Power Calculations for Project Proposals for Gen2 Ex11 / Omni1 Ex6

This document and an accompanying Excel workbook "**power calculations Ex11, Ex6 continuous X.xlsx**" give results from power calculations to facilitate your grant proposal development. The projected attendance is 1185 participants as detailed in separate documents.

For these calculations, **we assume that the primary predictor variable, X, has a continuous distribution and we assume X has been standardized (i.e., mean=0, SD=1).** The power calculation results are reported using the **Minimum Detectable Effect (MDE)** for three types of analyses: **linear regression of continuous Y on X, logistic regression of binary Y (0,1) on X, and proportional hazards [Cox] regression of time to event on X**.

MDE is the smallest value of the population parameter that corresponds with pre-specified statistical power under stipulated conditions. **For linear regression, we show MDE as a partial correlation coefficient; for logistic regression, we show the odds ratio per unit X; and for Cox regression, we show the hazards ratio per unit X.**

If you have discrete X, either binary or multi-category, please use SAS PROC POWER or other power-calculation software for your setting.

Generally, the provided tables cover four **sample sizes (N=1185, 889, 593 and 296)**, six values for the **statistical significance threshold (alpha = 5.0E-02 down to 5.0E-08** by powers of 10), and two values for **statistical power (0.80 and 0.90)**. For binary outcomes and time-to-event outcomes, the expected number of "events" also comes into play. *Probably a small subset of these combinations suits your individual proposal: choose those that seem appropriate.*

Sample Size. Four sample sizes cover a broad range of inclusion/exclusion filters and subset selection that represent the full sample stepping down to a 25% sub-sample. *You can pick one or more sample sizes that fit your specific proposal, or you can interpolate MDEs between two sample sizes if necessary.*

Alpha. Six values were chosen for alpha to cover a single hypothesis test at conventional statistical significance level 5% (alpha=5E-02) stepping down to the commonly used criterion for genome-wide association testing (alpha=5E-08). For each specific aim in your proposal, you might assess the total number of statistical tests as (number of response variables) * (number of predictors to test). Then you might calculate a Bonferroni significance threshold such as $alpha^{+}$ = 5.0E-2 / (number of tests). *Pick the tabulated alpha closest to your* $alpha^{+}$ *or interpolate the MDE between two alpha values that bracket yours.*

Power. The tables show MDE for power 0.80 and 0.90.

<u>1. Linear Models: see the Linear tab in the workbook.</u> We assume a multiple linear regression model with Y versus X plus 10 covariates (e.g., Z_1 to Z_{10}). Note that MDE expressed as partial correlation is especially useful because it is independent of R^2(Y on X, Z) and of R^2 (X on Z); also, with these large sample sizes, MDE is almost invariant to the number of covariates.

The MDE for partial correlation of Y with X, when the sample is 100% (N=1185), significance level alpha=0.05 for which power is 0.80, is MDE = 0.082 (see top panel, top left – that is, row 6, column D). Even accounting for 100 tests, such that alpha = 5.0E-04, the MDE= 0.126 (ro2 6, column F), still modest.

As the table shows, MDE increases as sample size decreases (MDE is 41% larger for N=593 vs N=1185, and 100% larger for N=296 vs N=1185), and it increases as significance level decreases (MDE is about 2-fold as large for alpha=5E-08 than for alpha=5E-02); the MDE is modestly larger for 90% power than for 80% power (7% to 15 % increase with parameters specified for this table).

2. Logistic models: see the Logistic tab in the workbook. For a binary response variable (Y is 0 or 1), we use the setting of a multiple logistic regression model, regressing log odds (Y=1) versus {X plus 10 covariates}. We assume that covariates explain 25% of variance of the primary predictor X. In this setting, power depends on one additional parameter, the probability of response: we examine 10%, 20% and 30% response probabilities. To simplify calculations, we use Pr(Y = 1 at the mean of X, namely X=0).

The MDE is the odds ratio per 1 unit of X (i.e., 1 SD of X). For example, with N=1185 and 10% response probability, with a test at 5% significance level, for 80% power, the MDE is an odds ratio of 1.37 (see top panel, top left; row 6, column E).

With the set of parameters reported in this table, the MDE increases as sample size decreases, and as significance level decreases, as the probability of response decreases, and MDE increases as desired power increases. Note that the MDE may be large when response probability is low and/or number of tests is large.

3. Time to event (Cox) models: see the Cox tab in the workbook. Some of the research proposals involve events that will occur during follow up after the baseline examination. Therefore, we also provide power calculations for Cox models to handle that situation. As before, we assume that X has been standardized to mean=0 and SD=1. Here, we express the MDE as the hazards ratio (HR) for the event per 1 unit of X (i.e., 1 SD of X). We assume that covariates explain 25% of the variance of the primary predictor X.

In addition to the usual parameters (sample size, alpha, power), to carry out power calculations we need to know the expected number of events, say d. We can express d = N * event rate (%), where the event rate is the percentage of participants that we expect to have an event over some time frame (such as 1, 2 or 5 years).

For instance, we want to detect an association of event hazard rate with predictor X, using a test at 5% significance level, and we want 80% power. With sample size N=1185, if the expected event rate is 4% during the follow up period (top panel, top left – row 6, column D), then the MDE is HR=1.60 per 1 SD of X; note that if the expected event rate is higher, say 10% (row 8, column D), the MDE is 1.35).

The hazards ratio MDE decreases as the event count increases since more events corresponds with more information for testing association. This is true whether due to higher event rate or longer follow up. As in linear and logistic models, the MDE increases as alpha decreases, and as the desired power increases. Note that the MDE is high when the expected even count is low; even when testing with a 5% significance level, a fairly large number of events is needed to have power 80% to detect association when HR is moderate, say < 1.50.

REFERENCES

1. F. Y. Hsieh, Daniel A. Bloch and Michael D. Larson. A Simple Method of Sample Size Calculation for Linear and Logistic Regression. Statistics in Medicine, 17:1623-1634 (1998).

2. F.Y. Hsieh and Philip W. Lavori. Sample-Size Calculations for the Cox Proportional Hazards Regression Model with Nonbinary Covariates. Controlled Clinical Trials, 21:552–560 (2000).