Dataset Integrity Check for the Restoring Insulin Secretion – Pediatric BetaFat Study (RISE BetaFat)

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Contents

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

BetaFat, a component of the Restoring Insulin Secretion (RISE) Consortium, was a two-arm, unblinded clinical trial. Study participants were recruited at the University of Southern California and randomized into two intervention groups. One group received gastric banding surgery and the other group was treated with metformin. Patients underwent assessments at baseline and at predetermined intervals during the 24-month study period. Beta-cell function, insulin sensitivity, and blood glucose levels were regularly evaluated during the study period. Participants were also monitored for adverse effects to the interventions.

3 Archived Datasets

All data files, as provided by the Data Coordinating Center (DCC), are located in the RISE BetaFat study data package. For this replication, variables were taken from the derived datasets: risebetafat_basedata.sas7bdat, betafat_otherlabdata.sas7bdat, risebetafat_vitalsigndata.sas7bdat, betafat_clampdata.sas7bdat, betafat_ogttdata.sas7bdat, and betafat_screendata.sas7bdat.

4 Statistical Methods

Analyses were performed to duplicate results for the data published by Anny Xiang [1] in *Diabetes Care* in 2018. To verify the integrity of the datasets, descriptive statistics were computed.

5 Results

For Table 1 in the publication [1], Table 1 – Demographic, physical, and metabolic characteristics of study participants at baseline for all randomized participants and for participants who completed 24-month testing, Table A lists the variables that were used in the replication and Tables B-1 to B-4 compare the results calculated from the archived data file to the results published in Table 1.

6 Conclusions

The results of the replication are within expected variation to the published results. Only the race stratification for "White" was provided and could be verified.

7 References

[1] Anny Xiang. "Impact of Gastric Banding Versus Metformin on b-Cell Function in Adults With Impaired Glucose Tolerance or Mild Type 2 Diabetes" *Diabetes Care* 2018 Dec; 41(12): 2544-2551. https://doi.org/10.2337/dc18-1662.

Table A: Variables used to replicate Table 1 – Demographic, physical, and metabolic characteristics of study participants at baseline for all randomized participants and for participants who completed 24-month testing

Characteristic	dataset.variable
Weight (kg)	risebetafat_vitalsigndata.weight
Height	risebetafat_vitalsigndata.height
HbA1c (mol/mmol)	betafat_otherlabdata.hba1c
Fasting glucose (mmol/L)	betafat_ogttdata.GLUC_05
2-h glucose (mmol/L)	betafat_ogttdata.gluc120
Sex	risebetafat_basedata.sex
Race	risebetafat_basedata.race
Glucose status	betafat_screendata.diabetes
Treatment Group	risebetafat_basedata.treatment

Table B-1: Comparison of values computed in integrity check to reference article Table 1 values. Randomized Cohort (N, %)

		Randomized											
		Gastric band						**metformin alone**					
		N=44	**40**	**4**	**%**			**N=44**	**37**	**7**	**%**		
		Manuscript	**DSIC**	**Diff**	**Manuscript**	**DSIC**	**Diff**	**Manuscript**	**DSIC**	**Diff**	**Manuscript**	**DSIC**	**Diff**
Sex	**Women**	34	31	3.0	77	77.5	-0.5	35	30	5	79	81.1	-2.1
Race/ethnicity	**White**	15	15	0.0	34	37.5	-3.5	10	10	0	23	27	-4
	Black	7	N/A	N/A	16	N/A	N/A	9	N/A	N/A	20	N/A	N/A
	Hispanic (any)	19	N/A	N/A	43	N/A	N/A	21	N/A	N/A	48	N/A	N/A
	Asian	3	N/A	N/A	7	N/A	N/A	4	N/A	N/A	9	N/A	N/A
Glucose status	**IGT**	25	23	2.0	57	57.5	-0.5	26	23	3	59	62.2	-3.2
	Diabetes	19	17	2.0	43	42.5	0.5	18	14	4	41	37.8	3.2

Table B-2: Comparison of values computed in integrity check to reference article Table 1 values. Completed 24 months testing Cohort (N, %)

		Completed 24 months testing											
		Gastric band						**metformin alone**					
		N=36	**33**	**3**	**%**			**N=34**	**28**	**6**	**%**		
		Manuscript	**DSIC**	**Diff**	**Manuscript**	**DSIC**	**Diff**	**Manuscript**	**DSIC**	**Diff**	**Manuscript**	**DSIC**	**Diff**
Sex	**Women**	29	27	2	81	81.8	-0.8	27	23	4	79	82.1	-3.1
Race/ethnicity	**White**	9	9	0	25	27.3	-2.3	9	9	0	26	32.1	-6.1
	Black	7	N/A	N/A	20	N/A	N/A	7	N/A	N/A	21	N/A	N/A
	Hispanic (any)	17	N/A	N/A	47	N/A	N/A	16	N/A	N/A	47	N/A	N/A
	All other	3	N/A	N/A	8	N/A	N/A	2	N/A	N/A	6	N/A	N/A
Glucose status	**IGT**	18	17	1	50	51.5	-1.5	20	18	2	59	64.3	-5.3
	Diabetes	18	16	2	50	48.5	1.5	14	10	4	42	35.7	6.3

Table B-3: Comparison of values computed in integrity check to reference article Table 1 values. Randomized Cohort (Mean, SD)

		Randomized											
		Gastric band						metformin alone					
		Mean			SD			Mean			SD		
		Manuscript	DSIC	Diff	Manuscript	DSIC	Diff	Manuscript	DSIC	Diff	Manuscript	DSIC	Diff
	Weight (kg)	97.5	96.55	0.95	12.2	11.12	1.08	96.1	96.55	-0.45	10.9	11.12	-0.22
	BMI (kg/m2)	35.7	35.16	0.54	2.9	3	-0.10	35	35.16	-0.16	2.9	3	-0.1
Glucose status	Fasting glucose (mmol/L)	6.2	6.12	0.08	0.7	0.73	-0.03	6.2	6.12	0.08	0.8	0.73	0.07
	2-h glucose (mmol/L)	10.4	10.55	-0.15	2.7	2.53	0.17	10.5	10.55	-0.05	2.6	2.53	0.07
	HbA1c (mol/mmol)	41.2	40.22	0.98	4.6	4.49	0.11	40.1	40.22	-0.12	4.5	4.49	0.01

Table B-4: Comparison of values computed in integrity check to reference article Table 1 values. Metformin Alone Cohort (Mean, SD)

		Completed 24 months testing											
		Gastric band						metformin alone					
		Mean			SD			Mean			SD		
		Manuscript	DSIC	Diff	Manuscript	DSIC	Diff	Manuscript	DSIC	Diff	Manuscript	DSIC	Diff
	Weight (kg)	97	97.84	-0.84	12.2	11.83	0.37	95.9	95.65	0.25	10.5	11.43	-0.93
	BMI (kg/m2)	35.7	35.72	-0.02	2.9	3.23	-0.33	34.8	34.9	-0.1	2.8	3.04	-0.24
Glucose status	**Fasting glucose (mmol/L)**	6.2	6.17	0.03	0.8	0.8	0	6.2	6.07	0.13	0.9	0.8	0.1
	2-h glucose (mmol/L)	10.6	10.4	0.2	2.7	2.82	-0.12	10.5	10.51	-0.01	2.5	2.45	0.05
	HbA1c (mol/mmol)	41.5	41.15	0.35	4.5	4.66	-0.16	40.8	40.99	-0.19	4.6	4.6	0

Attachment A: SAS Code

```
options nocenter validvarname=upcase fmtsearch=(formats) nofmterr;

title '/prj/niddk/ims_analysis/RISE/prog_initial_analysis/RISE_BetaFat/RISE.BetaFat.dsic.sas';
run;

* Peds primary outcome.pdf ;

**********;
* INPUT   ;
**********;
libname orig   '/prj/niddk/ims_analysis/RISE/private_orig_data/betafat_lab_and_base/';
libname orig2 '/prj/niddk/ims_analysis/RISE/private_orig_data/betafat_lab_and_base/10_30_20/';
libname orig3 '/prj/niddk/ims_analysis/RISE/private_orig_data/betafat_lab_and_base/12_29_20/';

/*
libname fmts '/prj/niddk/ims_analysis/LOGIC/private_created_data/';

PROC FORMAT CNTLIN = fmts.algsformats;

  */


***********;
* MACROS    ;
***********;
%macro readin(lib, ds);
  data &ds;
    set &lib..&ds;
  run;

  proc contents data=&ds;
  title3 "&ds";
  run;
%mend;


* produce n and %;
%macro npercent(rownum, ds, var, varf, subset, subsetname);
  proc freq data=analy&ds noprint;
    where &subset = 1;
    tables &var/list missing out=tbl1&subsetname;
  run;

  data tbl1&subsetname;
    length covar covarf $100;
    set tbl1&subsetname;
```

```
    covar = "&var";
    covarf = put(&var,&varf..);
    rownum = &rownum;
  run;

  data prnt&subsetname;
    set prnt&subsetname tbl1&subsetname;
  run;

%mend;


%macro univ(rownum, ds, var, subset, subsetname);

  proc univariate data=analy&ds outtable= univ&subsetname noprint;
    where &subset=1;
    var &var
       ;
  run;

  data univ&subsetname;
    length covarf $100 _var_ $25;
    set univ&subsetname;
        covarf = "&subset";
        rownum = &rownum;
  run;

  data prntuniv&subsetname;
    set prntuniv&subsetname univ&subsetname;
  run;

%mend;



*************;
* FORMATS    ;
*************;
proc format;
  value novalue
      . = "No Value"
  other = "   Value"
  ;

  value racegf
  1='White'
  2='Other'
  ;
```

```
  value sexf
  1='Male'
  2='Female'
  ;

  value ynf
    1 = 'yes'
  .,2 = 'no'
  ;

run;


%readin(orig, betafat_basedata);
%readin(orig3, risebetafat_basedata);

proc compare base=betafat_basedata compare=risebetafat_basedata listvar;
run;


%readin(orig, betafat_clampdata);
%readin(orig, betafat_ogttdata);
%readin(orig, betafat_otherlabdata);
%readin(orig2, betafat_screendata);
%readin(orig3, risebetafat_vitalsigndata);

proc freq data=betafat_basedata;
  tables treatment/missing list;
  title3 "prelim freqs";
  run;

proc freq data=betafat_OTHERLABDATA;
  tables visit/missing;
run;

proc freq data=risebetafat_vitalsigndata;
  tables visit weight*height/missing list;
  format weight height novalue.;
run;

proc freq data=betafat_screendata;
  tables visit diabetes/missing;
run;


* combine;

* completed 24-month testing;
proc sort data=risebetafat_vitalsigndata out=subset_m24;
```

```
  where visit="M24";
  by RISE_REPOSITORY_ID;
run;

proc sort data=risebetafat_basedata;
  by RISE_REPOSITORY_ID;
run;

proc sort data=betafat_OTHERLABDATA;
  where visit="BAS";
  by RISE_REPOSITORY_ID;
run;

proc sort data=risebetafat_vitalsigndata;
  where visit="BAS";
  by RISE_REPOSITORY_ID;
run;

proc sort data=betafat_clampdata;
  where visit="BAS";
  by RISE_REPOSITORY_ID;
run;

proc sort data=betafat_ogttdata;
  where visit="BAS";
  by RISE_REPOSITORY_ID;
run;

proc sort data=betafat_screendata;
  by RISE_REPOSITORY_ID;
run;



data analyrand;
  merge risebetafat_basedata   (in=in1 keep=rise_repository_id treatment agegroup race sex)
        betafat_otherlabdata   (in=in2 keep=rise_repository_id hba1c  )
        risebetafat_vitalsigndata(in=in3 keep=rise_repository_id weight height)
       betafat_clampdata        (in=in5 keep=rise_repository_id GLUC_05
                                        rename=(GLUC_05=clamp_GLUC_05))
       betafat_ogttdata        (in=in7 keep=rise_repository_id GLUC_05 CPEP_05 gluc120)
       betafat_screendata      (in=in8 keep=rise_repository_id diabetes gluc000s gluc120s)
       subset_m24               (in=in9 keep=rise_repository_id)
       ;
  by rise_repository_id;

  if in9 then subset_m24=1;

  if treatment = 'LapBand'    then do;
```

```
    treat_grp1 = 1;
    if subset_m24=1 then treat_grp1b=1;
  end;
  if treatment = 'METFORMIN'  then do;
    treat_grp2 = 1;
    if subset_m24=1 then treat_grp2b=1;
  end;

  * Conversions provided by Sharon in email 10/6/20:                ;

  *  Glucose: multiply by 0.0555                      ;
  GLUC_05mod = GLUC_05*0.0555;
  gluc120mod = gluc120*0.0555;

  clamp_GLUC_05mod = clamp_GLUC_05*0.0555;

  *  C-peptide: divide by 3.003003                    ;
  CPEP_05_nmol_l = CPEP_05/3.003003                   ;

  *  HbA1c: Multiply by 10.93 and then subtract 23.5  ;
  HbA1c_mol_mmol = HbA1c*10.93-23.5;

  * calculate BMI (kg/m2);
  height_m = height/100;
  bmi = weight/(height_m**2);


run;

proc freq data=analyrand;
  tables subset_m24*treat_grp1*treat_grp2/list missing;
run;


proc freq data=analyrand;
  where treat_grp1=1;
  tables sex race diabetes/missing;
run;


* Cohort: Gastric band;

* med, q1, q3;
data prntunivg_m;
 * length _VAR_ $100;
  set _null_;
run;

* Age continuous is NOT provided, skip   ;
```

```
%univ(8    , rand, Weight          , treat_grp1 , G_M);
%univ(8    , rand, bmi             , treat_grp1 , G_M);
*%univ(12   , rand, clamp_GLUC_05mod, treat_grp1 , G_M);  * Hyperglycemic clamp: Fasting glucose (mmol/L)  ;
%univ(12   , rand, GLUC_05mod      , treat_grp1 , G_M);  * OGTT: Fasting glucose (mmol/L)  ;
%univ(15   , rand, gluc120mod      , treat_grp1 , G_M);  * OGTT: 2-h glucose (mmol/L)        ;
%univ(10   , rand, HbA1c_mol_mmol  , treat_grp1 , G_M);

data prntunivg_m;
  set prntunivg_m;
   _median_  = round(_median_ , 0.1);
   _q1_      = round(_q1_     , 0.1);
   _q3_      = round(_q3_     , 0.1);
   _mean_    = round(_mean_   , 0.01);
   _std_     = round(_std_    , 0.01);
run;

proc print data=prntunivg_m;
 var rownum _var_ covarf _nobs_/* _median_ _q1_ _q3_ _min_ _max_*/ _mean_ _std_;
 title3 "Cohort: Gastric band (all randomized participants)";
run;


data prntg_m;
 * length _VAR_ $100;
  set _null_;
run;

%npercent(1, rand, Sex          , SEXF   , treat_grp1, g_m);
%npercent(3, rand, Race         , RACEgF , treat_grp1, g_m);   * ??;
%npercent(4, rand, diabetes     , ynf    , treat_grp1, g_m); * IGT/Diabetes ;

data prntg_m;
  set prntg_m;
  percent = round(percent,0.1);
run;

proc sort data=prntg_m;
  by rownum covarf;
  run;

proc print data=prntg_m;
  var rownum covar covarf count percent;
run;



* Cohort: Metformin;
```

```
* med, q1, q3;
data prntuniv_m;
 * length _VAR_ $100;
  set _null_;
run;

* Age continuous is NOT provided, skip   ;
%univ(8    , rand, Weight          , treat_grp2 , _M);
%univ(8    , rand, bmi             , treat_grp2 , _M);
*%univ(12   , rand, clamp_GLUC_05mod, treat_grp2 , _M);  * Hyperglycemic clamp: Fasting glucose (mmol/L)  ;
%univ(12   , rand, GLUC_05mod      , treat_grp2 , _M);  * OGTT: Fasting glucose (mmol/L)  ;
%univ(15   , rand, gluc120mod      , treat_grp2 , _M);  * OGTT: 2-h glucose (mmol/L)         ;
%univ(10   , rand, HbA1c_mol_mmol  , treat_grp2 , _M);

data prntuniv_m;
  set prntuniv_m;
   _median_  = round(_median_ , 0.1);
   _q1_      = round(_q1_     , 0.1);
   _q3_      = round(_q3_     , 0.1);
   _mean_    = round(_mean_   , 0.01);
   _std_     = round(_std_    , 0.01);
run;

proc print data=prntuniv_m;
 var rownum _var_ covarf _nobs_/* _median_ _q1_ _q3_ _min_ _max_*/ _mean_ _std_;
 title3 "Cohort: Metformin (all randomized participants)";
run;


data prnt_m;
 * length _VAR_ $100;
  set _null_;
run;

%npercent(1, rand, Sex          , SEXF   , treat_grp2, _m);
%npercent(3, rand, Race         , RACEgF , treat_grp2, _m);   * ??;
%npercent(4, rand, diabetes     , ynf    , treat_grp2, _m); * IGT/Diabetes ;

data prnt_m;
  set prnt_m;
  percent = round(percent,0.1);
run;

proc sort data=prnt_m;
  by rownum covarf;
  run;

proc print data=prnt_m;
  var rownum covar covarf count percent;
```

```
run;


********** completed 24-month testing *********************************;

* Cohort: Gastric band;

* med, q1, q3;
data prntunivg_m24;
 * length _VAR_ $100;
  set _null_;
run;

* Age continuous is NOT provided, skip   ;
%univ(8    , rand, Weight          , treat_grp1b , G_M24);
%univ(8    , rand, bmi             , treat_grp1b , G_M24);
*%univ(12   , rand, clamp_GLUC_05mod, treat_grp1b , G_M);  * Hyperglycemic clamp: Fasting glucose (mmol/L)  ;
%univ(12   , rand, GLUC_05mod      , treat_grp1b , G_M24);  * OGTT: Fasting glucose (mmol/L)  ;
%univ(15   , rand, gluc120mod      , treat_grp1b , G_M24);  * OGTT: 2-h glucose (mmol/L)     ;
%univ(10   , rand, HbA1c_mol_mmol  , treat_grp1b , G_M24);

data prntunivg_m24;
  set prntunivg_m24;
   _median_  = round(_median_ , 0.1);
   _q1_      = round(_q1_     , 0.1);
   _q3_      = round(_q3_     , 0.1);
   _mean_    = round(_mean_   , 0.01);
   _std_     = round(_std_    , 0.01);
run;

proc print data=prntunivg_m24;
 var rownum _var_ covarf _nobs_/* _median_ _q1_ _q3_ _min_ _max_*/ _mean_ _std_;
 title3 "Cohort: Gastric band (completed 24-month testing)";
run;


data prntg_m24;
 * length _VAR_ $100;
  set _null_;
run;

%npercent(1, rand, Sex          , SEXF   , treat_grp1b, g_m24);
%npercent(3, rand, Race         , RACEgF , treat_grp1b, g_m24);   * ??;
%npercent(4, rand, diabetes     , ynf    , treat_grp1b, g_m24); * IGT/Diabetes ;

data prntg_m24;
  set prntg_m24;
  percent = round(percent,0.1);
run;
```

```
proc sort data=prntg_m24;
  by rownum covarf;
  run;

proc print data=prntg_m24;
  var rownum covar covarf count percent;
run;



* Cohort: Metformin;

* med, q1, q3;
data prntuniv_m24;
 * length _VAR_ $100;
  set _null_;
run;

* Age continuous is NOT provided, skip   ;
%univ(8    , rand, Weight          , treat_grp2b , _m24);
%univ(8    , rand, bmi             , treat_grp2b , _m24);
*%univ(12   , rand, clamp_GLUC_05mod, treat_grp2b , _m24);  * Hyperglycemic clamp: Fasting glucose (mmol/L)  ;
%univ(12   , rand, GLUC_05mod      , treat_grp2b , _m24);  * OGTT: Fasting glucose (mmol/L)  ;
%univ(15   , rand, gluc120mod      , treat_grp2b , _m24);  * OGTT: 2-h glucose (mmol/L)      ;
%univ(10   , rand, HbA1c_mol_mmol  , treat_grp2b , _m24);

data prntuniv_m24;
  set prntuniv_m24;
   _median_  = round(_median_ , 0.1);
   _q1_      = round(_q1_     , 0.1);
   _q3_      = round(_q3_     , 0.1);
   _mean_    = round(_mean_   , 0.01);
   _std_     = round(_std_    , 0.01);
run;

proc print data=prntuniv_m24;
 var rownum _var_ covarf _nobs_/* _median_ _q1_ _q3_ _min_ _max_*/ _mean_ _std_;
 title3 "Cohort: Metformin (completed 24-month testing)";
run;


data prnt_m24;
 * length _VAR_ $100;
  set _null_;
run;

%npercent(1, rand, Sex          , SEXF   , treat_grp2b, _m24);
%npercent(3, rand, Race         , RACEgF , treat_grp2b, _m24);   * ??;
```

```
%npercent(4, rand, diabetes     , ynf    , treat_grp2b, _m24); * IGT/Diabetes ;

data prnt_m24;
  set prnt_m24;
  percent = round(percent,0.1);
run;

proc sort data=prnt_m24;
  by rownum covarf;
  run;

proc print data=prnt_m24;
  var rownum covar covarf count percent;
run;
```