Power Analysis

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# Notes

* Feb 18, 2021: I have only run models assuming between-cluster variance of about 10%. I am guessing that this is a high estimate. Also, I have assumed that we will have all 300 participants in both arms with the outcome variable not missing. Future analyses should consider other estimates of between-cluster variance and should evaluate the potential impact of attrition.
* Feb 21, 2021: I added a simulation estimating power for the GEE model in which reSET-O yields a reduction in the OR of 40% with only 5% of the total variance between cluster (as opposed to the 10% I had assumed before). With a 5% between-cluster variance, we could expect to detect a 40% reduction in odds with approximately , the target power.

# Prepare workspace

Load the required packages.

require( clusterPower )  
require( powerSurvEpi )

# GEE Models

## 10% Between-Cluster Variance

Each of the models in this section assume that the between-cluster variance accounts for 10% of the total variance within both the reSET-O and TAU groups.

### GEE Model Assuming OR=0.50

Estimate power for rejecting the null hypothesis that difference in the odds of non-abstinence (0=abstinent; 1=used drugs) across the reSET-O and treatment as usual care (TAU) conditions is 0 at weeks 9-12 of the study. The model assumes the following:

* Random allocation of half the total cluster (k=6) to reSET-O and half (k=6) to TAU
* Equal cluster sizes of 50 patients (300 patients in each group)
* Probability of non-abstinence in TAU assumed to be 40% based on [Maricich et al., 2020](https://www.tandfonline.com/doi/full/10.1080/03007995.2020.1846022)
* Probability of non-abstinence in reSET-O assumed to be 25% based on [Maricich et al., 2020](https://www.tandfonline.com/doi/full/10.1080/03007995.2020.1846022)
* This comes to an assumed odds ratio (OR) = 0.5, a 50% reduction in odds.

# geesim1 <- cps.binary( nsim = 1000,  
# nsubjects = 50, # 50 participants per cluster assuming equal sizes  
# nclusters = 6, # 6 clusters per treatment arm  
# p1=.40, # 40% non-abstinence rate in TAU in Maricich et al. (2020)  
# p2=.25, # 25% non-abstinence rate in reSET-0 group in Maricich et al. (2020)  
# sigma\_b\_sq=0.024, # variance = p(1-p)=0.24; assume 10% variance is between)  
# sigma\_b\_sq2=0.019, # variance = p(1-p)=0.1875; assume 10% variance is between)  
# alpha=.05,  
# method='gee',  
# quiet=F,  
# seed=0218211,  
# lowPowerOverride = TRUE)  
load( 'geesim1.RData' )  
geesim1["power"]

## $power  
## Power Lower.95.CI Upper.95.CI Alpha Beta Converged Requested  
## Arm.2 0.956 0.9413796 0.9678505 0.05 0.044 1000 1000

This simulation suggests that our power would be between 0.94-0.97 – i.e., well powered.

### GEE Model Assuming OR=0.55

Next, we will calculate power using a simulation assuming an in-between effect where reSET-O results in a ~45% reduction in the odds.

* Assume a 40% non-abstinence rate in TAU
* Assume a 27% non-abstinence rate in reSET-O
* Keep all of the rest of the assumptions the same as in the previous simulation

# geesim5 <- cps.binary( nsim = 1000,  
# nsubjects = 50, # 50 participants per cluster assuming equal sizes  
# nclusters = 6, # 6 clusters per treatment arm  
# p1=.40, # 40% non-abstinence rate in TAU in Maricich et al. (2020)  
# p2=.27, # 27% non-abstinence rate in reSET-0 group   
# sigma\_b\_sq=0.024, # variance = p(1-p)=0.24; assume 10% variance is between)  
# sigma\_b\_sq2=0.022, # variance = p(1-p)=0.21; assume 10% variance is between)  
# alpha=.05,  
# method='gee',  
# quiet=F,  
# seed=0218211,  
# lowPowerOverride = TRUE )  
load( 'geesim5.RData' )  
geesim5["power"]

## $power  
## Power Lower.95.CI Upper.95.CI Alpha Beta Converged Requested  
## Arm.2 0.875 0.852893 0.8948702 0.05 0.125 1000 1000

This simulation suggests that our power would be well-powered 0.85-0.89 to detect an OR=0.55.

### GEE Model Assuming OR=0.60

Next, we will calculate power using a simulation assuming an in-between effect where reSET-O results in a ~40% reduction in the odds.

* Assume a 40% non-abstinence rate in TAU
* Assume a 29% non-abstinence rate in reSET-O
* Keep all of the rest of the assumptions the same as in the previous simulation

# geesim4 <- cps.binary( nsim = 1000,  
# nsubjects = 50, # 50 participants per cluster assuming equal sizes  
# nclusters = 6, # 6 clusters per treatment arm  
# p1=.40, # 40% non-abstinence rate in TAU in Maricich et al. (2020)  
# p2=.29, # 29% non-abstinence rate   
# sigma\_b\_sq=0.024, # variance = p(1-p)=0.24; assume 10% variance is between)  
# sigma\_b\_sq2=0.021, # variance = p(1-p)=0.21; assume 10% variance is between)  
# alpha=.05,  
# method='gee',  
# quiet=F,  
# seed=0218211,  
# lowPowerOverride = TRUE )  
load( 'geesim4.RData' )  
geesim4["power"]

## $power  
## Power Lower.95.CI Upper.95.CI Alpha Beta Converged Requested  
## Arm.2 0.763 0.7353915 0.7890505 0.05 0.237 1000 1000

This simulation suggests that our power would be between 0.74-0.79 – i.e., approaching the goal of 0.80.

### GEE Model Assuming OR=0.65

Now we will calculate power using a simulation assuming an in-between effect where reSET-O results in a ~35% reduction in the odds.

* Assume a 40% non-abstinence rate in TAU
* Assume a 30% non-abstinence rate in reSET-O
* Keep all of the rest of the assumptions the same as in the previous simulation

# geesim3 <- cps.binary( nsim = 1000,  
# nsubjects = 50, # 50 participants per cluster assuming equal sizes  
# nclusters = 6, # 6 clusters per treatment arm  
# p1=.40, # 40% non-abstinence rate in TAU in Maricich et al. (2020)  
# p2=.30, # 30% non-abstinence rate  
# sigma\_b\_sq=0.024, # variance = p(1-p)=0.24; assume 10% variance is between)  
# sigma\_b\_sq2=0.021, # variance = p(1-p)=0.21; assume 10% variance is between)  
# alpha=.05,  
# method='gee',  
# quiet=F,  
# seed=0218211,  
# lowPowerOverride = TRUE )  
load( 'geesim3.RData' )  
geesim3["power"]

## $power  
## Power Lower.95.CI Upper.95.CI Alpha Beta Converged Requested  
## Arm.2 0.688 0.6582616 0.7166268 0.05 0.312 1000 1000

This simulation suggests that our power would be between 0.66-0.71 – i.e., moderately powered.

### GEE Model Assuming OR=0.80

Now we will calculate power using a simulation assuming a more modest effect where reSET-O results in a 20% reduction in the odds.

* Assume a 40% non-abstinence rate in TAU
* Assume a 35% non-abstinence rate in reSET-O
* Keep all of the rest of the assumptions the same as in the previous simulation

# geesim2 <- cps.binary( nsim = 1000,  
# nsubjects = 50, # 50 participants per cluster assuming equal sizes  
# nclusters = 6, # 6 clusters per treatment arm  
# p1=.40, # 40% non-abstinence rate in TAU in Maricich et al. (2020)  
# p2=.35, # 35% non-abstinence rate   
# sigma\_b\_sq=0.024, # variance = p(1-p)=0.24; assume 10% variance is between)  
# sigma\_b\_sq2=0.023, # variance = p(1-p)=0.2275; assume 10% variance is between)  
# alpha=.05,  
# method='gee',  
# quiet=F,  
# seed=0218211,  
# lowPowerOverride = TRUE )  
load( 'geesim2.RData' )  
geesim2["power"]

## $power  
## Power Lower.95.CI Upper.95.CI Alpha Beta Converged Requested  
## Arm.2 0.263 0.2359435 0.2914594 0.05 0.737 1000 1000

This simulation suggests that our power would be between 0.23-0.29 – i.e., poorly powered.

## 5% Between-Cluster Variance

In this section, we rerun the simulation models that fell short of the desired power () with 10% between-cluster variability assuming just 5% between-cluster variability, which seems more probably given the design.

### 

Rerun geesim4, which assumes a ~40% reduction in the odds but with only 5% of the total variance between clusters. The geesim4 model assuming 10% between-cluter variance yielded a power estimate (0.74-0.79) that fell just short of the goal.

* Assume a 40% non-abstinence rate in TAU
* Assume a 29% non-abstinence rate in reSET-O

# geesim6 <- cps.binary( nsim = 1000,  
# nsubjects = 50, # 50 participants per cluster assuming equal sizes  
# nclusters = 6, # 6 clusters per treatment arm  
# p1=.40, # 40% non-abstinence rate in TAU in Maricich et al. (2020)  
# p2=.29, # 29% non-abstinence rate in reSET-0  
# sigma\_b\_sq=0.012, # variance = p(1-p)=0.24; assume 5% variance is between)  
# sigma\_b\_sq2=0.010, # variance = p(1-p)=0.21; assume 5% variance is between)  
# alpha=.05,  
# method='gee',  
# quiet=F,  
# seed=0221211,  
# lowPowerOverride = TRUE )  
load( 'geesim6.RData' )  
geesim6["power"]

## $power  
## Power Lower.95.CI Upper.95.CI Alpha Beta Converged Requested  
## Arm.2 0.806 0.7801051 0.8300789 0.05 0.194 1000 1000

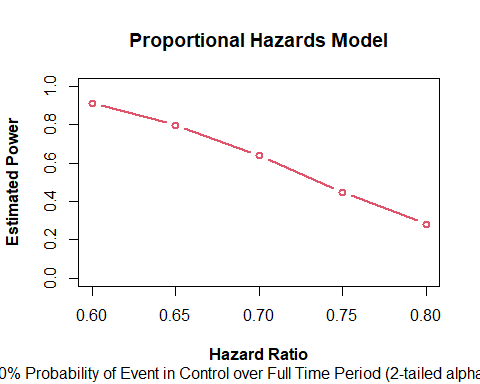
This simulation suggests that our power would be between 0.74-0.79 – i.e., approaching the goal of 0.80.

# Cox Propotional Hazards Model

These models should be taken with a **big** grain of salt. Power analysis for a proportional hazards model with individuals clustered within groups is a bit beyond my capabilities. I believe this would require simulations that are beyond my expertise. I ran a number of quick-and-dirty models varying the probability of an event (drug use) over the full follow-up period in the reSET-O group and the assumed hazard ratio. For all models, I assumed that 40% of TAU participants would have an event over the full follow-up. As with the previous examples, I am assuming 300 participants per treatment arm ().

The consequence of failing to account for clustering is having too small standard error estimates. I used a conservative to try to counteract this – a terribly unsophisticated approach. The [powerSurvEpi package](https://cran.r-project.org/web/packages/powerSurvEpi/powerSurvEpi.pdf) was used to obtain these estimates.

surv.80 <- powerCT.default(nE = 300,  
 nC = 300,  
 pE = 0.35,  
 pC = 0.40,  
 RR = 0.8,  
 alpha = 0.025 )  
surv.75 <- powerCT.default(nE = 300,  
 nC = 300,  
 pE = 0.33,  
 pC = 0.40,  
 RR = 0.75,  
 alpha = 0.025 )  
surv.70 <- powerCT.default(nE = 300,  
 nC = 300,  
 pE = 0.32,  
 pC = 0.40,  
 RR = 0.7,  
 alpha = 0.025 )  
surv.65 <- powerCT.default(nE = 300,  
 nC = 300,  
 pE = 0.30,  
 pC = 0.40,  
 RR = 0.65,  
 alpha = 0.025 )  
surv.60 <- powerCT.default(nE = 300,  
 nC = 300,  
 pE = 0.29,  
 pC = 0.40,  
 RR = 0.60,  
 alpha = 0.025 )  
  
plot( sort( seq(.80,.60,-.05), decreasing = T ),  
 c(surv.80[1], surv.75[1], surv.70[1], surv.65[1], surv.60[1]),  
 type='b',  
 ylim = c(0,1),  
 lwd=2,  
 col=2,  
 ylab='Estimated Power',  
 xlab='Hazard Ratio',  
 main='Proportional Hazards Model',  
 sub='40% Probability of Event in Control over Full Time Period (2-tailed alpha=.025)',  
 font.lab=2)



As can be seen in the plot above, these very unsophisticated power estimates suggest that we could detect a hazard ratio of approximately to achieve .