Medtronic

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IMPROVE SCA

Statistical Analysis Plan

Version 1
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[redacted]

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1 PURPOSE

This Statistical Analysis Plan has been designed to document, before data is analyzed, the rationale for the study design, and the planned analyses that will be included in study reports. This plan does not limit the analysis provided in reports, and additional analysis of the study data beyond this plan is expected.

The Statistical Analysis Plan was developed based on version 1.0 of the Improve SCA Study Clinical Investigation Plan dated December 23, 2013.

2 STUDY OVERVIEW

The study design and rationale can be found in the Clinical Investigational Plan (CIP). The Improve SCA study is a prospective, non-randomized, non-blinded, global, interventional, multi-site post-market study. The study purpose is to demonstrate that primary prevention patients with one or more additional risk factors (1.5 prevention criteria: syncope/pre-syncope, non-sustained ventricular tachycardia (NSVT), frequent pre-ventricular contractions (PVCs), and low left ventricular ejection fraction (LVEF)) are at a similar risk of life-threatening ventricular arrhythmias (LTVA) when compared to secondary prevention patients, and would receive similar benefit from an implantable cardioverter defibrillator (ICD), or cardiac resynchronization therapy- defibrillator (CRT-D) implant. Additional objectives evaluating mortality, cost effectiveness, reason for implant refusal, and Chagas disease will be analyzed.

3 DESCRIPTION OF ANALYSIS

3.1 General Summaries

The Medtronic statisticians who are assigned to the project will conduct all statistical analyses. The primary objective is to compare 1.5 prevention patients with secondary prevention patients regarding the time to first appropriately treated VT/VF. There is also a secondary objective to compare the mortality rates between patients with an implanted device (ICD/ CRT-D) and those without, for patients meeting 1.5 prevention criteria. [redacted]

3.1.1 Description of Baseline Variables

A number of characteristics will be reported for each enrolled subject at time of enrollment. The variables collected will include demographics, medical history, NYHA classification, and cardiovascular medications. Tables and descriptive statistics will be used to summarize subject data with respect to these variables.

3.1.2 Special Considerations

Medtronic statisticians will perform the statistical analyses. Sample size estimates were calculated using SAS Version 9.2 (SAS Institute Inc.).

Analysis Cohort

Patients with any of the following deviations from the study protocol will be excluded from all statistical analysis, as if they were never enrolled in the study:

- Patients that violate any of the inclusion/exclusion criteria.

- Primary prevention patients that did not have LVEF measured at baseline or the 1.5 criteria assessment
- Patients with LVEF measured prior to 40 days post-MI OR prior to 90 days post-MI with revascularization.
- Primary ICD indication patient that is not Class I.
- Primary prevention patients without history of any 1.5 criteria and no Holter test performed
- Primary prevention patients without history of any 1.5 criteria and Holter test performed more than 12 months prior to enrollment or more than 3 months after enrollment.
- Primary prevention patients with no 1.5 criteria assessment.
- Patients with a Baseline or Medical History CRF dated after implant.
- Patients with consent date after implant decision date.
- Patients with previous ICD or CRT-D.
- Patients implanted with a Non-Medtronic device.
- Patients exiting the study or dying prior to completing the Medical History CRF, or the Implant CRF.

3.1.3 Reports for which this Statistical Analysis Plan applies

This analysis plan shall apply to the final report. Statistical analysis for study related publications will not be limited to this plan. However, it is the intent that the main study publication will follow the methods detailed in this plan, which in some cases supersede the investigational plan.

3.2 Primary Objective: Appropriate Therapy

The primary objective is to demonstrate that appropriate VT/VF therapy rates (shock and ATP) for subjects meeting 1.5 prevention criteria implanted with a Medtronic device (ICD/CRT-D) are equivalent (within 30%) to rates in subjects meeting secondary prevention criteria.

The primary objective will be evaluated by using post-implant time to first appropriate VT/VF therapy (shock and ATP). More specifically, the following hypothesis will be tested:

Hypothesis
H_o: Hazard ratio of Implanted 1.5 patients to implanted secondary patients ≤ 0.70
H_a: Hazard ratio of Implanted 1.5 patients to implanted secondary patients > 0.70

Endpoint Definition
The event of interest for this objective is appropriate VT/VF therapy. To qualify as an event, a VT/VF event observed by the ICD/CRT must be adjudicated to be one of the following by the Episode Review Committee:

- Polymorphic VT/VF
- Monomorphic VT
- Non-sustained VT/VF
- Other VT/VF, specify:

Additionally, the episode must have been treated either by ATP, shock, or both by the device.

Performance Requirement
The null hypothesis will be rejected if the one-sided 95% lower confidence bound of the hazard ratio of implanted 1.5 subjects to implanted secondary prevention subjects is greater than 0.70.

Analysis Methods
A Cox proportional hazard model will be used to compare the hazard rates of first appropriate VT/VF therapy between implanted subjects meeting 1.5 prevention criteria and secondary prevention subjects. Because secondary and 1.5 patients are known to be different in many potential covariates, the Cox proportional hazards model will not include any covariates. The one-sided hypothesis test will be performed by computing a 90% two-tailed confidence interval for the hazard ratio between the groups and using the lower limit of this estimated 90% CI as a rejection boundary of the null hypothesis. In particular, if the 90% CI lower limit is greater than 0.7 then the null hypothesis will be rejected.

The analysis will be performed using SAS code similar to:

```
proc phreg data = alldata;
where group in ('A','C');
class group (ref = 'A');
model time2event*eventStatus(0)= group/ rl alpha = 0.1;
run;
```

Additionally, Kaplan-Meier estimates of the survival curves will be displayed for each prevention criteria group.

Determination of Patients/Data for Analysis

- All 1.5 prevention and secondary prevention subjects with an ICD/CRT-D implant and at least one device interrogation available in the database will be included in the primary analysis hypothesis test. This includes subjects implanted with a device after the initial enrollment period. These later implants will be included if they are secondary or 1.5 at the time of implant.
- Time 0 is the implant date and, if no events occur, subjects will be censored on the date of their latest device interrogation.
- VT/VF episodes that cannot be adjudicated (due to not saving full episode data or any other reason) will be ignored. Often, these episodes are followed by episodes that can be adjudicated, and since the endpoint is time to first episode, effects on the results from these events will be minimal. In addition, these should be balanced between the comparison groups.

Sample Size Calculation
The minimum required sample size for this study has been estimated to be 4800 subjects based on the following:

- 60% of enrollments will be secondary prevention and 40% primary prevention
- 50% of primary subjects will be in the 1.5 group
- 57% of secondary subjects will get an ICD (includes CRT-D)
- 45% of 1.5 subjects will get an ICD
- 22% of 1.0 subjects will get an ICD
- Annual attrition (includes exits and deaths) will be 10%
- The study will end two years after the last enrollment
- 4000 patients will take 2 years to enroll with enrollment beginning slowly, and then accelerating to a steady 246 per month
- Expected rates of appropriately treated VT/VF in secondary subjects follow Figure 2, with a higher rate in the first year (22.5%), then a constant rate (11.1%) thereafter
- The hazard ratio of 1.5 to secondary is 0.91

Under the above assumptions and using the hypothesis test stated above, 4800 subjects will have 80% power to reject the null hypothesis. With 4800 enrolled patients, it is expected that approximately 1650 secondary prevention subjects will be implanted, 430 1.5 prevention subjects will be implanted, and 200 1.0 subjects will be implanted.

More details, including the simulation program can be found in the Appendix.

Sample Size Re-estimation
Because most of the assumptions above are based only on investigator opinion, the sample size will be re-estimated during the study using the same simulation methods, but changing the following assumptions using the study data:

- % of enrollments will be secondary prevention
- % of primary patients in the 1.5 group
- % of secondary patients who will get an ICD (includes CRT-D)
- % of 1.5 patients who will get an ICD
- % of 1.0 patients who will get an ICD
- Annual attrition (includes exits and deaths)
- Enrollment rate

With this re-estimation of sample size, the length of follow-up after the last enrollment may be changed as well. Because no comparisons will be done at the point of re-estimation, alpha is not affected and the final analysis can compare the p-value to a 0.05 alpha level.

The sample size re-estimation will occur at the later of:
- One year after the 400th subject has been enrolled
- The time of the 2000th enrollment.

The database will be frozen for the sample size re-estimation with a visit cut-off date of 4 weeks after the 2000th enrollment, and an enrollment cut-off of the date of the 2000th enrollment. That will allow collection of 1.5 Criteria and implant/implant refusal data for the last subjects enrolled prior to the enrollment cut-off. The enrollment cut-off means any subject consented after that date will not be included in analysis.

Subjects who meet the “excluded” criteria in section 3.1.2 will not be included in the sample size re-estimation calculations. This will mean less than 2000 subjects will be included. Additionally, the new sample size will add subjects to replace the excluded subjects. For example, if 1900 subjects are not

excluded at the time of database freeze and the sample size re-estimate calls for 3000 subjects, then 1100 more non-excluded subjects will need to be enrolled in the study.

It is the study sponsor's discretion to increase (to a maximum of 8000 subjects) or decrease the sample size, or increase or decrease the length of follow-up after last enrollment.

If fewer subjects are required, the study sponsor may either lower the sample size, or increase the power of the study (possibly keeping the original sample size). If more subjects are required, the study sponsor may elect to not increase the sample size, but may increase the length of follow-up to ensure adequate power for the study.

Study sites will be notified of any change in sample size and length of follow-up (if applicable) at that time. The investigational plan will not be changed.

3.3 Secondary Objective: Mortality

The secondary objective is to compare the mortality rates for patients meeting 1.5 prevention criteria between those implanted with a device (ICD/CRT-D) and those not implanted.

Hypothesis
Although this is an exploratory objective and is not powered, a hypothesis test will be done and compared to an alpha level of 0.05.

H_o: Hazard ratio of non-implanted to implanted 1.5 patients = 1
H_a: Hazard ratio of non-implanted to implanted 1.5 patients ≠ 1

Analysis Methods
A Cox proportional hazards model will be used to compare the mortality rates between subjects with device implant and without, in subjects who meet the 1.5 prevention criteria. In addition to the implant/no implant variable, the Cox proportional hazards model will include baseline covariates that are known to be associated with mortality and that might be unbalanced between the groups due to the non-randomized study design. These covariates are:

- age at consent
- sex
- QRS duration
- ischemic cardiomyopathy (yes/no)
- left bundle branch block (LBBB) (yes/no)
- NYHA Classification (treated as an ordinal variable, including 0 for those without HF)
- diabetes (Type 1 or 2 only, gestational not counted) (yes/no)
- LVEF (taken from the 1.5 Visit CRF, if it exists, or from the Baseline CRF)
- syncope qualifying as 1.5 (yes/no)
- NSVT qualifying as 1.5 (yes/no)
- PVCs qualifying as 1.5 (yes/no)

Note that all 3 categorical 1.5 covariates can be found at the end of the 1.5 Criteria CRF. The NSVT and PVC variables on the Baseline CRF do not include the minimum thresholds of 3 consecutive >100 bpm beats for NSVT and 10 or more PVCs per hour.

Country of enrollment was to be included as a covariate according to the CIP, but it will not be included as subjects in the study (who all have medical care) may not have significantly different mortality rates between countries. Also, some countries may have a small number of enrollments. The idea was to have covariates with known mortality risks.

LBBB and diabetes are added covariates from the CIP based on steering committee input. LBBB was added because it is a well-known mortality risk factor. Diabetes was not originally collected in the study, but was added later and is being collected for all subjects, including those enrolled prior to it being added to the Medical History CRF.

Due to the large sample size, it is likely that some subjects will have covariates missing. To circumvent this problem, multiple imputation methods will be used. More specifically:

- The number of imputed datasets to be created will be 20.
- The imputation of missing values will be done using the fully conditional specification (FCS) method, where the covariates in the imputation model are the same covariates in the Cox proportional model (except the covariate being imputed) plus implant/no implant, the event indicator and the Nelson-Aalen estimator of the cumulative hazard function as suggested by White and Royston (2009).
- The imputation for missing binary variables (e.g., gender) will be done via the FCS logistic regression method, and for missing continuous variables (e.g., QRS) it will be done via the FCS linear regression method.
- Missing NYHA will be imputed via FCS ordinal logistic regression.
- All continuous variables will be standardized before the imputation phase, in order to avoid the FCS linear regression imputing values that are not realistic (e.g., negative LVEF).
- The null hypothesis will be rejected if the pooled p-value for the implant/no-implant covariate is less than 0.05.

The analysis will be performed using SAS code similar to:

```
/*Nelson-Aalen Estimates for Cumulative Hazard Function*/

proc phreg data=alldataneeded1p5 noprint;
  model SURVTIME*EVENT(0) =;
  output out=alldataneeded1p5_2 logsurv=logs / method=emp;
run;

data Alldataneeded1p5_2;
  set Alldataneeded1p5_2;
  cumhaz = -logs;
run;

proc standard  data = Alldataneeded1p5_2 mean = 0 std=1 out=
Alldataneeded1p5_3;
  var AGE LVEF0 QRS;
run;

/*Imputation Phase*/
proc mi data= Alldataneeded1p5_3 nimpute = 5 out = mi_alldata_1p5 ;
class SEXCHAR CMYISCH LBBB NYHA0 DIABETES CRIT15SYNC CRIT15NSVT CRIT15PVC
GROUP EVENT;
var AGE SEXCHAR QRS CMYISCH LBBB NYHA0 DIABETES LVEF0 CRIT15SYNC CRIT15NSVT
CRIT15PVC GROUP CUMHAZ EVENT;
fcs logistic(SEXCHAR CMYISCH LBBB NYHA0 DIABETES CRIT15SYNC CRIT15NSVT
CRIT15PVC GROUP EVENT);
run;

/*Analysis Phase*/
proc phreg data = mi_alldata_1p5;
class SEXCHAR CMYISCH LBBB NYHA0 DIABETES CRIT15SYNC CRIT15NSVT CRIT15PVC
GROUP EVENT;
```

```
model SURVTIME*EVENT(0) = AGE SEXCHAR QRS CMYISCH LBBB NYHA0 DIABETES LVEF0
CRIT15SYNC CRIT15NSVT CRIT15PVC GROUP ;
by _Imputation_;
ods output ParameterEstimates=coxReg_fcs;
ods output Type3=type3table;
run;

/*Pooling Phase*/
proc mianalyze parms(classvar=ClassVal) = coxReg_fcs;
class SEXCHAR CMYISCH LBBB NYHA0 DIABETES CRIT15SYNC CRIT15NSVT CRIT15PVC
GROUP;
modeleffects  AGE SEXCHAR QRS CMYISCH LBBB NYHA0 DIABETES LVEF0 CRIT15SYNC
CRIT15NSVT CRIT15PVC GROUP ;
run;
```

Kaplan-Meier estimates of the survival curves will be displayed for each group.

The same analysis will be performed comparing implanted and not implanted 1.0 subjects.

Time to Event Considerations

- Time 0 is the enrollment date and subjects will be censored on the last date they were confirmed to be alive.
- Non-implanted patients that later decided to implant the ICD/CRT-D, will have their time to event censored at the day of the implant procedure.
- Implanted patients that explanted the device (without replacement) will continue to be followed as part of the implanted group. These cases will be rare, and unless the explant is completely voluntary (i.e., not due to infection, or imminent subject end-of-life), censoring subjects at explant would bias the results in favor of implant. This is an intention-to-treat approach.
- Patients that had heart transplant will have their time to event censored at the day of the transplant.

3.3.1 Power

This objective is not powered and the likelihood of a statistically significant test is not known. Therefore, it should not be a surprise if the endpoint is not statistically significant.

The following table shows what the power of the endpoint would be under various scenarios if doing a log-rank test (see PASS screen shot in the appendix for details). It is not known what effect adding covariates in a Cox proportional hazards model will have on the power.

In a retrospective analysis of SCD-HeFT, 1.5 prevention subjects without an ICD had a 25.7% mortality rate at 3 years compared to 18.5% for 1.5 subjects with an ICD. Under the sample size assumptions, it is expected that approximately 430 1.5 subjects will be implanted and 540 will not.

Power for 1.5 Prevention Mortality Endpoint

1.5 implanted sample size	1.5 **not** implanted sample size	Assumed 3-year Mortality				
		26% no ICD 18% ICD	26% no ICD 20% ICD	26% no ICD 22% ICD	22% no ICD 14% ICD	30% no ICD 22% ICD
450	550	88%	63%	32%	93%	82%
350	650	85%	60%	30%	91%	79%
360	440	80%	53%	27%	87%	73%
350	350	74%	48%	24%	83%	67%

3.3.2 Determination of Patients/Data for Analysis

All subjects in the 1.5 prevention cohort at the time of enrollment who do not meet the criteria in section 3.1.2 of this document will be included. The same criteria apply for the 1.0 subjects in their mortality analysis.

[redacted]

Hypothesis
Although this is an exploratory objective and is not powered, a hypothesis test will be done and compared to an alpha level of 0.05.

H_o: Hazard ratio of patients with Chagas disease to patients without Chagas disease = 1
H_a: Hazard ratio of patients with Chagas disease to patients without Chagas disease ≠ 1

Only subjects with implant (regardless the prevention criteria group) will be included in the analysis. Subjects with missing information regarding Chagas disease will not be included.

The hypothesis will be tested separately for 1.0, 1.5, and secondary groups.

Analysis Methods
A Cox proportional hazard model will be used to compare the hazard rates of first appropriate VT/VF therapy between subjects with Chagas disease and subjects without Chagas disease within each group (1.0, 1.5, and secondary). The Cox proportional hazards model will only include the Chagas disease indicator. The null hypothesis will be rejected if the p-value for the Chagas disease indicator covariate is less than 0.05.
The analysis will be performed using SAS code similar to:

```
proc phreg data=alldataneeded ;
  class chagas;
  model firstVTVFappropTreat*event(0) = chagas;
run;
```

Time to Event Considerations

- Time 0 is the implant date and, if no events occur, subjects will be censored on the date of their latest device interrogation. Only spontaneous, appropriately treated VT/VF episodes as adjudicated by the episode review committee will count toward the endpoint.
- VT/VF episodes that cannot be adjudicated (due to not saving full episode data or any other reason) will be ignored. Often, these episodes are followed by episodes that can be adjudicated, and since the endpoint is time to first episode, effects on the results from these events will be minimal. In addition, these should be balanced between the comparison groups.

4 REFERENCES

1. White, I.R. and Royston P. (2009) *Imputing missing covariate values for the Cox model*. Statistics in Medicine **28**: 1982 – 1998.

5 APPENDIX

Sample size details

The % in each study group was based on estimates from the steering committee. It was assumed 1/3 would be enrolled in India, 1/3 in China, and 1/3 in the rest of the world. The table below shows the estimates from steering committee members, and the overall estimate, which was derived in a non-formulatic way from the physicians' estimates.

			% Implanted					
	%Secondary		Secondary		1.5		1.0	
Physician	My center	Others in my country	My center	Other centers in my country	My center	Other centers in my country	My center	Other centers in my country
Chasnoits (Belarus)	75	No ans.	98	90	65	65	40	40
Singh (India)	70	80	80	10-80	No answer		15	15
Zhang (China)	50	50	50	15	60	25	40	10
Huang (China)	30	55	50	30	40	30	30	30
Overall estimate	60*		57		45		22	

* Takes into account efforts to promote enrolling primary prevention subjects.

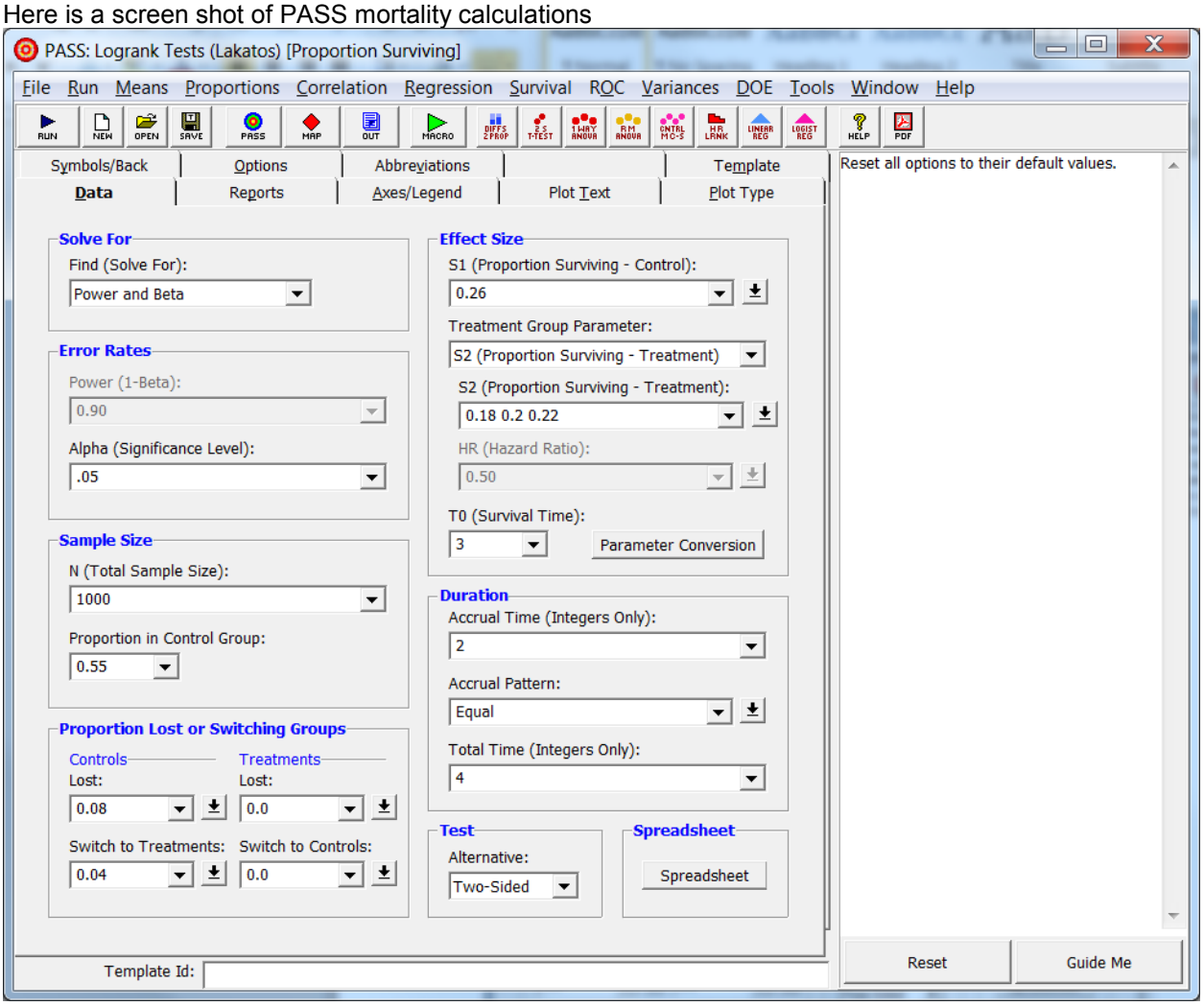
The program sim.sas produced power calculations based on the sample size assumptions. The program was run feeding in sample sizes from 4000-5000. Each study sample size was simulated 10,000 times, and the resulting power (% of time the lower one-sided 95% confidence limit of the hazard ratio (HR) was above 0.70) and the average hazard ratio for the 10,000 simulations are shown.

Sample size	Power	HR
4000	73.6	0.904
4050	74.9	0.904
4100	75.2	0.904
4150	74.6	0.903
4200	76.0	0.905
4250	75.6	0.904
4300	77.6	0.905
4350	76.7	0.903
4400	77.7	0.904
4450	78.1	0.903
4500	78.2	0.903
4550	79.2	0.904
4600	79.0	0.904
4650	79.5	0.905
4700	79.9	0.903
4750	80.5	0.903
4800	80.4	0.903
4850	80.6	0.902
4900	81.6	0.904
4950	81.8	0.904
5000	82.3	0.903

HR is included because those further away from 0.91 are under-estimating power.

4800 was chosen because the 4750 estimate of 80.5 may be too high (compared to 4700 and 4800).

Here is a screen shot of PASS mortality calculations



PROGRAM SIM.SAS

```
/*************************************************************************
*********************************
  Program Name: SIM.SAS

  Study: IMPROVE SCA

  Purpose: Determing study sample size

  Inputs: None

  Outputs: None

  Cautions: None

  Revision
  History:      Version     Date        Author                  Description
                -------     ---------   -------------------     -------------
------------------------------
                      1     09DEC13     Jeff Cerkvenik          Initial
Version
*************************************************************************
*********************************/

OPTIONS PS=56;

/*
SS: TOTAL SAMPLE SIZE OF STUDY
PROBSEC: PROBABILITY OF SECONDARY (AS OPPOSED TO PRIMARY) PREVENTION
PROB15: PROBABILITY OF BEING 1.5 GIVEN THEY ARE PRIMARY
IMPSEC: PROBABILITY THAT A SECONDARY PREVENTION PATIENT GETS AN IMPLANT
IMP15: PROBABILITY THAT A 1.5 PATIENT GETS AN IMPLANT
IMPPRIM: PROBABILITY THAT A PRIMARY (NON-1.5) PATIENT GETS AN IMPLANT
FAILA12: PROBABILITY THAT A GROUP A PATIENT WILL HAVE AN APPROPRIATE VT/VF IN
THE FIRST 12 MONTHS
FAILALONG: PROBABILITY THAT A GROUP A PATIENT WILL HAVE AN APPROPRIATE VT/VF
IN A GIVEN YEAR IN ANY YEAR AFTER THE FIRST 12 YEAR
HRAC: ASSUMED HAZARD RATIO OF GROUP A TO GROUP C
HRCE: ASSUMED HAZARD RATIO OF GROUP C TO GROUP E
YEARSENROLL: YEARS TO GET FULL ENROLLMENT
YEARLYATTRITION: ANNUAL ATTRITION DUE TO DEATH OR EXIT (IMPLANTED GROUPS A,
C, AND E ONLY)
YEARSFOLLOW: YEARS OF FOLLOW-UP FOLLOWING THE LAST ENROLLMENT
*/

%MACRO STUDY (
SS,
PROBSEC,
PROB15,
IMPSEC,
IMP15,
IMPPRIM,
FAILA12,
FAILALONG,
HRAC,
HRCE,
YEARSENROLL,
```

```
YEARLYATTRITION,
YEARSFOLLOW);

DATA STUDY;
DO PT=1 TO &SS;
   IMPDT=.; ENDDT=.; ATRTIME=.; FAILTIME=.; FAIL=.; SURVTIME=.;
   *ICD INDICATION;
   A=RAND('UNIFORM');
   IF A<&PROBSEC THEN IND='SECONDARY'; ELSE IND='PRIMARY';

   *1.0 OR 1.5?;
   B=RAND('UNIFORM');
   IF B<&PROB15 THEN LEVEL='1.5'; ELSE LEVEL='1.0';

   *ACCEPT IMPLANT?;
   C=RAND('UNIFORM');
   IF IND='SECONDARY' THEN DO;
      IF C<&IMPSEC THEN IMP=1; ELSE IMP=0;
   END;
   IF IND='PRIMARY' THEN DO;
      IF LEVEL='1.5' THEN DO;
         IF C<&IMP15 THEN IMP=1; ELSE IMP=0;
      END;
      IF LEVEL='1.0' THEN DO;
         IF C<&IMPPRIM THEN IMP=1; ELSE IMP=0;
      END;
   END;

   IF IND='SECONDARY' AND IMP=1 THEN GROUP='A';
   IF IND='SECONDARY' AND IMP=0 THEN GROUP='B';
   IF IND='PRIMARY' AND LEVEL='1.5' AND IMP=1 THEN GROUP='C';
   IF IND='PRIMARY' AND LEVEL='1.5' AND IMP=0 THEN GROUP='D';
   IF IND='PRIMARY' AND LEVEL='1.0' AND IMP=1 THEN GROUP='E';
   IF IND='PRIMARY' AND LEVEL='1.0' AND IMP=0 THEN GROUP='F';

   *GET 10-YEAR PROBABILITY OF APPROPRIATE THERAPY (ASSUMING NO DEATH, EXIT,
OR END OF STUDY);
       FAILMONTH=.;
       DO MONTH=1 TO 120;  *MONTHS;
          *MORE FAILURES IN FIRST YEAR;
          D=RAND('UNIFORM');
          IF GROUP='A' AND FAILMONTH=. THEN DO;
             IF MONTH LE 12 THEN DO;
                IF D<1-(1-&FAILA12)**(1/12) THEN FAILMONTH=MONTH;
             END;
             IF MONTH>12 THEN DO;
                IF D<1-(1-&FAILALONG)**(1/12) THEN FAILMONTH=MONTH;
             END;
          END;
          IF GROUP='C' AND FAILMONTH=. THEN DO;
             IF MONTH LE 12 THEN DO;
                IF D<1-(1-&FAILA12*&HRAC)**(1/12) THEN FAILMONTH=MONTH;
             END;
             IF MONTH>12 THEN DO;
                IF D<1-(1-&FAILALONG*&HRAC)**(1/12) THEN FAILMONTH=MONTH;
             END;
          END;
```

```
          IF GROUP='E' AND FAILMONTH=. THEN DO;
             IF MONTH LE 12 THEN DO;
                IF D<1-(1-&FAILA12*&HRAC*&HRCE)**(1/12) THEN FAILMONTH=MONTH;
             END;
             IF MONTH>12 THEN DO;
                IF D<1-(1-&FAILALONG*&HRAC*&HRCE)**(1/12) THEN
FAILMONTH=MONTH;
             END;
          END;
       END;

       E=RAND('UNIFORM');
       FAILTIME=ROUND((FAILMONTH-1)*365.25/12+E*30);



   *CENSOR PATIENTS ALONG THE WAY;
       *JAN 1, 2014 IS FIRST POSSIBLE DATE OF IMPLANT;
       FORMAT IMPDT ENDDT LASTSTUDYDT DATE7.;
       IF GROUP IN ('A','C','E') THEN DO;
          *ASSUME SLOW ENROLLMENT TO BEGIN, WITH INCREASING ENROLLMENT OVER
REST OF TIME PERIOD;
             F=RAND('CHISQ',2);
             IF F>4 OR F<0.1 THEN F=RAND('CHISQ',2);
             IF F>4 OR F<0.1 THEN F=RAND('CHISQ',2);
             IF F>4 OR F<0.1 THEN F=RAND('CHISQ',2);
             *ABOVE WILL CAPTURE>99%.  FOR A FEW, JUST GIVE A MIDDLE VALUE;
             IF F>4 OR F<0.1 THEN F=1+E;
             XX=(F*(-1/3.9)+4/3.9);
             IMPDT='01JAN14'D+ROUND((F*(-
1/3.9)+4/3.9)*(&YEARSENROLL*365.25));

          *ATTRITION DUE TO DEATH/EXIT;
             ATRMONTH=.;
             DO MONTH=1 TO 120;
                G=RAND('UNIFORM');
                IF ATRMONTH=. AND G<1-(1-&YEARLYATTRITION)**(1/12) THEN
ATRMONTH=MONTH;
             END;
             H=RAND('UNIFORM');
             ATRTIME=ROUND((ATRMONTH-1)*365.25/12+H*30);

       *FIND OUT ATRITION DATE AND EVENT DATE, THEN USE THE EARLIER OF THE
TWO;
          IF FAILTIME NE . AND ATRTIME NE . THEN
ENDDT=IMPDT+MIN(FAILTIME,ATRTIME);
          IF FAILTIME = . AND ATRTIME NE . THEN ENDDT=IMPDT+ATRTIME;
          IF FAILTIME NE . AND ATRTIME = . THEN ENDDT=IMPDT+FAILTIME;
          IF FAILTIME = . AND ATRTIME = . THEN ENDDT=IMPDT+3653;
          IF ENDDT=IMPDT+FAILTIME AND FAILTIME NE . THEN FAIL=1; ELSE
FAIL=0;

       *GET END OF STUDY;
          ENDSTUDYDT='01JAN14'D+INT((&YEARSENROLL+&YEARSFOLLOW)*365.25);
          *ASSUME LAST FOLLOW-UP WILL BE WITHIN 3 MONTHS OF END STUDY;
          I=RAND('UNIFORM');
```

```
            LASTSTUDYDT=ENDSTUDYDT-INT(I*91);

            IF ENDDT>LASTSTUDYDT THEN DO;
               ENDDT=LASTSTUDYDT;
               FAIL=0;
            END;

            SURVTIME=(ENDDT-IMPDT)/365.25*12;
        END;

*FOR PHREG SO THE HR IS C/A;
GROUP2='   ';
IF GROUP='C' THEN GROUP2=' C';
IF GROUP='A' THEN GROUP2='A';
IF GROUP='E' THEN GROUP2='  E';

OUTPUT;
END;
RUN;

ODS LISTING CLOSE;
PROC LIFETEST timelist=(12,24,36) DATA=STUDY;
STRATA GROUP;
TIME SURVTIME*FAIL(0);
SURVIVAL out=CI conftype=loglog stderr;
RUN;

DATA CI;
SET CI;
FAILURE=1-SURVIVAL;
FUCL=1-SDF_LCL;
FLCL=1-SDF_UCL;
RUN;

DATA CI12;
SET CI;
WHERE SDF_LCL NE . AND SURVTIME<12;
RUN;

PROC SORT;
BY GROUP SURVTIME;
RUN;

DATA CI12;
SET CI12;
BY GROUP SURVTIME;
IF NOT LAST.GROUP THEN DELETE;
RUN;

DATA CI24;
SET CI;
WHERE SDF_LCL NE . AND SURVTIME<24;
RUN;

PROC SORT;
BY GROUP SURVTIME;
RUN;
```

```
DATA CI24;
SET CI24;
BY GROUP SURVTIME;
IF NOT LAST.GROUP THEN DELETE;
RUN;

DATA CI36;
SET CI;
WHERE SDF_LCL NE . AND SURVTIME<36;
RUN;

PROC SORT;
BY GROUP SURVTIME;
RUN;

DATA CI36;
SET CI36;
BY GROUP SURVTIME;
IF NOT LAST.GROUP THEN DELETE;
RUN;

PROC PHREG DATA=STUDY;
WHERE GROUP IN ('A','C');
CLASS GROUP2;
*ALPHA=0.1 GIVES ONE-SIDED 95% CONFIDENCE INTERVAL;
MODEL SURVTIME*FAIL(0)=GROUP2 / RL ALPHA=0.1;
ODS OUTPUT ParameterEstimates=HRAC;
RUN;

PROC PHREG DATA=STUDY;
WHERE GROUP IN ('E','C');
CLASS GROUP2;
MODEL SURVTIME*FAIL(0)=GROUP2 / RL;
ODS OUTPUT ParameterEstimates=HRCE;
RUN;

PROC PHREG DATA=STUDY;
WHERE GROUP IN ('A','E');
CLASS GROUP2;
MODEL SURVTIME*FAIL(0)=GROUP2 / RL;
ODS OUTPUT ParameterEstimates=HRAE;
RUN;

PROC LIFETEST DATA=STUDY;
WHERE GROUP IN ('A','E');
STRATA GROUP;
TIME SURVTIME*FAIL(0);
ODS OUTPUT HomTests=LOGRANKAE;
RUN;

PROC LIFETEST DATA=STUDY;
WHERE GROUP IN ('C','E');
STRATA GROUP;
TIME SURVTIME*FAIL(0);
ODS OUTPUT HomTests=LOGRANKCE;
RUN;
```

```
PROC FREQ DATA=STUDY NOPRINT;
TABLES GROUP / OUT=GROUPN;
RUN;
ODS LISTING;

DATA STUDYRES;
MERGE
CI12 (WHERE=(GROUP='A') RENAME=(FAILURE=FAIL_A12 FLCL=FLCL_A12 FUCL=FUCL_A12)
KEEP=GROUP FAILURE FLCL FUCL)
CI12 (WHERE=(GROUP='C') RENAME=(FAILURE=FAIL_C12 FLCL=FLCL_C12 FUCL=FUCL_C12)
KEEP=GROUP FAILURE FLCL FUCL)
CI12 (WHERE=(GROUP='E') RENAME=(FAILURE=FAIL_E12 FLCL=FLCL_E12 FUCL=FUCL_E12)
KEEP=GROUP FAILURE FLCL FUCL)
CI24 (WHERE=(GROUP='A') RENAME=(FAILURE=FAIL_A24 FLCL=FLCL_A24 FUCL=FUCL_A24)
KEEP=GROUP FAILURE FLCL FUCL)
CI24 (WHERE=(GROUP='C') RENAME=(FAILURE=FAIL_C24 FLCL=FLCL_C24 FUCL=FUCL_C24)
KEEP=GROUP FAILURE FLCL FUCL)
CI24 (WHERE=(GROUP='E') RENAME=(FAILURE=FAIL_E24 FLCL=FLCL_E24 FUCL=FUCL_E24)
KEEP=GROUP FAILURE FLCL FUCL)
CI36 (WHERE=(GROUP='A') RENAME=(FAILURE=FAIL_A36 FLCL=FLCL_A36 FUCL=FUCL_A36)
KEEP=GROUP FAILURE FLCL FUCL)
CI36 (WHERE=(GROUP='C') RENAME=(FAILURE=FAIL_C36 FLCL=FLCL_C36 FUCL=FUCL_C36)
KEEP=GROUP FAILURE FLCL FUCL)
CI36 (WHERE=(GROUP='E') RENAME=(FAILURE=FAIL_E36 FLCL=FLCL_E36 FUCL=FUCL_E36)
KEEP=GROUP FAILURE FLCL FUCL)
HRAC (RENAME=(HAZARDRATIO=HR_AC HRLOWERCL=HRL_AC HRUPPERCL=HRU_AC)
KEEP=HAZARDRATIO HRLOWERCL HRUPPERCL)
HRCE (RENAME=(HAZARDRATIO=HR_CE HRLOWERCL=HRL_CE HRUPPERCL=HRU_CE)
KEEP=HAZARDRATIO HRLOWERCL HRUPPERCL)
HRAE (RENAME=(HAZARDRATIO=HR_AE HRLOWERCL=HRL_AE HRUPPERCL=HRU_AE)
KEEP=HAZARDRATIO HRLOWERCL HRUPPERCL)
LOGRANKAE (WHERE=(TEST='Log-Rank') RENAME=(ProbChiSq=LOGRANKAE) KEEP=TEST
ProbChiSq)
LOGRANKCE (WHERE=(TEST='Log-Rank') RENAME=(ProbChiSq=LOGRANKCE) KEEP=TEST
ProbChiSq)
GROUPN (WHERE=(GROUP='A') RENAME=(COUNT=GROUPA_SS) KEEP=GROUP COUNT)
GROUPN (WHERE=(GROUP='B') RENAME=(COUNT=GROUPB_SS) KEEP=GROUP COUNT)
GROUPN (WHERE=(GROUP='C') RENAME=(COUNT=GROUPC_SS) KEEP=GROUP COUNT)
GROUPN (WHERE=(GROUP='D') RENAME=(COUNT=GROUPD_SS) KEEP=GROUP COUNT)
GROUPN (WHERE=(GROUP='E') RENAME=(COUNT=GROUPE_SS) KEEP=GROUP COUNT)
GROUPN (WHERE=(GROUP='F') RENAME=(COUNT=GROUPF_SS) KEEP=GROUP COUNT)
;

DROP GROUP TEST;
RUN;

%MEND;


*% ASSUMPTIONS CAME FROM QUESTIONS ASKED OF 2 CHINESE, 1 INDIAN, AND 1
BELARUSSION PHYSICIANS.  THEY WERE ASKED TO ESTIMATE %
    AT THEIR CENTER, THEN IN THE REST OF THEIR COUNTRY.  iT IS ASSUMED THAT
1/3 OF THE PTS WILL BE CHINA, 1/3 INDIA, AND 1/3 THE REST.

% OF SECONDARY:
Chasnoits: 75% HIS CENTER / 75% OTHERS
```

```
BALBIR: 70/80
ZHANGE: 50/50
HUANG: 30/55
52% CHINA, 78% INDIA, AND 75% ROW = 68%

% OF SECONDARY THAT GET IMPLANTED:
Chasnoits: 98/90
BALBIR: 80/45
ZHANGE: 50/15
HUANG: 50/30
30% CHINA, 50% INDIA, 91% ROW = 57%

% OF 1.5 THAT GET IMPLANTED:
Chasnoits: 65/65
BALBIR: NO GUESS
ZHANGE: 60/25
HUANG: 40/30
30% CHINA, 40% INDIA, 65% ROW = 45%

% OF 1.0 THAT GET IMPLANTED:
Chasnoits: 40/40
BALBIR: 15/5
ZHANGE: 40/10
HUANG: 30/30
20% CHINA, 6% INDIA, 40% ROW = 22%
;

%MACRO LOOP(NUM,SS,PROBSEC,YEARSENROLL,YEARSFOLLOW);
DATA ALLSTUDIES;
RUN;

%DO X = 1 %TO &NUM;
%STUDY(
SS=&SS,
PROBSEC=&PROBSEC,
PROB15=0.5,
IMPSEC=0.57,
IMP15=0.45,
IMPPRIM=0.22,
/*FAIL VARIABLES BELOW WERE CHOSEN TO BEST MATCH THE 12-MONTH FAILURE RATES
AND THE HAZARD RATIOS IN OMNI.  HR OF C TO A WAS 0.909.  HR OF E TO C WAS
0.678*/
FAILA12=0.225,
FAILALONG=0.1110,
HRAC=0.91,
HRCE=0.68,
YEARSENROLL=&YEARSENROLL,
YEARLYATTRITION=0.1,
YEARSFOLLOW=&YEARSFOLLOW);

DATA ALLSTUDIES;
SET ALLSTUDIES STUDYRES;
RUN;
%END;

DATA RESULTS;
SET ALLSTUDIES;
```

```
WHERE FAIL_A12 NE .;

*IF WE WANT STUDY RESULT TO BE THAT C IS CLOSER TO A THAN IT IS TO E;
    *BASED ON DIFFERENCES AT 36 MONTHS.  TOO UNSTABLE TO USE: SOMETIMES
FAIL_E > FAIL_C, YET HR_CE IS STILL <1;
/*        DIFFAC=FAIL_A-FAIL_C;*/
/*        DIFFCE=FAIL_C-FAIL_E;*/
/*        IF FAIL_E>0 THEN DO;*/
/*            IF DIFFCE>DIFFAC THEN OBS_SUCCESS=1; ELSE OBS_SUCCESS=0;*/
/*        END;*/
/*        ELSE DO;*/
/*            IF DIFFAC<0.04 THEN OBS_SUCCESS=1; ELSE OBS_SUCCESS=0;    */
/*        END;*/

    IF HR_AC>1 THEN OBS_SUCCESS2=1;
    ELSE IF FAIL_E12>0 THEN DO;
        IF HR_AC > HR_CE THEN OBS_SUCCESS2=1; ELSE OBS_SUCCESS2=0;
    END;
    ELSE DO;
        IF HR_AC> 0.9 THEN OBS_SUCCESS2=1; ELSE OBS_SUCCESS2=0;
    END;
    LABEL OBS_SUCCESS2='SUCEESSFUL TRIAL?  SUCCESS BASICALLY DEFINED AS HR OF
C TO A HIGHER THAN E TO C';

*NON-INFERIORITY TEST - MARGINS OF 20, 25, AND 30%;
    IF HRL_AC>0.7 THEN NONINF70=1; ELSE NONINF70=0;
    IF HRL_AC>0.75 THEN NONINF75=1; ELSE NONINF75=0;
    IF HRL_AC>0.8 THEN NONINF80=1; ELSE NONINF80=0;
    IF HRL_AC>0.85 THEN NONINF85=1; ELSE NONINF85=0;
    IF HRL_AC>0.9 THEN NONINF90=1; ELSE NONINF90=0;

*SUCCESS IF 2.0 IS HIGHER THAN 1.0 AND 1.5 IS HIGHER THAN 1.0;
    IF LOGRANKAE<0.05 AND LOGRANKCE<0.05 AND HR_CE<1 THEN SUPSUCCESS=1;
    ELSE IF LOGRANKAE<0.05 AND HR_AE<1 THEN SUPSUCCESS=0.2;
    ELSE IF LOGRANKCE<0.05 AND HR_CE<1 THEN SUPSUCCESS=0.1;
    ELSE SUPSUCCESS=0;

*OPC SUCCESS;
IF FLCL_C12>0.15 THEN OPC15SUCCESS12=1; ELSE OPC15SUCCESS12=0;
IF FLCL_C24>0.15 THEN OPC15SUCCESS24=1; ELSE OPC15SUCCESS24=0;
IF FLCL_C36>0.15 THEN OPC15SUCCESS36=1; ELSE OPC15SUCCESS36=0;
IF FLCL_C12>0.20 THEN OPC20SUCCESS12=1; ELSE OPC20SUCCESS12=0;
IF FLCL_C24>0.20 THEN OPC20SUCCESS24=1; ELSE OPC20SUCCESS24=0;
IF FLCL_C36>0.20 THEN OPC20SUCCESS36=1; ELSE OPC20SUCCESS36=0;
IF FLCL_C12>0.25 THEN OPC25SUCCESS12=1; ELSE OPC25SUCCESS12=0;
IF FLCL_C24>0.25 THEN OPC25SUCCESS24=1; ELSE OPC25SUCCESS24=0;
IF FLCL_C36>0.25 THEN OPC25SUCCESS36=1; ELSE OPC25SUCCESS36=0;

*NARROW CONFIDENCE INTERVAL SUCCESS;
CIWIDTH12=FUCL_C12-FLCL_C12;
CIWIDTH24=FUCL_C24-FLCL_C24;
CIWIDTH36=FUCL_C36-FLCL_C36;
IF CIWIDTH12<0.05 THEN CI05SUCCESS12=1; ELSE CI05SUCCESS12=0;
IF CIWIDTH24<0.05 THEN CI05SUCCESS24=1; ELSE CI05SUCCESS24=0;
IF CIWIDTH36<0.05 THEN CI05SUCCESS36=1; ELSE CI05SUCCESS36=0;
IF CIWIDTH12<0.08 THEN CI08SUCCESS12=1; ELSE CI08SUCCESS12=0;
IF CIWIDTH24<0.08 THEN CI08SUCCESS24=1; ELSE CI08SUCCESS24=0;
```

```
IF CIWIDTH36<0.08 THEN CI08SUCCESS36=1; ELSE CI08SUCCESS36=0;
IF CIWIDTH12<0.10 THEN CI10SUCCESS12=1; ELSE CI10SUCCESS12=0;
IF CIWIDTH24<0.10 THEN CI10SUCCESS24=1; ELSE CI10SUCCESS24=0;
IF CIWIDTH36<0.10 THEN CI10SUCCESS36=1; ELSE CI10SUCCESS36=0;
IF CIWIDTH12<0.12 THEN CI12SUCCESS12=1; ELSE CI12SUCCESS12=0;
IF CIWIDTH24<0.12 THEN CI12SUCCESS24=1; ELSE CI12SUCCESS24=0;
IF CIWIDTH36<0.12 THEN CI12SUCCESS36=1; ELSE CI12SUCCESS36=0;
IF CIWIDTH12<0.15 THEN CI15SUCCESS12=1; ELSE CI15SUCCESS12=0;
IF CIWIDTH24<0.15 THEN CI15SUCCESS24=1; ELSE CI15SUCCESS24=0;
IF CIWIDTH36<0.15 THEN CI15SUCCESS36=1; ELSE CI15SUCCESS36=0;
RUN;

TITLE "SAMPLE SIZE IS &SS, PROBSEC=&PROBSEC, YEARS OF ENROLLMENT:
&YEARSENROLL, YEARS OF FOLLOW-UP: &YEARSFOLLOW";

PROC FREQ;
TABLES OBS_SUCCESS2 NONINF70 NONINF75
OPC15SUCCESS12 OPC15SUCCESS24 OPC15SUCCESS36
OPC20SUCCESS12 OPC20SUCCESS24 OPC20SUCCESS36
OPC25SUCCESS12 OPC25SUCCESS24 OPC25SUCCESS36
CI05SUCCESS12 CI05SUCCESS24 CI05SUCCESS36
CI08SUCCESS12 CI08SUCCESS24 CI08SUCCESS36
CI10SUCCESS12 CI10SUCCESS24 CI10SUCCESS36
CI12SUCCESS12 CI12SUCCESS24 CI12SUCCESS36
CI15SUCCESS12 CI15SUCCESS24 CI15SUCCESS36;
RUN;

PROC MEANS N MEAN MEDIAN MAXDEC=3 DATA=ALLSTUDIES;
VAR FAIL_A12 FAIL_C12 FAIL_E12 FAIL_A24 FAIL_C24 FAIL_E24 HR_AC HR_CE
GROUPA_SS GROUPB_SS GROUPC_SS GROUPD_SS GROUPE_SS GROUPF_SS;
RUN;
%MEND;



%LOOP(10000,SS=4000,PROBSEC=0.6,YEARSENROLL=1.97,YEARSFOLLOW=2);
%LOOP(10000,SS=4050,PROBSEC=0.6,YEARSENROLL=1.99,YEARSFOLLOW=2);
%LOOP(10000,SS=4100,PROBSEC=0.6,YEARSENROLL=2.01,YEARSFOLLOW=2);
%LOOP(10000,SS=4150,PROBSEC=0.6,YEARSENROLL=2.02,YEARSFOLLOW=2);
%LOOP(10000,SS=4200,PROBSEC=0.6,YEARSENROLL=2.04,YEARSFOLLOW=2);
%LOOP(10000,SS=4250,PROBSEC=0.6,YEARSENROLL=2.06,YEARSFOLLOW=2);
%LOOP(10000,SS=4300,PROBSEC=0.6,YEARSENROLL=2.07,YEARSFOLLOW=2);
%LOOP(10000,SS=4350,PROBSEC=0.6,YEARSENROLL=2.09,YEARSFOLLOW=2);
%LOOP(10000,SS=4400,PROBSEC=0.6,YEARSENROLL=2.11,YEARSFOLLOW=2);
%LOOP(10000,SS=4450,PROBSEC=0.6,YEARSENROLL=2.12,YEARSFOLLOW=2);
%LOOP(10000,SS=4500,PROBSEC=0.6,YEARSENROLL=2.14,YEARSFOLLOW=2);
%LOOP(10000,SS=4550,PROBSEC=0.6,YEARSENROLL=2.16,YEARSFOLLOW=2);
%LOOP(10000,SS=4600,PROBSEC=0.6,YEARSENROLL=2.18,YEARSFOLLOW=2);
%LOOP(10000,SS=4650,PROBSEC=0.6,YEARSENROLL=2.19,YEARSFOLLOW=2);
%LOOP(10000,SS=4700,PROBSEC=0.6,YEARSENROLL=2.21,YEARSFOLLOW=2);
%LOOP(10000,SS=4750,PROBSEC=0.6,YEARSENROLL=2.23,YEARSFOLLOW=2);
%LOOP(10000,SS=4800,PROBSEC=0.6,YEARSENROLL=2.24,YEARSFOLLOW=2);
%LOOP(10000,SS=4850,PROBSEC=0.6,YEARSENROLL=2.26,YEARSFOLLOW=2);
%LOOP(10000,SS=4900,PROBSEC=0.6,YEARSENROLL=2.28,YEARSFOLLOW=2);
%LOOP(10000,SS=4950,PROBSEC=0.6,YEARSENROLL=2.29,YEARSFOLLOW=2);
%LOOP(10000,SS=5000,PROBSEC=0.6,YEARSENROLL=2.31,YEARSFOLLOW=2);
```

```
/*


%macro plot(name);
%LOOP(1,SS=3000,YEARSENROLL=1.6,YEARSFOLLOW=1);
DATA JJJ;
SET STUDY;
IF SURVTIME=. THEN DELETE;
IF GROUP='A' THEN G=1;
IF GROUP='C' THEN G=2;
IF GROUP='E' THEN G=3;
RUN;

PROC FORMAT;
VALUE type 1='A' 2='C' 3='E';
RUN;

PROC PRINT DATA=RESULTS;
VAR HR_AC   HR_CE;
RUN;

%MKMPlot(indata=JJJ,
        TRT=G,
            TRTfmt= TYPE.,
        PlotType=failure,
            SubjectID=PT,
            TimeToEvent=SURVTIME,
            EventIND=FAIL,
            Censored=0,
        ShowHazardRatio=Y,
        ShowLogRankPvalue=n,
        ShowCI=Y,
        SurvivalRateDataPointsSwap=y,
            xaxismax=36,xaxisby=6,
            Yaxismax=0.50,Yaxisby=.10,
        yaxislabel=%nrbquote(% with Appropriately Treated VT/VF),
        xaxislabel=%nrbquote(Months Since Implant),
            SubjectsatRiskBy=6,
            GraphfilePath=V:\Improve SCA\Sample Size,
        GraphFilename=&name,
        SurvivalRateDataPoints=12$24$36$48$60$72,
        StopPlotCount=20,
        AtRiskText=%str(Number Reamining)
                  );
%mend;

%PLOT(SIM1);
%PLOT(SIM2);
%PLOT(SIM3);
%PLOT(SIM4);
```

```
%PLOT(SIM5);
%PLOT(SIM6);
%PLOT(SIM7);
%PLOT(SIM8);
%PLOT(SIM9);
%PLOT(SIM10);
%PLOT(SIM11);
%PLOT(SIM12);
%PLOT(SIM13);
%PLOT(SIM14);
%PLOT(SIM15);
%PLOT(SIM16);
%PLOT(SIM17);
%PLOT(SIM18);
%PLOT(SIM19);
%PLOT(SIM20);




/*




PROC LIFETEST DATA=STUDY;
STRATA GROUP;
TIME SURVTIME*FAIL(0);
RUN;

PROC FREQ DATA=STUDY;
TABLES IMPDT;
RUN;

PROC PRINT DATA=STUDY;
WHERE GROUP IN ('A','C','E') AND SURVTIME=.;
RUN;

PROC SORT DATA=STUDY;
BY IMPDT;
RUN;

PROC PRINT DATA=STUDY;
VAR PT IMPDT ENDDT FAILMONTH ATRMONTH SURVTIME FAIL;
RUN;




*GET A VS. C ONLY;
DATA JJJ;
SET STUDY;
IF SURVTIME=. THEN DELETE;
IF GROUP='E' THEN DELETE;
IF GROUP='A' THEN G=1;
```

```
IF GROUP='C' THEN G=2;
IF GROUP='E' THEN G=3;
RUN;

PROC FORMAT;
VALUE type 1='A' 2='C' 3='E';
RUN;

%MKMPlot(indata=JJJ,
        TRT=G,
            TRTfmt= TYPE.,
        PlotType=failure,
            SubjectID=PT,
            TimeToEvent=SURVTIME,
            EventIND=FAIL,
            Censored=0,
        ShowHazardRatio=Y,
        ShowLogRankPvalue=y,
        ShowCI=Y,
        SurvivalRateDataPointsSwap=y,
            xaxismax=36,xaxisby=6,
            Yaxismax=0.50,Yaxisby=.10,
        yaxislabel=%nrbquote(% with Appropriately Treated VT/VF),
        xaxislabel=%nrbquote(Months Since Implant),
            SubjectsatRiskBy=6,
            GraphfilePath=V:\Improve SCA\Sample Size,
        GraphFilename=SIMULATIONAC,
        SurvivalRateDataPoints=12$24$36$48$60$72,
        StopPlotCount=20,
        AtRiskText=%str(Number Reamining)
                  );



*GET C VS. E ONLY;
DATA JJJ;
SET STUDY;
IF SURVTIME=. THEN DELETE;
IF GROUP='A' THEN DELETE;
IF GROUP='A' THEN G=1;
IF GROUP='C' THEN G=2;
IF GROUP='E' THEN G=3;
RUN;

PROC FORMAT;
VALUE type 1='A' 2='C' 3='E';
RUN;

%MKMPlot(indata=JJJ,
        TRT=G,
            TRTfmt= TYPE.,
        PlotType=failure,
            SubjectID=PT,
            TimeToEvent=SURVTIME,
            EventIND=FAIL,
            Censored=0,
```

```
ShowHazardRatio=Y,
ShowLogRankPvalue=y,
ShowCI=Y,
SurvivalRateDataPointsSwap=y,
    xaxismax=36,xaxisby=6,
    Yaxismax=0.50,Yaxisby=.10,
yaxislabel=%nrbquote(% with Appropriately Treated VT/VF),
xaxislabel=%nrbquote(Months Since Implant),
    SubjectsatRiskBy=6,
    GraphfilePath=V:\Improve SCA\Sample Size,
GraphFilename=SIMULATIONCE,
SurvivalRateDataPoints=12$24$36$48$60$72,
StopPlotCount=20,
AtRiskText=%str(Number Reamining)
          );
```