Dataset Integrity Check for Open Randomized Multicenter Study to Evaluate Safety and Efficacy of Low Molecular Weight Sulfated Dextran in Islet Transplantation – von Zur-Mühlen et al

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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 Clinical Islet Transplantation consortium 01 study was a phase II, multicenter, open label, active control, randomized study. Twenty-four subjects were randomized to peritransplant intraportal and systemic treatment with either LMW-DS or heparin, targeting an activated partial thromboplastin time of 150 ± 10 seconds and 50 ± 5 seconds, respectively. C-peptide response was measured with a mixed meal tolerance test at 75 and 365 days after transplant.

3 Archived Datasets

All the SAS data files, as provided by the Data Coordinating Center (DCC), are located in the CIT_01 folder in the data package. For this replication, variables were taken from the “clarke.sas7bdat,” “demographics.sas7bdat,” “drugs.sas7bdat,” and “insulin.sas7bdat” datasets.

4 Statistical Methods

Analyses were performed to duplicate results for the data published by von Zur-Mühlen et al [1] in the journal Transplantation in 2019. To verify the integrity of the dataset, descriptive statistics were computed.

5 Results

For Table 1 in the publication [1], Baseline demographic and metabolic data described as mean values and standard deviation (SD) were applicable, 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.

6 Conclusions

The NIDDK repository is confident that the CIT_01 data files to be distributed are a true copy of the study data.

7 References

[1] von Zur-Mühlen B, Lundgren T, Levent B, et al. Open Randomized Multicenter Study to Evaluate Safety and Efficacy of Low Molecular Weight Sulfated Dextran in Islet Transplantation. *Transplantation* volume 103, issue 3, pages 630-637 (Mar 2019).

Table A: Variables used to replicate Table 1: Baseline demographic and metabolic data described as mean values and standard deviation (SD) were applicable

Table Variable	**dataset.variable**
n	drugs.randdrugname
Sex: male/female	demographics.gender
Age	demographics.agetx1
Weight	demographics.weight
BMI	demographics.bmi
Duration of diabetes	demographics.duration
Insulin requirement U	insulin.insulin
Clarke score	clarke.clarke_score

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

Variable	LMW-DS/Heparin	MS n (%) or Median (Percentiles)	IMS n (%) or Median (Percentiles)	Difference
n	LMW-DS	10	10	0
Sex	LMW-DS	4/6	4/6	0/0
Age	LMW-DS	47.4 (27.5-59.7)	47.4 (27.5-59.7)	0 (0-0)
Weight	LMW-DS	74.2 (56-93)	74.2 (56-93)	0 (0-0)
BMI	LMW-DS	24.9 (20.1-28.7)	24.9 (20.1-28.7)	0 (0-0)
Duration of diabetes	LMW-DS	33.0 (18-49)	33.0 (18-49)	0 (0-0)
Insulin requirement U	LMW-DS	42.2 (20.9)	?	?
Clarke score	LMW-DS	5.3 (1.5)	5.3 (1.5)	0 (0)
n	Heparin	14	14	0
Sex	Heparin	6/8	6/8	0/0
Age	Heparin	51.8 (36.7-63.8)	51.8 (36.7-63.8)	0 (0-0)
Weight	Heparin	66.5 (51-86)	66.5 (51-86)	0 (0-0)
BMI	Heparin	22.8 (18.6-29.1)	22.8 (18.6-29.1)	0 (0-0)
Duration of diabetes	Heparin	33.6 (16-46)	33.6 (16-46)	0 (0-0)
Insulin requirement U	Heparin	36.3 (12.3)	?	?
Clarke score	Heparin	6.1 (1.1)	6.1 (1.1)	0 (0)

Attachment A: SAS Code

```
options mprint nocentre linesize=147 validvarname=upcase;

title "Program:  /prj/niddk/ims_analysis/CIT_01/prog_initial_analysis/DSIC.paper-check.CIT01.y2019m03d22.sas";
title2 "This program checks the CIT01 paper.";

/*********************************************************************

programmer:  Jane Rideau Demuth

platform:  LINUX SASv9.4

date:  22nd March 2019

purpose:  See title2.

*********************************************************************/

***************;
*** formats ***;
***************;
proc format;
  value nmsgf
    . = ' '
    low-high = '###'
    ;
  value $cmsgf
    ' ' = ' '
    other = '$$$'
    ;
  value posnegf
    . = ' '
    low-<0 = '---'
    0 = '0'
    0<-high = '+++'
    ;

*******************;
*** input files ***;
*******************;
libname pcsasin "/prj/niddk/ims_analysis/CIT_01/private_created_data/3_14_2019/";

%macro reader(ds);
data &ds.;
  set pcsasin.&ds.;
title3 "Input file:  /prj/niddk/ims_analysis/CIT_01/private_created_data/3_14_2019/&ds..sas7bdat";
proc contents data=&ds. varnum;
```

```
%mend reader;

%reader(clarke);
%reader(demographics);
%reader(drugs);
%reader(insulin);

*********************;
*** check Table 1 ***;
*********************;
/*proc freq data=insulin;
  title3 'Insulin ds';
  tables pstintvst*pstfinvst / missing list;*/

proc sort data=insulin out=insulinbl;
  where pstintvst = 1 and pstfinvst = 1;
  by accession numdaysinitial;

/*proc freq data=insulinbl;
  title4 'just baseline';
  tables numdaysinitial / missing list;*/

data insulinbl1;
  set insulinbl;
  by accession numdaysinitial;
  if first.accession;

data table1(keep=accession randdrugname gender agetx1 weight bmi duration insulin clarke_score);
  merge drugs(in=indrugs keep=accession randdrugname)
        demographics(in=indemo keep=accession gender agetx1 weight bmi duration)
        insulinbl1(in=ininsulin keep=accession insulin)
        clarke(in=inclarke keep=accession clarke_score pstintvst pstfinvst
               where=(pstintvst = 1 or pstfinvst = 1));
  by accession;
  if not(first.accession and last.accession) then abort;
  if not(pstintvst = 1 and pstfinvst = 1) then abort;

proc sort data=table1;
  by randdrugname;

proc freq data=table1;
  title3 'Table 1';
  tables gender*randdrugname / missing;

proc univariate data=table1 noprint;
  by randdrugname;
  var agetx1 weight bmi duration insulin clarke_score;
  output out=tbl1uni
         mean=age_mean weight_mean bmi_mean duration_mean insulin_mean clarke_mean
         min=age_min weight_min bmi_min duration_min insulin_min clarke_min
         max=age_max weight_max bmi_max duration_max insulin_max clarke_max
```

```
          std=age_std weight_std bmi_std duration_std insulin_std clarke_std;

proc print data=tbl1uni noobs;
  var randdrugname age_mean age_min age_max;

proc print data=tbl1uni noobs;
  var randdrugname weight_mean weight_min weight_max;

proc print data=tbl1uni noobs;
  var randdrugname bmi_mean bmi_min bmi_max;

proc print data=tbl1uni noobs;
  var randdrugname duration_mean duration_min duration_max;

proc print data=tbl1uni noobs;
  var randdrugname insulin_mean insulin_std;

proc print data=tbl1uni noobs;
  var randdrugname clarke_mean clarke_std;

endsas;
```