HW1ClinicalTrials

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3/21/2021

Problem 1: Consider the setting of a cardiovascular disease clinical trial conducted to compare the efficacy of two treatments in reducing the incidence of coronary heart disease (CHD) The outcome of interest is time from entry into the study to a diagnosis with CHD. Assume the following:

- The time-to-event of interest T is distributed according to an exponential distribution with parameters lambda0 and lambda1 in treatment groups 0 and 1, respectively.
- The median survival time in treatment group 0 is 6 years and that in treatment group 1 is 9 years
- A constant accrual rate of 120 subjects per year into your study Assuming that you would allocate subjects equally to both treatment groups, that the type I error rate is 0.05, power is 90%:

1) How many events are needed to satisfy the desired power of 90%?

```
#critical values
ZA2 <- abs(qnorm(p = .025, lower.tail = TRUE))
ZB <- abs(qnorm(p = 0.1, lower.tail = TRUE))

#hazard ratio
(lambda0 <- log(2)/6)
```

```
## [1] 0.1155245
```

```
(lambda1 <- log(2)/9)
```

```
## [1] 0.07701635
```

```
HR <- lambda1/lambda0

(d <- (4*(ZA2+ZB)^2)/log(HR)^2)
```

```
## [1] 255.652
```

The number of events needed to satisfy the desired power of 90% is approximately 256.

2) Assuming that there is no additional follow-up in the study (i.e. A = L), what is the number of subjects you would recruit into your study? How long would you plan for total follow up (i.e. L)?

```
L <- 7.48079
(events <- 60*(L - (exp(-0.1155245*L)/0.1155245)*(exp(0.1155245*L)- 1))+ 60*(L - (exp(-0.07701635*L)/0.0
```

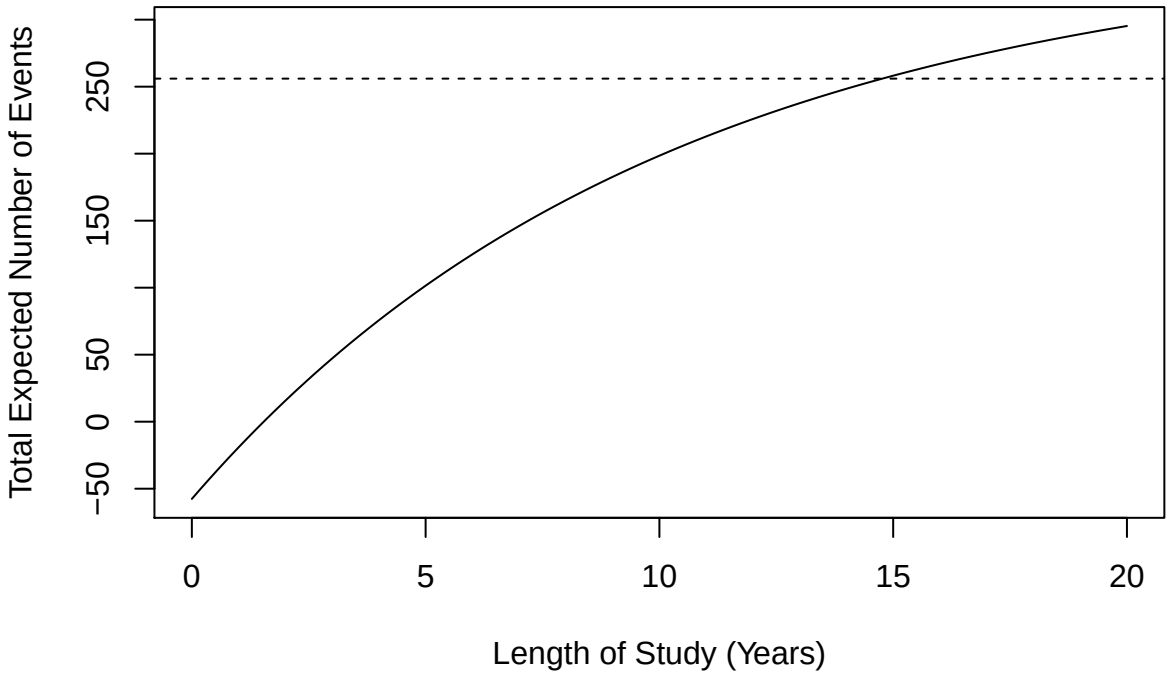
```
## [1] 256
```

then L = 7.48 years, the events equation is 256. I got this by solving for L in the above equation

So we would need to recruit

3) Assume that accrual would take 3 years (i.e. A = 3). Plot the total expected number of events in the study as a function of study length (L) in years.

```
curve(60*(3 - (exp(-0.1155245*x)/0.1155245)*(exp(0.1155245*3)- 1))+ 60*(3 - (exp(-0.07701635*x)/0.07701
abline(h = 256, lty = "dashed")
```



4) Assume that you would allocate subjects to treatment groups in the 1:4 ratio. How many events are needed to satisfy the desired power of 90%?

```
(d2 <- (ZA2+ZB)^2/(0.2*(1-0.2)*log(HR)^2))
```

```
## [1] 399.4563
```

Approximately 400 events are needed to satisfy the desired power of 90% with subjects being allocated into the treatment groups in a 1:4 ratio.

Problem 2) Consider a clinical trial comparing the efficacy of two cholesterol lowering drugs, A and B. 1. Find the sample size necessary to detect a difference in mean cholesterol levels. Delta = 60 mg/ml. standard deviation = 200 mg/ml. Assume a two-sided, 0.05 significance level and power of 80%. Use the function power.t.test in R

```
?power.t.test
```

```
## starting httpd help server ... done
```

```
power.t.test(delta= 60, sd = 200, power = .8, sig.level = 0.05, alternative = "two.sided")
```

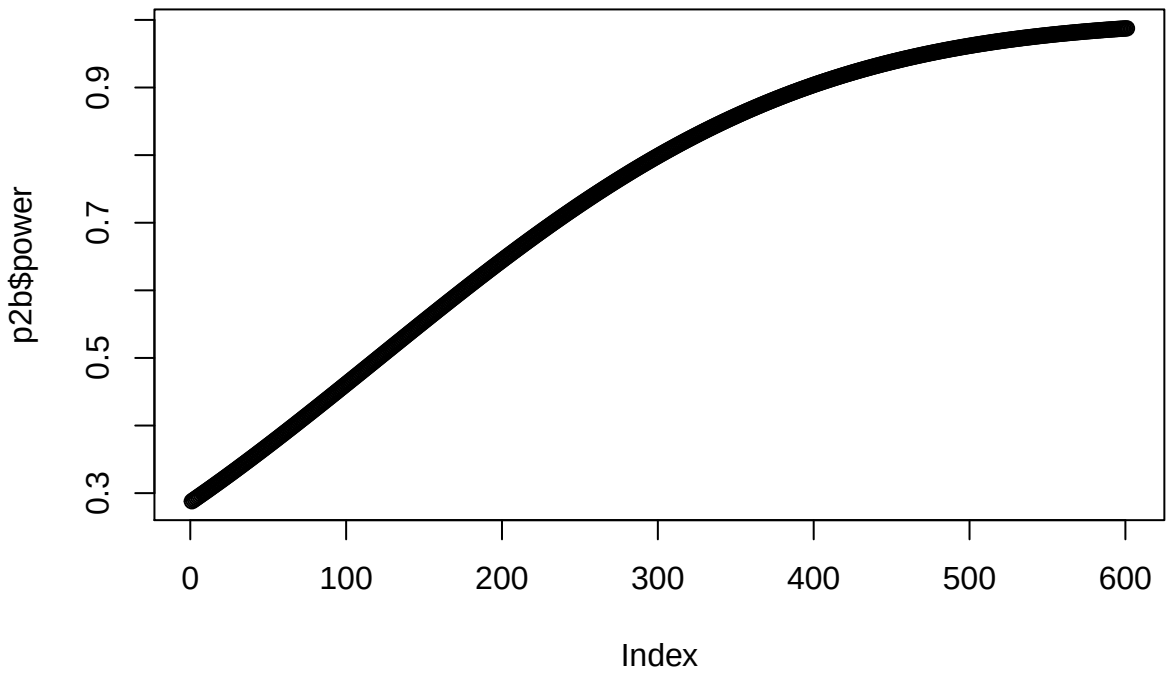
```
##
##      Two-sample t test power calculation
##
##               n = 175.3851
##           delta = 60
##              sd = 200
##       sig.level = 0.05
##           power = 0.8
##     alternative = two.sided
##
## NOTE: n is number in *each* group
```

The sample size needed would be 176.

2. Using same setting as above, assume delta varies between 30 mg/ml and 90 mg/ml. plot power curve and interpret findings.

```
p2b <- power.t.test(n = 175.3851, delta= seq(30, 90,by=0.1), sd = 200, sig.level = 0.05, alternative =

plot(p2b$power)
```

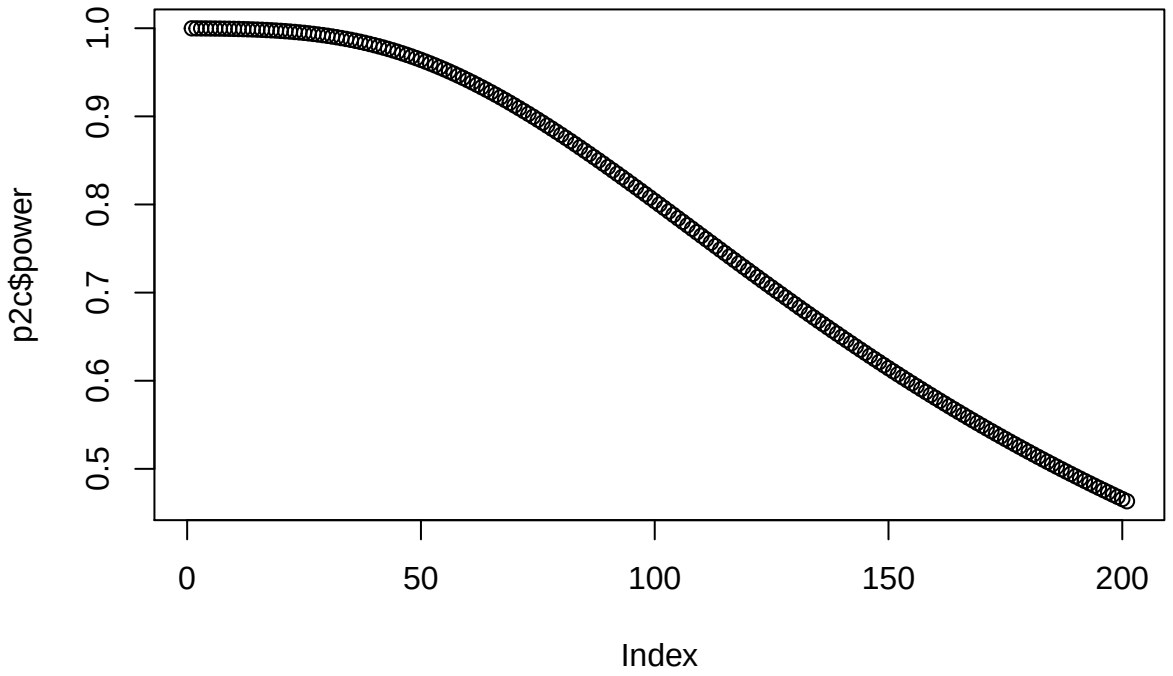


We see that power is the highest when the delta is higher and this is because it is more easy to detect a difference.

3. Assume standard deviation varies 100 and 300 mg/ml. plot power curve and interpret findings.

```
p2c <- power.t.test(n = 175.3851, delta= 60, sd = seq(100,300,by= 1), sig.level = 0.05, alternative = "

plot(p2c$power)
```



The power decreases as standard deviation increases because it is easier to reject the null hypothesis (easier to detect a difference) when the standard deviation is higher.