**SUPPLEMENTAL MATERIAL**

**How to impute study-specific standard deviations in meta-analyses of skewed continuous endpoints.**

**Appendix 1**

Example of SAS code to simulate a meta-analysis on 15 datasets with 15 records generated from a Gamma distribution (alpha=2 and beta=5 versus alpha=2 and beta=7 for the treatment and control group, respectively).

\* q is the assigned library;

\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*;

\* SIMULATIONS;

\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*;

%let s=gamma;

%let ndset=15;

\* Simulation of n=15 dataset using the Gamma distributions;

**%macro** ***simul***;

%do q=**1** %to &ndset;

%let seed=%sysevalf(1234567+&q);

%let num\_i=%sysevalf(&ndset);

%let v=%sysevalf(0+&q);

data s&q;

k=&q;

%do i=**1** %to &num\_i;

var1=**5**\*rangam(&seed,**2**);

var2=**7**\*rangam(&seed,**2**);

output;

%end;

run;

%end;

\* Dataset combining;

data simul\_&s;

set

%do w=**1** %to &ndset;

s&w

%end;

;

run;

**%mend**;

%***simul***;

\* Descriptive statistics for each dataset;

ods trace on;

ods output summary=summary\_&s;

**proc** **means** data=simul\_&s mean std median q1 q3;

class k;

var var1 var2;

**run**;

ods trace off;

**data** summary\_&s;

set summary\_&s;

l1=(var1\_Median-var1\_Q1)/**0.6745**;

l2=(var2\_Median-var2\_Q1)/**0.6745**;

u1=(var1\_Q3-var1\_Median)/**0.6745**;

u2=(var2\_Q3-var2\_Median)/**0.6745**;

if l1>u1 then MeSD\_v1\_cons=l1; else MeSD\_v1\_cons=u1;

if l2>u2 then MeSD\_v2\_cons=l2; else MeSD\_v2\_cons=u2;

if l1>u1 then MeSD\_v1\_prec=u1; else MeSD\_v1\_prec=l1;

if l2>u2 then MeSD\_v2\_prec=u2; else MeSD\_v2\_prec=l2;

MeSD\_v1\_mean=(var1\_Q3-var1\_Q1)/**1.349**;

MeSD\_v2\_mean=(var2\_Q3-var2\_Q1)/**1.349**;

\* Median difference;

MeD=var1\_Median-var2\_Median;

\*1 conservative estimate of standard deviation;

a1sd=((MeSD\_v1\_cons)\*\***2**)/NObs;

b1sd=((MeSD\_v2\_cons)\*\***2**)/NObs;

MeSD\_cons=sqrt(a1sd+b1sd);

\*2 less conservative estimate of standard deviation;

a2sd=((MeSD\_v1\_prec)\*\***2**)/NObs;

b2sd=((MeSD\_v2\_prec)\*\***2**)/NObs;

MeSD\_prec=sqrt(a2sd+b2sd);

\*3 mean estimate of standard deviation;

a3sd=((MeSD\_v1\_mean)\*\***2**)/NObs;

b3sd=((MeSD\_v2\_mean)\*\***2**)/NObs;

MeSD\_mean=sqrt(a3sd+b3sd);

\*4 Interquartile range;

a4sd=((var1\_Q3-var1\_Q1)\*\***2**)/NObs;

b4sd=((var2\_Q3-var2\_Q1)\*\***2**)/NObs;

MeSD\_iqr=sqrt(a4sd+b4sd);

\* Mean difference and pooled standard deviation;

MD=var1\_Mean-var2\_Mean;

asd=((var1\_StdDev)\*\***2**)/NObs;

bsd=((var2\_StdDev)\*\***2**)/NObs;

SD=sqrt(asd+bsd);

drop l1 l2 u1 u2 asd bsd a1sd b1sd a2sd b2sd a3sd b3sd a4sd b4sd;

**run**;

\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*;

\* Meta-analyses;

**data** sum\_&s;

set summary\_&s;

keep k NObs MeD MeSD\_cons MeSD\_prec MeSD\_mean MeSD\_iqr MD SD qq;

**run**;

\*1 Median and conservative estimate of standard deviation;

**data** meta\_&s.1;

set sum\_&s;

model="Conservative SD";

MDz=MeD;

SDz=MeSD\_cons;

w=**1**/(SDz\*\***2**);

MDw=MDz\*w;

keep model k NObs MDz SDz w MDw;

**run**;

\*2 Median and less conservative estimate of standard deviation;

**data** meta\_&s.2;

set sum\_&s;

model="Less Conservative SD";

MDz=MeD;

SDz=MeSD\_prec;

w=**1**/(SDz\*\***2**);

MDw=MDz\*w;

keep model k NObs MDz SDz w MDw;

**run**;

\*3 Median and mean estimate of standard deviation;

**data** meta\_&s.3;

set sum\_&s;

model="Mean SD";

MDz=MeD;

SDz=MeSD\_mean;

w=**1**/(SDz\*\***2**);

MDw=MDz\*w;

keep model k NObs MDz SDz w MDw;

**run**;

\*4 Median and interquartile range;

**data** meta\_&s.4;

set sum\_&s;

model="IQR";

MDz=MeD;

SDz=MeSD\_iqr;

w=**1**/(SDz\*\***2**);

MDw=MDz\*w;

keep model k NObs MDz SDz w MDw;

**run**;

\* Mean and standard deviation (reference);

**data** meta\_&s.5;

set sum\_&s;

model="Reference";

MDz=MD;

SDz=SD;

w=**1**/(SDz\*\***2**);

MDw=MDz\*w;

keep model k NObs MDz SDz w MDw;

**run**;

**proc** **format**;

value model

**1**="conservative SD"

**2**="Less Conservative SD "

**3**="Mean SD "

**4**="IQR"

**5**="Reference"

;

**run**;

\*\*\* Fixed effect model meta-analysis – Inverse of Variance method;

**%macro** ***meta\_iv***;

%do i=**1** %to **5**;

ods output Summary=somme&i;

proc means data=meta\_&s&i sum;

var MDw w;

run;

data somme&i;

set somme&i;

model=&i;

format model model.;

theta=MDw\_Sum/w\_Sum;

se\_theta=**1**/(sqrt(w\_sum));

lower=theta-(se\_theta\***1.96**);

upper=theta+(se\_theta\***1.96**);

mtheta=sqrt(theta\*\***2**);

CV=se\_theta/mtheta;

keep model theta se\_theta lower upper cv;

run;

%end;

data aaMeta\_&s;

set

%do w=**1** %to **5**;

somme&w

%end;

;

run;

title "distr=&s - k=&ndset";

proc print; run;

**%mend**;

%***meta\_iv***;

Supplemental Figure 1

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Supplemental Figure 2

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