
tables (country family female hla_5grps prob_expose_bf4wk formula_cat_1w formula_cat_3mo  
rs1004446_A rs10517086_A  
rs1143678_A rs12708716_G rs2292239_A rs2476601_A rs2816316_C rs3184504_A rs4597342_A  
rs4948088_A)*ia/norow nopercnt;  
run;
```

```
proc means data=m221.m_221_krischer_niddk_31jul2017_1 n mean std;  
var wtz_12m;  
class ia;  
run;
```

```
*Table B2;
```

```
proc freq data=m221.m_221_krischer_niddk_31jul2017_1;  
tables (country family female hla_5grps prob_expose_bf4wk formula_cat_1w formula_cat_3mo  
rs1004446_A rs10517086_A  
rs1143678_A rs12708716_G rs2292239_A rs2476601_A rs2816316_C rs3184504_A rs4597342_A  
rs4948088_A)*first_autoantibody/norow nopercnt;  
where first_autoantibody = 1 OR first_autoantibody = 2;  
run;
```

```
proc means data=m221.m_221_krischer_niddk_31jul2017_1 n mean std;  
var wtz_12m;  
class first_autoantibody;  
where first_autoantibody = 1 OR first_autoantibody = 2;  
run;
```

```
*Table B3;
```

```
proc freq data=m221.m_221_krischer_niddk_31jul2017_2;  
tables (country family female hla_5grps first_autoantibody rs1004446_A rs10517086_A rs1534422_G  
rs2327832_G)*T1D/norow nopercnt;  
run;
```

```
proc means data=m221.m_221_krischer_niddk_31jul2017_2 n mean std;  
var age_mab_mos;  
class T1d;  
run;
```