Data Set Integrity Check for the Trial of Mid-Urethral Slings (TOMUS) 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 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

Urinary incontinence affects up to 50% of women, resulting in substantial medical, social, and economic burdens. Among U.S. women with urinary incontinence, 15 to 80% have a component of stress incontinence, which results in leakage of urine during physical exertion, sneezing, and coughing. Of these women, 4 to 10% undergo surgery.

TOMUS is a 2-arm, unmasked, multi-center randomized controlled trial that compared two types of mid-urethral slings used for treatment of stress incontinence: the retropubic midurethral mesh sling (RMUS) and the transobturator mid-urethral sling (TMUS). RMUS procedures are less invasive than the fascial sling procedures that were reference standards at the start of the study. Specifically, a synthetic tape is passed transvaginally at the midurethral level through the retropubic space. TMUS procedures were developed to minimize the potential for bladder and bowel injuries associated with the retropubic sling, since the sling is passed through the obturator canal, avoiding the pelvic organs in the retropubic space. Eligible women 21 years of age or older who were planning to undergo surgery for the treatment of stress incontinence were invited to participate in TOMUS. Randomization was performed after anesthesia was administered. Women were randomly assigned with the use of a permuted-block randomization schedule, with stratification according to clinical site. After the surgery, information regarding the treatment assignment was not kept from the patient. Subjects were followed up at 12 and 24 months after the surgery.

### **3** Archived Datasets

All SAS data files, as provided by the Data Coordinating Center (DCC), are located in the TOMUS "Data" folder included in the data package. For this replication, variables were taken from the "tomusfinal" dataset. These datasets were analysis datasets created by the DCC from the forms datasets, which are also included.

### **4 Statistical Methods**

To verify the integrity of the datasets, descriptive counts and percentage of baseline, after 12 and 24 months treatment characteristics were computed, by treatment group (Table B, table D, and Figure 2).

# **5 Results**

Figure 1 in the publication [1], <u>Study enrollment, randomization and assessment, PP, per protocol</u>. Table A lists the variables that were used in our replication and Table B compares the results calculated from the archived data file to the results published in Figure 1. Most of the results of the replication are close to the published results. The biggest difference is the lost to follow-up for treatment success at 12 months numbers. The Data Coordinating Center noted that specific details that would allow the replication of the lost to follow-up for treatment success numbers were not included in this data package.

Figure 2 in the publication [1] <u>Objective and Subjective success rates with 95% Cls for retropubic and</u> <u>transobturator mid urethral sling at 12 and 24 months.</u> Table C lists the variables that were used in our replication and Table D compares the results calculated from the archived data file to the results published in Figure 2. The results of the replication are the same as published results. Figure 3 in the publication [1]: Proportion of failure of individual components of objective and subjective outcomes by surgery group. Table E lists the variables that were used in our replication and Figure 1 is the a copy of Figure 3 in the publication [1], and Figure 2 shows the results calculated from the archived data file to the results published in Figure 3. The results of the replication are similar to published results, within rounding error.

Note that the adverse event data that was used to create the adverse event table in the publication was not included in this data package.

# **6** Conclusions

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

### 7 References

Michael E. Albo, Heather J. Litman, Holly E. Richter, Gary E. Lemack, Larry T. Sirls, Toby C. Chai, Peggy Norton, Stephen R. Kraus, Halina Zyczynski, Kimberly Kenton, E. Ann Gormley and John W. Kusek for the Urinary Incontinence Treatment Network. Treatment Success of Retropubic and Transobturator Mid Urethral Slings at 24 Months. *The Journal of Urology Volume 188, Issue 6*, Pages 2281-2287, December 2012

 Table A: Variables used to replicate Table 1: Study enrollment, randomization and assessment, PP, per protocol

Figure Variable for total randomized subjects	Variables Used in Replication from the "tomusfinal" Dataset
Treatment group	retropubic
ineligible	inelig
crossover	crossover
Did not receive study surgery	nostudyproc

Figure Variable for 12 months after surgery subjects	Variables Used in Replication	Data set the variable from
Treatment group	retropubic	Tomusfinal
	FINAL_STATUS=2 and	
Lost to follow-up	perprotocol =1 and any_status = 2 and any_visit < 12	F380/ tomusfinal
	FINAL_STATUS=3 and	
withdraw consent	perprotocol =1 and any_status = 2 and any_visit < 12	F380/ tomusfinal
	FINAL_STATUS=6 and	
other	perprotocol =1 and any_status = 2 and any_visit < 12	F380/ tomusfinal

Figure Variable for 24 months after surgery subjects	Variables Used in Replication	Data set the variable from
	retropubic	Tomusfinal
Treatment group	retropuble	Tomusiinai
	FINAL_STATUS=2 and	
Lost to follow-up	perprotocol =1 and any_status = 2 and any_visit >= 12	F380/ tomusfinal
	FINAL_STATUS=3 and	
withdraw consent	perprotocol =1 and any_status = 2 and any_visit >= 12	F380/ tomusfinal
	FINAL_STATUS=6 and	
other	perprotocol =1 and any_status = 2 and any_visit >= 12	F380/ tomusfinal

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

total randomized	retropubic count [Manuscript]	retropubic count [DSIC]	retropubic count [Difference]	Transobturator count [Manuscript]	Transobturator count [DSIC]	Transobturato r count [Difference]
subjects	298	298	0	299	299	0
include pp	291	291	0	292	292	0
ineligible	4	4	0	6	6	0
crossover				1	1	0
ineligible and						
crossover	1	1	0		•	•
did not receive						
study surgery	2	2	0	•	•	•

Follow-up for treatment success at 12 months	retropubic count [Manuscript]	retropubic count [DSIC]	retropubic count [Difference]	Transobturator count [Manuscript]	Transobturator count [DSIC]	Transobturator count [Difference]
subjects	274	271	3	278	277	1
lost to follow up	8	9	-1	8	8	0
withdraw consent	7	7	0	5	5	0
Other	2	1	1	1	1	0

Follow-up for treatment success at 24 months	retropubic count [Manuscript]	retropubic count [DSIC]	retropubic count [Difference]	Transobturator count [Manuscript]	Transobturator count [DSIC]	Transobturator count [Difference]
subjects	253	252	0	263	263	0
lost to follow up	10	10	0	7	7	0
withdraw consent	3	3	0	5	5	0
Other	8	5	3	3	1	2

**Table C**: Variables used to replicate Table 2: Objective and Subjective success rates with 95% Cls for retropubic and transoburator mid urethral sling at 12 and 24 months

Figure Variable	Variables Used in Replication from the "tomusfinal" Dataset
Objective	objfail, obj_visit
Subjective	subjfail, subj_visit

Table D: Comparison of values computed in integrity check to reference article Figure 2 values

characteristic	retropubic count [Manuscript]	retropubic count [DSIC]	retropubic count [Difference]	Transobturator count [Manuscript]	Transobturator count [DSIC]	Transobturator count [Difference]
obj_success_rate_24	77.3	77.5168	-0.22	72.3	71.9064	0.39
obj_success_rate_12	80.8	81.5436	-0.74	77.7	77.9264	-0.23
subj_success_rate_24	55.7	56.0403	-0.34	48.3	47.4916	0.81
subj_success_rate_12	62.2	63.7584	-1.56	55.8	56.8562	-1.06

**Table E**: Variables used to replicate Table 3 <u>Proportion of failure of individual components of objective</u> and subjective outcomes by surgery group

Figure Variable	Variables Used in Replication from the "tomusfinal" Dataset
Stress test	st_failt
Pad test	pad_failt
Retreatment	retrm_failt
stress type UI	mesa_failt
3-day Voiding diary	vd_failt

Figure 1: Figure 3 in the publication



Figure 2: Results replicated form archived data file for figure 3 in the publication.



#### Attachment A: SAS Code

\*\*\*\*\* \*\*\*Program: /prj/niddk/ims\_analysis/TOMUS/prog initial analysis/TOMUS integrity check 04142014.sas; \*\*\*Programmer: Jane Wang \*\*\*Date Created: 4/14/2014 \*\*\*Purpose: To perform a Dataset Integrity Check (DSIC) between the TOMUS data and the primary outcome paper: \*\*\*Treatment Success of Retropubic and Transobturator Mid Urethral Slings at 24 Months \*\*\*Michael E. Albo, Heather J. Litman, Holly E. Richter, Gary E. Lemack, Larry T. Sirls, Toby C. Chai, Peggy Norton, Stephen R. Kraus \*\*\*Halina Zyczynski, Kimberly Kenton, E. Ann Gormley and John W. Kusek? for the Urinary Incontinence Treatment Network \*/; title1 "%sysfunc(getoption(sysin))"; title2 " "; options nofmterr linesize=180; \*\*\* Location of the TOMUS SAS dataset; %include '/prj/niddk/ims analysis/TOMUS/prog initial analysis/tomus format.sas'; \*\*\* Reading in the analysis datasets used for the DSIC; libname sas data "/prj/niddk/ims analysis/TOMUS/private orig data/Tomus Data/Ready to send/3. TOMUS Data/Data/"; data f380 ; set sas data.f380 ; ; set sas\_data.tomusbase ; set sas\_data.tomusfinal data tomusbase ; data tomusfinal ; \*\*\* Data from the Primary outcome paper that was converted to .csv format so that the DSIC data could be easily compared; FILENAME fig 1 '/prj/niddk/ims analysis/TOMUS/private created data/tomus fig1 data.csv'; '/prj/niddk/ims\_analysis/TOMUS/private\_created\_data/tomus\_fig2\_data.csv'; FILENAME fig 2 \*\*\* Output CSV files that will be converted to .xls before being added to the DSIC document; FILENAME out f1 '/prj/niddk/ims analysis/TOMUS/private created data/tomus fig1 dsic 04142014.csv'; FILENAME out f2 '/prj/niddk/ims analysis/TOMUS/private created data/tomus fig2 dsic 04142014.csv'; FILENAME out f3 '/prj/niddk/ims\_analysis/TOMUS/private\_created\_data/tomus fig3 dsic 04142014.csv'; proc freq data = tomusfinal; tables retropubic/list missing noprint out= fig1 totalcount; proc print data = fig1 totalcount; title3 'total count'; proc freq data = tomusfinal; tables retropubic \* inelig \* crossover \* nostudyproc retropubic; ods output CrossTabFreqs = fig1\_freq; proc print data = fig1 freq; title3 'beginning exclude count'; data fig1 freq(keep = ineli count crossover count include pp retropubic ineli cross count nosurg count ); set fig1 freq; if (crossover ne . and nostudyproc ne . and Frequency ne 0); if retropubic = 0 then do; if inelig =1 and crossover =2 and nostudyproc = 2 then ineli count = Frequency; else if inelig =2 and crossover =1 and nostudyproc = 2 then crossover count = Frequency; else if inelig =2 and crossover =2 and nostudyproc = 2 then include\_pp = Frequency; end;

```
else if retropubic = 1 then do;
      if inelig =1 and crossover =1 and nostudyproc = 2 then ineli cross count = Frequency;
      else if inelig =1 and crossover =2 and nostudyproc = 2 then ineli_count = Frequency;
else if inelig =2 and crossover =2 and nostudyproc = 1 then nosurg count = Frequency.
                                                     nostudyproc = 1 then nosurg count = Frequency;
      else if inelig =2 and crossover =2 and
                                                    nostudyproc = 2 then include pp = Frequency;
  end:
data fig1_freq(keep = retropubic count chara
  set fig1_freq (in = in1) fig1_totalcount (in = in2);
                                       count characteristic);
  length characteristic $45 ;
  if in2 then characteristic = 'total';
if in1 then do;
  if ineli count ne . then do;
    count = ineli count;
    characteristic = 'ineli count';
  end;
  else if crossover count ne . then do;
    count = crossover count;
    characteristic = 'crossover count';
  end;
  else if include pp ne . then do;
   count = include_pp;
    characteristic = 'include pp';
  end;
  else if ineli cross count ne . then do;
    count = ineli_cross_count;
    characteristic = 'ineli cross count';
  end:
  else if nosurg count ne . then do;
    count = nosurg count;
    characteristic = 'nosurg count';
  end;
end;
proc print data = fig1 freq;
  title3 'beginning exclude count, include total';
/*
Code below from Anne Stoddard,
From: Anne Stoddard [mailto:AStoddard@neriscience.com]
Sent: Friday, April 04, 2014 5:06 PM
To: DelVecchio, Corey (IMS)
Subject: RE: Code to identify subjects in the TOMUS flow diagram
* /
proc sort data = f380; by aid;
proc sort data = tomusfinal; by aid;
data all;
  merge tomusfinal f380;
  by aid;
  if perprotocol =1 then do;
    if any_status = 2 and any_visit < 12 then fu_12m = final_status;
    else fu 12m = 1;
    if any status = 2 and any visit >= 12 then fu 24m = final status;
    else fu 24m = 1;
    if fu 12m >1 then fu 24m = .;
  end:
  label fu 12m = 'Follow-up for succes at 12m'
         fu 24m = 'Follow-up for success at 24m';
proc freq data = all;
  where perprotocol= 1;
  tables fu_12m*retropubic/list missing noprint out= fig1a_freq;
data figla freg(keep = retropubic
                                     COUNT
                                                characteristic);
  set fig1a_freq;
  length characteristic $45 ;
  if fu 12m = 1 then characteristic = 'final 12 count';
```

```
else if fu 12m = 2 then characteristic = 'lost days 12 count';
  else if fu 12m = 3 then characteristic = 'cw days 12 count';
  else if fu 12m = 5 then characteristic = 'Death';
  else if fu_12m = 6 then characteristic = 'adm_days_12_count';
proc print data = figla freq;
  title3 'fu 12 count';
proc freq data = all;
  where perprotocol=1 and fu 12m = 1;
  tables fu 24m*retropubic/list missing noprint out= fig1b_freq;
data fig1b freg(keep = retropubic
                                   COUNT
                                             characteristic);
  set fig1b freq;
  length characteristic $45 ;
  if fu 24m = 1 then characteristic = 'final 24 count';
  else if fu 24m = 2 then characteristic = 'lost days 24 count';
  else if fu_24m = 3 then characteristic = 'cw_days_24_count';
  else if fu_24m = 5 then characteristic = 'Death';
 else if fu 24m = 6 then characteristic = 'adm days 24 count';
proc print data = fig1b freq;
 title3 'fu 24 count';
data fig1 freq;
 set fig1 freq fig1a freq fig1b freq;
proc sort data = fig1 freq;
 by characteristic;
data fig1 freq trans fig1 freq retro;
 set fig1 freq;
  if characteristic not in ('', 'Death');
  if retropubic = 1 then output fig1_freq_retro;
  else if retropubic = 0 then output fig1 freq trans;
proc print data = fig1_freq;
 title3 'fig 1 before transpose';
data fig1 freq transpose (drop =retropubic);
 merge fig1_freq_retro(rename = (count =retro_compare)) fig1_freq_trans(rename = (count =
Trans compare));
 by characteristic;
proc print data = fig1_freq_transpose;
 title3 'fig 1 after transpose';
data fig1 data;
 infile fig 1 delimiter = ',' MISSOVER DSD firstobs=2 ls=1080;
  length characteristic $45 ;
  input
 characteristic $ Retro
                            Trans test $
data fig1 data;
 set fig1 data;
 sort_order = _n_;
proc print data = fig1_data;
 title3 'manuscript fig 1';
proc sort data = fig1 data;
 by characteristic;
data compare fig1;
 merge fig1 data(in = in1) fig1 freq transpose (in = in2);
 by characteristic;
data compare fig1(drop = test);
```

```
set compare fig1;
 diff_Retro = round((round(Retro,1) - round(retro_compare
diff_Trans = round((round(Trans,1) - round(Trans_compare
                                                                ,1)),1);
                                                                ,1)),1);
 label
    Retro
                  = "retropubic count [Manuscript]"
    retro compare = "retropubic count [DSIC]
                 = "retropubic count [Difference]"
= "Transobturator count [Manuscript]"
    diff Retro
    Trans
    Trans_compare = "Transobturator count [DSIC]
                = "Transobturator count [Difference]"
    diff Trans
 ;
proc sort data = compare fig1;
 by sort order;
ods csv file = out f1;
run;
proc print data = compare fig1 NOOBS label;
      var characteristic Retro retro compare diff Retro Trans Trans compare diff Trans
;
      title3 "DSIC Check of Figure 1: Count of retropubic treatment";
run;
ods csv close;
****
*** Macro to create a dataset that matches Figure 2 of the primary outcome paper;
%macro baseline freq(var name1,var name2);
 proc freq data = tomusfinal;
       table retropubic * &var name1. * &var name2;
       title3 "Frequency table of the &var name1. variable in the analysis dataset";
       *** Outputting the frequency data to work.&var name. cross using the ODS output;
 ods output CrossTabFreqs = work.&var name1. cross;
 data &var_name1._cross (keep = retropubic &var_name1. &var_name2 Frequency);
   set &var name1. cross;
   if &var name1 = 1 and not missing(&var name2);
proc transpose data=&var_name1._cross out=&var_name1._trans ;
  by retropubic;
  ID &var name2.;
 data &var name1. trans (keep = retropubic &var name1. success rate 12
&var_name1._success_rate_24);
   set &var name1. trans;
   if NAME = 'Frequency';
   if retropubic = 1 then do;
     &var name1. success rate 12 = (298- 0 - 6 - 12)/298 * 100;
&var_name1._success_rate 24 = (298- 0 - 6 - 12- 24)/298 * 100;
   end;
   else if retropubic = 0 then do;
     &var_name1._success_rate_12 = (299-_0 - _6 - _12)/299 * 100;
&var_name1._success_rate_24 = (299-_0 - _6 - _12-_24)/299 * 100;
   end;
```

%mend;

```
proc freq data = tomusfinal;
       table retropubic * &var name1. ;
        title3 "Frequency table of the &var namel. variable in the analysis dataset";
       *** Outputting the frequency data to work.&var name. cross using the ODS output;
 ods output CrossTabFreqs = work.&var name1. cross;
 data &var name1. cross (keep = retropubic RowPercent rename = (RowPercent = &var name1. pct));
   set &var_name1._cross;
   if &var name1 = 1 and retropubic ne .;
proc transpose data=&var_name1._cross out=&var_name1._trans ;
  by retropubic;
%mend;
*** Running the baseline_freq on the categorical variables in the Figure 2 manuscript file;
%baseline freq(objfail,obj visit );
%baseline freq(subjfail, subj visit
                                      );
data combine_fig2;
 set objfail trans subjfail trans;
proc sort data = combine fig2;
 by retropubic;
proc transpose data=combine fig2 out=combine fig2 trans ;
  by retropubic;
*proc print data = combine fig2 trans;
data fiq2 ret (keep= compare Retro characteristic ) fig2_tran (keep = compare_Trans
characteristic);
 set combine fig2 trans;
  if _name _ = 'objfail_success_rate_24 ' then characteristic = 'obj_success_rate_24 ';
 if _name_ = 'objfail_success_rate_12 ' then characteristic = 'obj_success_rate_12 ';
if _name_ = 'subjfail_success_rate_24' then characteristic = 'subj_success_rate_24';
  if _name_ = 'subjfail_success_rate_12' then characteristic = 'subj success rate 12';
  if retropubic = 0 then do;
      if coll ne . then compare Trans = coll;
      else if col2 ne . then compare_Trans = col2;
      output fig2_tran;
  end;
  if retropubic = 1 then do;
     if COL1 ne . then compare Retro = COL1;
      else if COL2 ne . then compare Retro = COL2;
      output fig2_ret;
 end:
proc sort data = fig2 ret;
 by characteristic;
proc sort data = fig2_tran;
 by characteristic;
*** Merging the two frequency datasets together;
data all fig2;
 merge fig2_ret fig2_tran;
 by characteristic;
*proc print data = all fig2;
 title3 'all fig2';
data fig2 data;
 infile fig 2 delimiter = ',' MISSOVER DSD firstobs=2 ls=1080;
  length characteristic $45 ;
  input
 characteristic $ Retro
                             Trans test $
```

```
*proc print data = fig2 data;
data fig2 data;
 set fig2 data;
 sort_order = _n_;
proc sort data = fig2_data;
 by characteristic;
proc sort data = all_fig2;
 by characteristic;
*** Merging the DSIC data with the Figure 2 data from the primary outcome paper;
*** Variables that contain the differences between the two datasets are created;
data compare fig2;
 merge fig2_data(in = in1) all_fig2 (in = in2);
 by characteristic;
data compare fig2;
 set compare_fig2;
 diff_Retro = round((round(Retro,0.01) - round(compare_Retro
diff_Trans = round((round(Trans,0.01) - round(compare_Trans
                                                               ,0.01)),0.01);
                                                               ,0.01)),0.01);
 label
                 = "retropubic count [Manuscript]"
    Retro
    compare Retro = "retropubic count [DSIC]
                 = "retropubic count [Difference]"
    diff Retro
               = "retropuble count [Diricitant]
= "Transobturator count [Manuscript]"
    Trans
    compare_Trans = "Transobturator count [DSIC]
    diff Trans
                 = "Transobturator count [Difference]"
;
proc sort data = compare fig2;
 by sort order;
ods csv file = out f2;
run;
proc print data = compare fig2 NOOBS label;
      var characteristic Retro compare Retro diff Retro Trans compare Trans diff Trans
:
      title3 "DSIC Check of Figure 2: Objective and Subjective success rate";
run;
ods csv close;
*** Running the baseline freq on the categorical variables in the Figure 3 manuscript file;
%baseline_freq_f3(st_failt );
%baseline_freq_f3(pad_failt );
%baseline freq f3(mesa failt
                            );
%baseline_freq_f3(vd_failt
                         );
data combine fig3 trans;
 set retrm_failt_trans st_failt_trans
    pad failt trans
     mesa failt trans
     vd_failt_trans
     ;
*proc print data = combine fig3 trans;
data fig3 ret (keep= compare Retro characteristic ) fig3 tran (keep = compare Trans
characteristic);
```

;

```
set combine_fig3_trans;
  characteristic= __name_;
if retropubic = 0 then do;
     if coll ne . then compare_Trans = coll;
      output fig3_tran;
  end;
  if retropubic = 1 then do;
      if COL1 ne . then compare_Retro = COL1;
      output fig3_ret;
  end;
proc sort data = fig3_ret;
 by characteristic;
proc sort data = fig3_tran;
 by characteristic;
*** Merging the two frequency datasets together;
data all fig3;
 merge fig3_ret fig3_tran;
by characteristic;
ods csv file = out_f3;
run;
proc print data = all_fig3 NOOBS label;
       var characteristic compare_Retro compare_Trans
;
       title3 "DSIC Check of Figure 3: Porportion of failure";
run;
ods csv close;
```