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*simulate repeated measures data;
*compare bias and power of t-test and means model;
*single time point comparison;
*ELA April 2, 2015;

libname dbox 'c:\simulations\results';

%let n = 200;*sample size;
%let NumSamples = 10000;*number of simulated data sets;

*** rho = .7 *****;
%let varb = 77;*between-person variance;
%let vare = 33;*within-person variance;
*****;
/*** rho = .5 *****;
%let varb = 55;*between-person variance;
%let vare = 55;*within-person variance;
*****/;
/*** rho = .3 *****;
%let varb = 33;*between-person variance;
%let vare = 77;*within-person variance;
*****/;

%macro ODSoff(); /* Call prior to BY-group processing */
ods graphics off;
ods exclude all;
ods noresults;
%mend;

%macro ODSon(); /* Call after BY-group processing */
ods graphics on;
ods exclude none;
ods results;
%mend;

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*****;
*** SIMULATE COMPLETE DATA *****;

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*****;
*one row per person;
data wide;
  call streaminit(20090520);
  do SampleID =1 to &NumSamples;
    do id=1 to &n;
      b = rand('Normal',0, sqrt(&varb));*between-person effects;
      if mod(id,2)=0 then do;
        trt = 0; *control group;
        do until((y1>=0 & y1<=100));
          y1 = rand('Normal',50, sqrt(&vare)) + b;
        end;
        do until((y2>=0 & y2<=100));
          y2 = rand('Normal',50, sqrt(&vare)) + b;
        end;
        do until((y3>=0 & y3<=100));
          y3 = rand('Normal',50, sqrt(&vare)) + b;
        end;
        do until((y4>=0 & y4<=100));
          y4 = rand('Normal',50, sqrt(&vare)) + b;
        end;
      end;
      else do;
        trt = 1; *active treatment group;
        do until((y1>=0 & y1<=100));
          y1 = rand('Normal',50, sqrt(&vare)) + b;
        end;
        do until((y2>=0 & y2<=100));
          y2 = rand('Normal',51.393, sqrt(&vare)) + b;
        end;
        do until((y3>=0 & y3<=100));
          y3 = rand('Normal',52.7867, sqrt(&vare)) + b;
        end;
        do until((y4>=0 & y4<=100));
          y4 = rand('Normal',54.18, sqrt(&vare)) + b;
        end;
      end;
      output;
    end;
  end;

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        end;
    end;
run;

*****;
*** MCAR with equal dropout of 40% in each group *****;
*****;
proc sort data=wide; by sampleid trt; run;
proc surveystest data=wide
    method=SRS n=40 seed=2015 out=mcAR;
    strata sampleid trt;
run;
proc sort data=mcAR; by sampleid id; run;
proc sort data=wide; by sampleid id; run;

data wideMCAR;
    merge wide
        mcar(in=m keep=sampleid id);
    by sampleid id;
    call streaminit(2015);
    if m then do;
        U = rand('Uniform');
        if U < 1/3 then do;
            y2=.; y3=.; y4=.;
        end;
        else if U < 2/3 then do;
            y3=.; y4=.;
        end;
        else if U < 1 then do;
            y4=.;
        end;
    end;
run;
*****;
*** 2. MAR with unequal dropout of 30% and 50% in each group *****;
*** participants in the treatment group have a dropout rate of 30%;
*** participants in the control group have a dropout rate of 50%;
*** a) One reason for dropout: feeling poorly (low score);

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*****;
*set probability of missing in control arm;
%let TRTOPMT2=.15;
%let TRTOPMT3=.3;
%let TRTOPMT4=.5;
*set probability of missing in treatment arm;
%let TRT1PMT2=.1;
%let TRT1PMT3=.2;
%let TRT1PMT4=.3;

data wideMARA2;
    set wide;
    call streaminit(2015);

    EY1=50;*expectation for Y at time 1;

    if trt=0 then p2 = ((100*TRTOPMT2)/(100-EY1))*(100 - y1)/100;*probability of missing at t2 depends on y at t1;
    else if trt=1 then p2 = ((100*TRT1PMT2)/(100-EY1))*(100 - y1)/100;

    m2 = rand("Bernoulli", p2);
    if m2=1 then do; y2=.; y3=.; y4=.; end;*dropout at t2;
run;

*calculate the mean of y2 now in each arm;
proc sql noprint;
    select mean(y2) into :EY2trt0 - :EY2trt1 from widemara2
    group by trt;
quit;
%put _user_;

data widemara3;
    set widemara2;
    if m2=0 then do;
        if trt = 0 then p3 = (1 - (1-TRTOPMT3)/(1-TRTOPMT2))*(100/(100-EY2trt0)) * (100 - y2)/100;*probability of mis
        else if trt = 1 then p3 = (1 - (1-TRT1PMT3)/(1-TRT1PMT2))*(100/(100-EY2trt1)) * (100 - y2)/100;
        m3 = rand("Bernoulli", p3);
        if m3=1 then do; y3=.; y4=.; end;*dropout at t3;
    end;
end;

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run;

*calculate the mean of y3 now in each arm;
proc sql noprint;
  select mean(y3) into :EY3trt0 - :EY3trt1 from widemara3
  group by trt;
quit;
%put _user_;

data widemara4;
  set widemara3;
  if m3 =0 then do;
    if trt = 0 then p4 = (1 - (1- &TRTOPMT4)/(1- &TRTOPMT3))*(100/(100- &EY3trt0)) * (100 - y3)/100;*probability of
    else if trt =1 then p4 = (1 - (1- &TRT1PMT4)/(1- &TRT1PMT3))*(100/(100- &EY3trt1)) * (100 - y3)/100;
    m4 = rand("Bernoulli", p4);
    if m4=1 then do; y4=.; end;*dropout at t4;
  end;
run;

*****;
*****;
*** 2. MAR with unequal dropout of 30% and 50% in each group *****;
*** participants in the treatment group have a dropout rate of 30%;
*** participants in the control group have a dropout rate of 50%;
*** b) Different reasons for dropout: feeling poorly (low score) or feeling well (high score);
*****;
*set probability of missing in control arm;
%let TRTOPMT2=.15;
%let TRTOPMT3=.3;
%let TRTOPMT4=.5;
*set probability of missing in treatment arm;
%let TRT1PMT2=.1;
%let TRT1PMT3=.2;
%let TRT1PMT4=.3;

data wideMARB2;
  set wide;
  call streaminit(2015);

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EY1=50;*expectation for Y at time 1;

if trt=0 then c = &TRTOPMT2 / (.6 * (((55-EY1)/55)**2) + .4);
else if trt=1 then c = &TRT1PMT2 / (.6 * (((55-EY1)/55)**2) + .4);

p2 = c * (.6 * (((55-y1)/55)**2) + .4);*probabilty of missing at t2 depends on y1;

m2 = rand("Bernoulli", p2);
if m2=1 then do; y2=.; y3=.; y4=.; end;*dropout at t2;
run;

*calculate the mean of y2 now in each arm;
proc sql noprint;
  select mean(y2) into :EY2trt0 - :EY2trt1 from widemarb2
  group by trt;
quit;
%put _user_;

data widemarb3;
  set widemarb2;
  if m2=0 then do;

    if trt=0 then c = (1 - (1 - &TRTOPMT3)/(1 - &TRTOPMT2)) / (.6 * (((55-&EY2trt0)/55)**2) + .4);
    else if trt=1 then c = (1 - (1 - &TRT1PMT3)/(1 - &TRT1PMT2)) / (.6 * (((55-&EY2trt1)/55)**2) + .4);

    p3 = c * (.6 * (((55-y2)/55)**2) + .4);*probabilty of missing at t3 depends on y2;

    m3 = rand("Bernoulli", p3);
    if m3=1 then do; y3=.; y4=.; end;*dropout at t3;
  end;
run;

*calculate the mean of y3 now in each arm;
proc sql noprint;
  select mean(y3) into :EY3trt0 - :EY3trt1 from widemarb3
  group by trt;
quit;

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%put _user_;

data widemarb4;
  set widemarb3;
  if m3 =0 then do;
    if trt=0 then c = (1 - (1 - &TRTOPMT4)/(1 - &TRTOPMT3)) / (.6 * (((55-&EY3trt0)/55)**2) + .4);
    else if trt=1 then c = (1 - (1 - &TRT1PMT4)/(1 - &TRT1PMT3)) / (.6 * (((55-&EY3trt1)/55)**2) + .4);

    p4 = c * (.6 * (((55-y3)/55)**2) + .4);*probability of missing at t4 depends on y3;

    m4 = rand("Bernoulli", p4);
    if m4=1 then do; y4=.; end;*dropout at t4;
  end;
run;

*****;
*****;
*** 3. MAR with equal dropout of 40% in each group *****;
*** Different reasons for dropout: feeling poorly (low score) or feeling well (high score);
*****;
*set probability of missing in control arm;
%let TRTOPMT2=.15;
%let TRTOPMT3=.25;
%let TRTOPMT4=.4;
*set probability of missing in treatment arm;
%let TRT1PMT2=.15;
%let TRT1PMT3=.25;
%let TRT1PMT4=.4;
data wideMAR32;
  set wide;
  call streaminit(2015);

  EY1=50;*expectation for Y at time 1;

  if trt=0 then c = &TRTOPMT2 / (.6 * (((55-EY1)/55)**2) + .4);
  else if trt=1 then c = &TRT1PMT2 / (.6 * (((55-EY1)/55)**2) + .4);

  p2 = c * (.6 * (((55-y1)/55)**2) + .4);*probabilty of missing at t2 depends on y1;

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  m2 = rand("Bernoulli", p2);
  if m2=1 then do; y2=.; y3=.; y4=.; end;*dropout at t2;
run;

*calculate the mean of y2 now in each arm;
proc sql noprint;
  select mean(y2) into :EY2trt0 - :EY2trt1 from widemar32
  group by trt;
quit;
%put _user_;

data widemar33;
  set widemar32;
  if m2=0 then do;

    if trt=0 then c = (1 - (1 - &TRTOPMT3)/(1 - &TRTOPMT2)) / (.6 * (((55-&EY2trt0)/55)**2) + .4);
    else if trt=1 then c = (1 - (1 - &TRT1PMT3)/(1 - &TRT1PMT2)) / (.6 * (((55-&EY2trt1)/55)**2) + .4);

    p3 = c * (.6 * (((55-y2)/55)**2) + .4);*probability of missing at t3 depends on y2;

    m3 = rand("Bernoulli", p3);
    if m3=1 then do; y3=.; y4=.; end;*dropout at t3;
  end;
run;

*calculate the mean of y3 now in each arm;
proc sql noprint;
  select mean(y3) into :EY3trt0 - :EY3trt1 from widemar33
  group by trt;
quit;
%put _user_;

data widemar34;
  set widemar33;
  if m3 =0 then do;
    if trt=0 then c = (1 - (1 - &TRTOPMT4)/(1 - &TRTOPMT3)) / (.6 * (((55-&EY3trt0)/55)**2) + .4);
    else if trt=1 then c = (1 - (1 - &TRT1PMT4)/(1 - &TRT1PMT3)) / (.6 * (((55-&EY3trt1)/55)**2) + .4);

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p4 = c * (.6 * (((55-y3)/55)**2) + .4);*probability of missing at t4 depends on y3;

m4 = rand("Bernoulli", p4);
if m4=1 then do; y4=.; end;*dropout at t4;
end;
run;

*****;
*** 4. MNAR with unequal dropout of 30% and 50% in each group *****;
*** participants in the treatment group have a dropout rate of 30%;
*** participants in the control group have a dropout rate of 50%;
*** a) One reason for dropout: feeling poorly (low score);
*****;
*set probability of missing in control arm;
%let TRTOPMT2=.15;
%let TRTOPMT3=.3;
%let TRTOPMT4=.5;
*set probability of missing in treatment arm;
%let TRT1PMT2=.1;
%let TRT1PMT3=.2;
%let TRT1PMT4=.3;

data wideMNARa;
set wide;
call streaminit(2015);

EY2trt0=50;*expectation for Y at time 2 in the control group;
EY3trt0=50;
EY4trt0=50;

EY2trt1=51.393;*expectation for Y at time 2 in the treatment group;
EY3trt1=52.7867;
EY4trt1=54.18;

if trt=0 then p2 = ((100*TRTOPMT2)/(100-EY2trt0))*(100 - y2)/100;*probability of missing at t2 depends on y at t2;
else if trt=1 then p2 = ((100*TRT1PMT2)/(100-EY2trt1))*(100 - y2)/100;

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m2 = rand("Bernoulli", p2);
if m2=1 then do; y2=.; y3=.; y4=.; end;*dropout at t2;
else do;
if trt=0 then p3=(1 - (1-TRTOPMT3)/(1-TRTOPMT2))*(100/(100-EY3trt0))*(100-y3)/100;
else if trt=1 then p3=(1 - (1-TRT1PMT3)/(1-TRT1PMT2))*(100/(100-EY3trt1))*(100-y3)/100;

m3 = rand("Bernoulli", p3);
if m3=1 then do; y3=.; y4=.; end;*dropout at t3;
else do;
if trt=0 then p4=(1 - (1-TRTOPMT4)/(1-TRTOPMT3))*(100/(100-EY4trt0))*(100-y4)/100;
else if trt=1 then p4=(1 - (1-TRT1PMT4)/(1-TRT1PMT3))*(100/(100-EY4trt1))*(100-y4)/100;

m4 = rand("Bernoulli", p4);
if m4=1 then do; y4=.; end;*dropout at t4;
end;
end;
run;

*****;
*** 4. MNAR with unequal dropout of 30% and 50% in each group *****;
*** participants in the treatment group have a dropout rate of 30%;
*** participants in the control group have a dropout rate of 50%;
*** b) Different reasons for dropout: feeling poorly (low score) or feeling well (high score);
*****;
*set probability of missing in control arm;
%let TRTOPMT2=.15;
%let TRTOPMT3=.3;
%let TRTOPMT4=.5;
*set probability of missing in treatment arm;
%let TRT1PMT2=.1;
%let TRT1PMT3=.2;
%let TRT1PMT4=.3;

data wideMNARb;
set wide;
call streaminit(2015);

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EY2trt0=50;*expectation for Y at time 2 in the control group;
EY3trt0=50;
EY4trt0=50;

EY2trt1=51.393;*expectation for Y at time 2 in the treatment group;
EY3trt1=52.7867;
EY4trt1=54.18;

if trt=0 then c = &TRTOPMT2 / (.6 * (((55-EY2trt0)/55)**2) + .4);
else if trt=1 then c = &TRT1PMT2 / (.6 * (((55-EY2trt1)/55)**2) + .4);

p2 = c * (.6 * (((55-y2)/55)**2) + .4);*probabilty of missing at t2 depends on y2;

m2 = rand("Bernoulli", p2);
if m2=1 then do; y2=.; y3=.; y4=.; end;*dropout at t3;
else do;
  if trt=0 then c = (1 - (1 - &TRTOPMT3)/(1 - &TRTOPMT2)) / (.6 * (((55-EY3trt0)/55)**2) + .4);
  else if trt=1 then c = (1 - (1 - &TRT1PMT3)/(1 - &TRT1PMT2)) / (.6 * (((55-EY3trt1)/55)**2) + .4);

  p3 = c * (.6 * (((55-y3)/55)**2) + .4);*probability of missing at t3 depends on y3;

  m3 = rand("Bernoulli", p3);
  if m3=1 then do; y3=.; y4=.; end;*dropout at t3;
  else do;
    if trt=0 then c = (1 - (1 - &TRTOPMT4)/(1 - &TRTOPMT3)) / (.6 * (((55-EY4trt0)/55)**2) + .4);
    else if trt=1 then c = (1 - (1 - &TRT1PMT4)/(1 - &TRT1PMT3)) / (.6 * (((55-EY4trt1)/55)**2) + .4);

    p4 = c * (.6 * (((55-y4)/55)**2) + .4);*probability of missing at t4 depends on y4;

    m4 = rand("Bernoulli", p4);
    if m4=1 then do; y4=.; end;*dropout at t4;
  end;
end;
run;

*****
*** 5. MNAR with equal dropout of 40% in each group *****

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```

*** Different reasons for dropout: feeling poorly (low score) or feeling well (high score);
*****;
*set probability of missing in control arm;
%let TRTOPMT2=.15;
%let TRTOPMT3=.25;
%let TRTOPMT4=.4;
*set probability of missing in treatment arm;
%let TRT1PMT2=.15;
%let TRT1PMT3=.25;
%let TRT1PMT4=.4;

data wideMNAR5;
  set wide;
  call streaminit(2015);

  EY2trt0=50;*expectation for Y at time 2 in the control group;
  EY3trt0=50;
  EY4trt0=50;

  EY2trt1=51.393;*expectation for Y at time 2 in the treatment group;
  EY3trt1=52.7867;
  EY4trt1=54.18;

  if trt=0 then c = &TRTOPMT2 / (.6 * (((55-EY2trt0)/55)**2) + .4);
  else if trt=1 then c = &TRT1PMT2 / (.6 * (((55-EY2trt1)/55)**2) + .4);

  p2 = c * (.6 * (((55-y2)/55)**2) + .4);*probabilty of missing at t2 depends on y2;

  m2 = rand("Bernoulli", p2);
  if m2=1 then do; y2=.; y3=.; y4=.; end;*dropout at t3;
  else do;
    if trt=0 then c = (1 - (1 - &TRTOPMT3)/(1 - &TRTOPMT2)) / (.6 * (((55-EY3trt0)/55)**2) + .4);
    else if trt=1 then c = (1 - (1 - &TRT1PMT3)/(1 - &TRT1PMT2)) / (.6 * (((55-EY3trt1)/55)**2) + .4);

    p3 = c * (.6 * (((55-y3)/55)**2) + .4);*probability of missing at t3 depends on y3;

    m3 = rand("Bernoulli", p3);
    if m3=1 then do; y3=.; y4=.; end;*dropout at t3;
  end;
end;

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else do;
  if trt=0 then c = (1 - (1 - &TRTOPMT4)/(1 - &TRTOPMT3)) / (.6 * (((55-EY4trt0)/55)**2) + .4);
  else if trt=1 then c = (1 - (1 - &TRT1PMT4)/(1 - &TRT1PMT3)) / (.6 * (((55-EY4trt1)/55)**2) + .4);

  p4 = c * (.6 * (((55-y4)/55)**2) + .4);*probability of missing at t4 depends on y4;

  m4 = rand("Bernoulli", p4);
  if m4=1 then do; y4=.; end;*dropout at t4;
end;
end;
run;

*****;
*** DATA ANALYSIS OF SIMULATED DATA *****;
*****;
%macro analysis(data);
*one row per person PER TIMEPOINT;
data long;
  set &data;*read in wide data;

  time = 1; y = y1; output;
  time = 2; y = y2; output;
  time = 3; y = y3; output;
  time = 4; y = y4; output;
  drop y1 y2 y3 y4 b;
run;

*** t-test bias and power *****;
proc ttest data=long;
  by SampleId;
  where time=4; *only consider last timepoint;
  class trt;
  var Y;
  ods output ttests=Tpvalues statistics=Tmeans;
run;

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```

options nonotes;

*** MMRM with Compound Symmetric variance-covariance matrix assumed ****;
proc mixed data=long;
  by SampleID;
  class id trt time;
  model y = trt time trt*time / noint;
  repeated time / type=CS subject=id;
  estimate 'MM t4' trt -1 1 trt*time 0 0 0 -1 0 0 0 1/cl ;
  ODS OUTPUT estimates = MMRMCS;
run;

*** MMRM with unstructured variance-covariance matrix *****;
proc mixed data=long;
  by SampleID;
  class id trt time;
  model y = trt time trt*time / noint;
  repeated time / type=UN subject=id;
  estimate 'MM t4' trt -1 1 trt*time 0 0 0 -1 0 0 0 1/cl ;
  ODS OUTPUT estimates = MMRMUN;
run;
options notes;

*** output the results to dropbox *****;
data dbox.Tpvalues_&data&vare; set Tpvalues; run;

data dbox.Tmeans_&data&vare; set Tmeans; run;

data dbox.MMRMCS_&data&vare; set MMRMCS; run;

data dbox.MMRMUN_&data&vare; set MMRMUN; run;
*****;
%mend;

%ODSoff;

%analysis(wide);

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```
%analysis(wideMCAR);  
%analysis(wideMARA4);  
%analysis(wideMARb4);  
%analysis(wideMAR34);  
%analysis(wideMNARa);  
%analysis(wideMNARb);  
%analysis(wideMNAR5);  
%ODSon;
```