Lecture 5: Statistical power

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Intro to statistical power

Let's return to the setting of Lectures 2 & 3: n pairs of same-sex twins discordant for psoriasis and in x of the pairs the psoriatic individual has larger BMI than the non-psoriatic one.

Let's see how the sample size n affects our inference on the population-level proportion p of twin pairs where the psoriatic twin has a higher BMI than the non-psoriatic one. Let's consider two data sets with sample sizes of 20 and 100, and let's assume that the point estimate for the proportion in both cases is 70%. (That is, we have observed 14 and 70 successes from the data sets of sizes 20 and 100, respectively.) Let's do the binomial test in both data sets.

```
p.est = 0.70 #our point estimate, x/n, is 70% in both cases
n = c(20, 100) #two sample sizes
x = n*p.est #two observations, one for each sample size, both giving a point estimate of 70%
x #14 and 70
```

```
## [1] 14 70
```

```
binom.test(x[1], n[1])
```

```
##
##  Exact binomial test
##
## data:  x[1] and n[1]
## number of successes = 14, number of trials = 20, p-value = 0.1153
## alternative hypothesis: true probability of success is not equal to 0.5
## 95 percent confidence interval:
##  0.4572108 0.8810684
## sample estimates:
## probability of success
##                    0.7
```

```
binom.test(x[2], n[2])
```

```
##
##  Exact binomial test
##
## data:  x[2] and n[2]
## number of successes = 70, number of trials = 100, p-value = 7.85e-05
## alternative hypothesis: true probability of success is not equal to 0.5
```

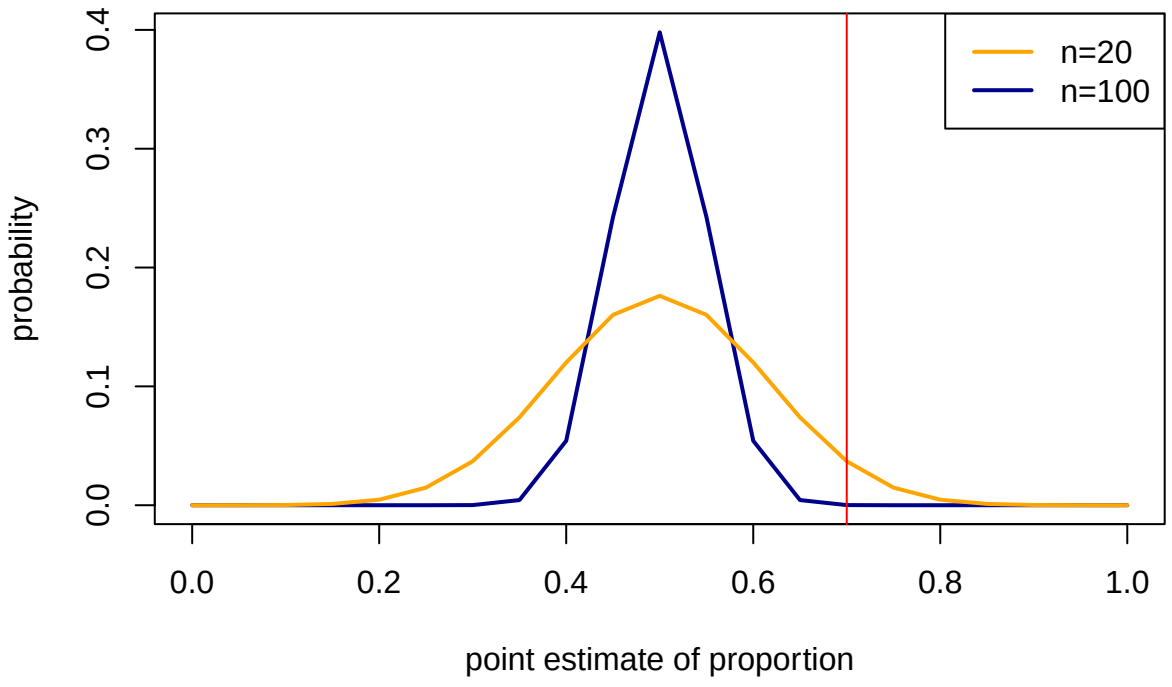
```
## 95 percent confidence interval:
##  0.6001853 0.7875936
## sample estimates:
## probability of success
##                    0.7
```

We see that the confidence interval around the point estimate 0.70 shrinks as the sample size n grows. This is because with larger n we have more information about where exactly the value of the population proportion parameter p is, and this is reflected in a smaller standard error and a narrower CI. With more information there is less uncertainty about the value of p. This is why statisticians always want to have a larger sample size.

There is also a striking difference in P-values (0.12 vs 8e-5). Let's try to understand why the sample size affects statistical testing and P-value.

The null hypothesis is that BMI and psoriasis are independent. This is equivalent to the assumption that the observed value x follows distribution Bin(n,$p = 0.5$), that is, x is distributed like the total number of heads in n tosses of a fair coin. Let's plot in the same figure the probability mass functions under the null hypothesis for possible point estimate values $\widehat{p} = x/n$ for the two sample sizes.

```
p.range = seq(0, 1, 0.05) #values at which density will be evaluated at steps of 1/20=0.05
n = c(20, 100)
y.1 = dbinom(p.range*n[1], size = n[1], p = 0.5) #null distribution when n = 20
y.2 = dbinom(p.range*n[2], size = n[2], p = 0.5) #null distribution when n = 100
#renormalize so that both distributions sum to 1 and are thus comparable
y.1 = y.1 / sum(y.1)
y.2 = y.2 / sum(y.2)
plot(p.range, y.2, col = "darkblue",t = "l", lwd = 2,
     xlab = "point estimate of proportion", ylab = "probability")
lines(p.range, y.1, col = "orange",t = "l", lwd = 2) #add line for n=20
legend("topright", legend = paste0("n=",n), col = c("orange","darkblue"), lty = 1, lwd = 2)
abline(v = 0.7, col = "red") # Mark observation 70% in red
```



We see that the null distribution for the larger sample size $n = 100$ is more concentrated near the null hypothesis value 0.5 than the distribution with $n = 20$. By looking at the probability mass to the right of the red line, we can conclude that if the true association between BMI and psoriasis in the populaiton was such that in 70% of discordant twin pairs the psoriatic one had a larger BMI, then, with the sample size $n = 100$, we would expect to distinguish that association from the null hypothesis with clear statistical evidence (small P-value because observation is so improbable under the blue null distribution), but, for $n = 20$, we might not distinguish it clearly (P-value can well be > 0.05 because the observation near 70% could happen also under the orange null distribution every now and then). We say that the larger sample size gives larger **statistical power** to detect a true deviation from the null hypothesis.

This logic is verified by the binomial tests above, where we saw that the P-values corresponding to the point estimate 70% in these two sample sizes are quite different: 0.12 for $n = 20$ but less than 1e-4 for $n = 100$.

Example 5.1. Suppose that the biomarker B is distributed according to N(1,1) in the healthy population and according to N(2,1) in the diabetes cases. Generate a random set of n samples from the healthy population and another sample of the same size from the diabetics. We know that the distributions have different means (namely, 1 and 2), and we want to see how statistically clearly we could detect that difference with different sample sizes. Test whether the means are different using a t-test when

(i) $n = 5$

(ii) $n = 25$

(iii) $n = 50$

Do the means look statistically different based on the P-values in these three scenarios?

```
ns = c(5, 25, 50)
for(n in ns){ #With for-loop we do not need to copy-paste the code separately for each value
  x.1 = rnorm(n, 1, 1) #healthy
  x.2 = rnorm(n, 2, 1) #diabetics
  print(paste("n =",n))
  print(t.test(x.1, x.2)) #Needs "print()" inside for-loop to print out the result of t-test.
}
```

```
## [1] "n = 5"
##
##  Welch Two Sample t-test
##
## data:  x.1 and x.2
## t = -2.2419, df = 7.0118, p-value = 0.05985
## alternative hypothesis: true difference in means is not equal to 0
## 95 percent confidence interval:
##  -2.09460386  0.05545062
## sample estimates:
## mean of x mean of y
##  0.857512  1.877089
##
## [1] "n = 25"
##
##  Welch Two Sample t-test
##
## data:  x.1 and x.2
## t = -2.3704, df = 43.329, p-value = 0.02229
```

```
## alternative hypothesis: true difference in means is not equal to 0
## 95 percent confidence interval:
##  -1.3441528 -0.1085158
## sample estimates:
## mean of x mean of y
##  1.297058  2.023392
##
## [1] "n = 50"
##
##  Welch Two Sample t-test
##
## data:  x.1 and x.2
## t = -5.4251, df = 97.976, p-value = 4.185e-07
## alternative hypothesis: true difference in means is not equal to 0
## 95 percent confidence interval:
##  -1.522608 -0.707022
## sample estimates:
## mean of x mean of y
##  1.041062  2.155877
```

Here the P-values get smaller with increasing sample size, reflecting that we will detect the same magnitude of true difference in means with more statistical evidence using a larger sample size than using a smaller sample size.

P-values and Type I error rate

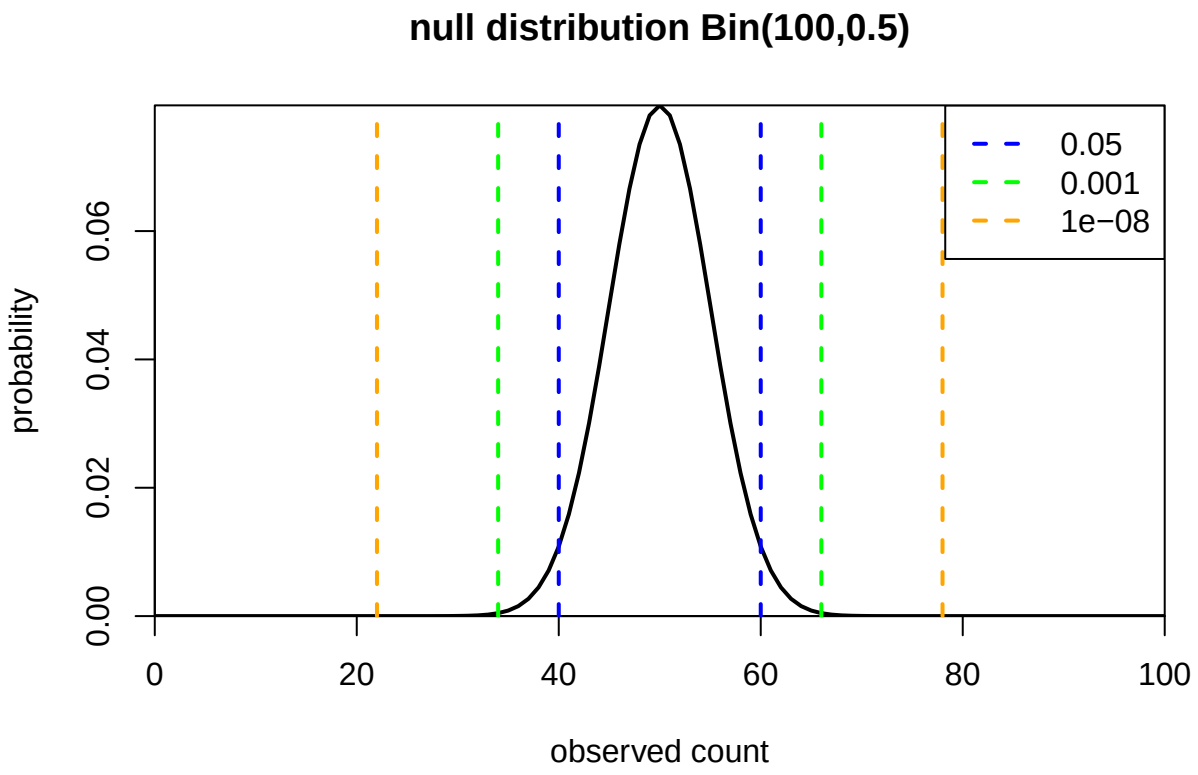
So far we have observed data and computed the P-value of observing such kind of data under the null hypothesis. The idea has been that if P-value is small, then the observed data seem unlikely to rise under the null hypothesis and hence we have a reason to suspect the null hypothesis.

We can also imagine a statistical testing procedure where, before seeing data and computing a P-value, we set a **significance level** (α, "alpha", e.g. 0.05, 0.01 or 0.001) and if the observed data reach that significance level (i.e. the computed P-value $\leq \alpha$), we "reject" the null hypothesis because it seems implausible. The motivation for pre-defining the significance level is that then the testing procedure has the following property: If the null hypothesis was true, then in repeated experiments we would falsely "reject" the null hypothesis for a proportion α of the experiments. By controlling α, we can control the level of false rejections of the null hypothesis. If $\alpha = 0.05$, then we would make a false call in about 1 out of every 20 of those experiments where the null hypothesis was actually true; if α is 0.001, then about 1 out of every 1000 cases where the null hypothesis is true were falsely rejected etc. The significance level α of the testing procedure is also called Type I error rate, since a false rejection of the null hypothesis is called a type I error. "**Type I error**: Falsely declaring an effect found when there truly is no effect."

Let's draw a picture of the null distribution of 100 flips of a fair coin, (analogous to twin pairs where higher BMI an psoriasis status go together), and mark the two-sided significance thresholds for values of $\alpha = 0.05$, 0.001 and 1e-8.

```
n = 100 # twin pairs
p0 = 0.5 # null hypothesis value for proportion
x = 0:n # plotting range 0,...,n
#Plot the null distribution
plot(x, dbinom(x, n, p0), t = "l", lwd = 2, main = "null distribution Bin(100,0.5)",
     xlab = "observed count", ylab = "probability", xaxs = "i", yaxs = "i")
#Plot thresholds corresponding to different significance levels using different colors
sig.threshold = c(0.05, 0.001, 1e-8)
```

```r
cols = c("blue", "green", "orange")
for(ii in 1:length(sig.threshold) ){ #goes through all sig.thresholds
  abline(v = qbinom(sig.threshold[ii]/2, n, p0),
         col = cols[ii], lwd = 2, lty = 2) #mark left cutpoint
  abline(v = qbinom(1-sig.threshold[ii]/2, n, p0),
         col = cols[ii], lwd = 2, lty = 2) # mark also right cutpoint
}
legend("topright", col = cols, legend = sig.threshold, lwd = 2, lty = 2)
```



We see that in order to get a significant deviation from the null hypothesis at significance level 0.05, we need to have either <40 or >60 successes. On the other hand, to get statistical significance at level 1e-8, we would need as extreme a result as <22 or >78 successes. This reflects the fact that we need much more evidence against the null in order to reject the null hypothesis at level 1e-8 than we need to reject the null at level 0.05. Consequently, we will make less Type I errors if our significance level is 1e-8 than if it is 0.05. But at the same time, at level 1e-8, we will miss some real deviations from the null hypothesis that we would detect at level 0.05. That is, we do more Type II errors at a lower significance level than at a higher significance level. "**Type II error**: Not rejecting the null hypothesis when it does not hold."

Typically, a significance level is chosen purely by Type I error rate, that is, by our tolerance for false rejection of the null hypothesis. This tolerance varies between contexts. In clinical trials, the significance level could be 0.05, but, for example, in genome-wide analyses we get excited about a new association between a genetic variant and a disease only when it reaches a significance level 5e-8 = 0.00000005! As another example, in 2012, the physicists claimed that they had "found" the Higgs' boson after they had gathered statistical evidence that reached their "5 sigma rule" (observation is 5 standard deviations away from the null hypothesis value) that corresponds to a significance level of 6e-7.

Rationale for such differences could be that, in a clinical trial, we only study one hypothesis (a therapy works) that possibly already has some prior evidence why it has been developed in the first place. Thus, we do not require a lot of additional statistical evidence at that point to get to the next step of the process, and we do not want to make a Type II error and miss a promising new therapy. In genome-wide analyses,

we are starting with a fishing experiment where we have millions of genetic variants and no prior evidence of any real association with diseases. Thus, we need a lot of statistical evidence to start believing that this one variant (out of millions of possible ones) is truly associated with the disease. Finally, with the Higgs' boson, we again have only one hypothesis to test, but here the price of making a wrong claim (Type I error) is large: Physicists don't want to publish a result about existence of a new particle unless they are (very) certain. Hence, they require much more statistical evidence from their experiment than clinical trials do.

Examples 5.2.

1. Your null hypothesis is that a coin is fair ($p = 50\%$). If you toss the coin n times and count the number of heads, what are the critical points below and above the null value 50% at which the outcome starts showing statistically significantly that the coin is biased, when

(i) $n = 10, \alpha = 0.05$

(ii) $n = 100, \alpha = 0.05$

(iii) $n = 10, \alpha = 0.0001$

(iv) $n = 100, \alpha = 0.0001$.

```
p = 0.5
ns = rep(c(10, 100), 2)
a = rep(c(0.05, 0.0001), each = 2)
for(ii in 1:length(ns)){ #for-loop over 4 sets of parameters n and alpha
  print(paste("n =",ns[ii],"alpha =",a[ii],": at most",
              qbinom(a[ii]/2, ns[ii], p) - 1,"or at least",
              qbinom(1 - a[ii]/2, ns[ii], p) + 1))
}
```

```
## [1] "n = 10 alpha = 0.05 : at most 1 or at least 9"
## [1] "n = 100 alpha = 0.05 : at most 39 or at least 61"
## [1] "n = 10 alpha = 1e-04 : at most -1 or at least 11"
## [1] "n = 100 alpha = 1e-04 : at most 30 or at least 70"
```

We see that, for $n = 10$, no observation can ever reach the significance level of $\alpha = 0.001$ as the critical points are outside the range 0,...,10.

2. Compute these critical points for a fixed $\alpha = 0.05$ as n goes through 10, 50, 100, 200, ... 1000. Compute which proportions they correspond to and show the results on screen.

```
a = 0.05
ns = c(10, 50, seq(100, 1000, 100))
res = c() #empty vector that will be filled to be a matrix with 3 columns:
#1st col = n; 2nd col = lower critical point; 3rd col = upper critical point
for(ii in 1:length(ns)){
  res = rbind(res,
              c(ns[ii], qbinom(a/2, ns[ii], p) - 1, qbinom(1 - a/2, ns[ii], p) + 1))
}
res[,2:3] = res[,2:3]/res[,1] #propotions are columns 2 and 3 divided by column 1
res #show results on screen
```

```
##       [,1]      [,2]      [,3]
##  [1,]   10 0.1000000 0.9000000
##  [2,]   50 0.3400000 0.6600000
##  [3,]  100 0.3900000 0.6100000
##  [4,]  200 0.4250000 0.5750000
##  [5,]  300 0.4400000 0.5600000
##  [6,]  400 0.4475000 0.5525000
##  [7,]  500 0.4540000 0.5460000
##  [8,]  600 0.4583333 0.5416667
##  [9,]  700 0.4614286 0.5385714
## [10,]  800 0.4637500 0.5362500
## [11,]  900 0.4666667 0.5333333
## [12,] 1000 0.4680000 0.5320000
```

We see that in order to get a significant result at significance level 0.05, with the sample size of 10, we need <20% or >80% success rate, while with the sample size of 1000, it is enough if we get a success rate <47% or >53%. The sample size really matters when it comes to determining which point estimate value is significant at a fixed significance level!

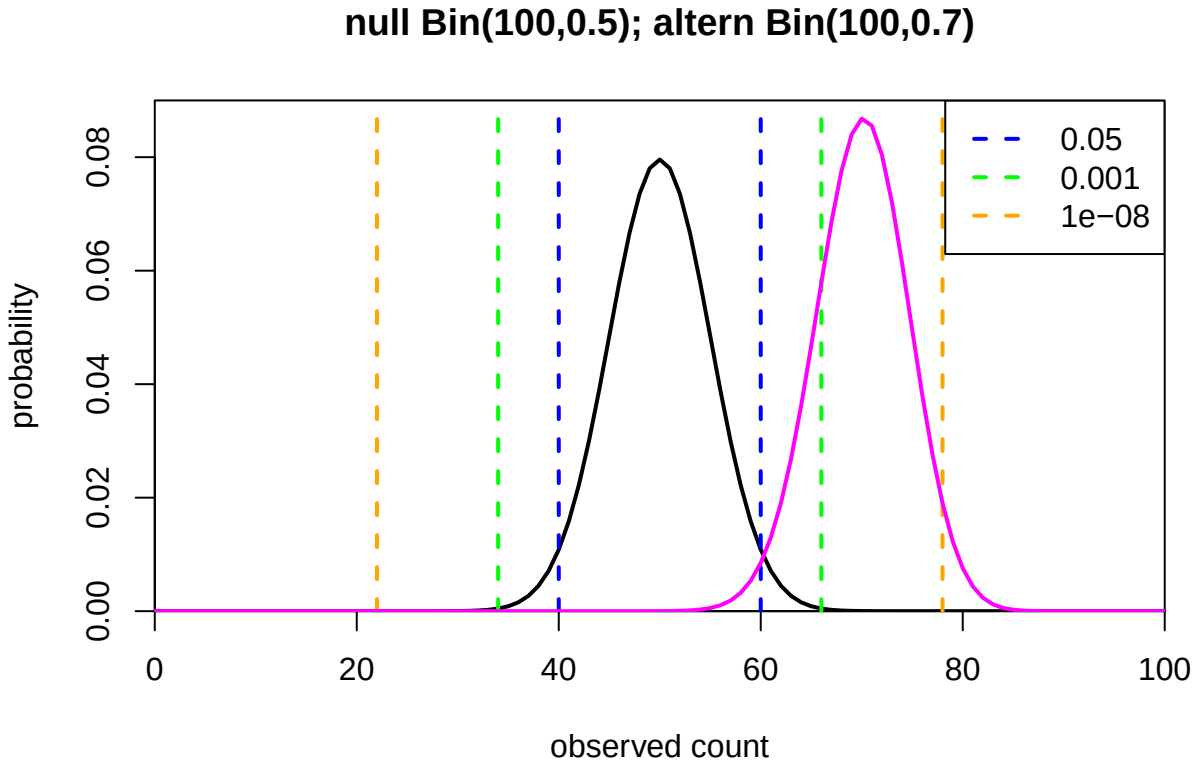
Statistical Power

Statistical power is a probability of detecting a given effect size, with a given sample size at a given significance level.

Typical context where statistical power comes up is the following. Let's say that in order to be convinced that there is an association between psoriasis and BMI we want to see a P-value of 0.001 (or less) if true parameter value is $p = 0.70$ (or larger), when we compare the observed twin-pair data to the null hypothesis value of $p = 0.50$. How large a study should we collect in order that the power with these parameters is at least 90%?

Before computing the power, let's add to our picture of the significance regions also the distribution of the **alternative hypothesis** that is defined by a non-null value of the parameter p. Here we consider the alternative hypothesis to be Bin(100, 0.7).

```
n = 100 #twin pairs
p0 = 0.5 #null hypothesis value
x = 0:n #plotting range 0,...,n
#Plot the null distribution
plot(x, dbinom(x, n, p0), t = "l", lwd = 2, main = "null Bin(100,0.5); altern Bin(100,0.7)",
     xlab = "observed count", ylab = "probability", xaxs = "i", yaxs = "i", ylim = c(0,0.09))
#Plot thresholds corresponding to different significance levels using different colors
sig.threshold = c(0.05, 0.001, 1e-8)
cols = c("blue", "green", "orange")
for(ii in 1:length(sig.threshold)){
  abline(v = qbinom(sig.threshold[ii]/2, n, p0),
         col = cols[ii], lwd = 2, lty = 2) #add left cutpoint
  abline(v = qbinom(1 - sig.threshold[ii]/2, n, p0),
         col=cols[ii],lwd = 2, lty = 2) #add also right cutpoint
}
legend("topright", col = cols, legend = sig.threshold, lwd = 2, lty = 2)
# and add the distribution under alternative hypothesis in magenta.
p1 = 0.7
lines(x, dbinom(x, n, p1), lwd = 2, col = "magenta")
```



Let's illustrate how the power calculation proceeds. For a fixed sample size n (=100), a significance level α (=0.001) and an effect size (null $p = 0.50$, alternative $p = 0.70$) we need to

1. Find the set S of possible observations that would give a P-value smaller than α under the null hypothesis. (Here this set consists of the values outside of the green lines.)
2. Find which proportion of the observations under the alternative hypothesis falls in set S (and hence would give a P-value $< \alpha$ under the null hypothesis).

```
n = 100
a = 0.001
#Cutpoints for significant results at level 0.001 under the null value p = 0.5
left.cut = qbinom(a/2, n, 0.5) - 1
right.cut = qbinom(1-a/2, n, 0.5) + 1
#For observations 0...left.cut and right.cut...100 we would thus have P<0.001 for n=100 and p=0.5.
S = c(0:left.cut, right.cut:100) #Set of observations which give small enough P-value

#What is a probability of observing a value in set S, under the alternative?
#Let's sum the probabilities over the set S:
sum(dbinom(S, size = n, p = 0.7))
```

```
## [1] 0.7792578
```

Thus we have a power of about 80%, (more accurately 78%), to discover a deviation from the null hypothesis (50% success rate), at significance level 0.001 (that is, with a P-value < 0.001), when the sample size is 100 and the true success rate in the population is 70%.

Let's compare this to a ready-made function. For that we need to `install.packages("pwr")` as you may have done already at Learn R part of the course material.

```r
#install.packages("pwr") #if you haven't done this yet, do it now
library(pwr) #load package "pwr"
#Compute power for binomial test at alpha = 0.001 and n = 100
#ES.h(0.5, 0.7) gives the "effect size" between null (0.5) and alternative (0.7) hypotheses
pwr.p.test(ES.h(0.5,0.7), sig.level = 0.001, n = 100)
```

```
##
##      proportion power calculation for binomial distribution (arcsine transformation)
##
##               h = 0.4115168
##               n = 100
##       sig.level = 0.001
##           power = 0.7952125
##     alternative = two.sided
```

This package gives power of ~80%, which agrees well with our manual calculation above. The `h` value in the output is the transformed effect size that corresponds to the difference between values 50% and 70%, and it was given by the `ES.h(0.5,0.7)` function call above.

We can leave also some other parameter than power away from the call to `pwr.p.test` and R will then compute the missing value for us. For example, we may want to know what n should be to get power of 90% at significance level 0.001.

```r
#Compute n for given power by leaving out n from the parameters
pwr.p.test(ES.h(0.5,0.7), sig.level = 0.001, power = 0.9)
```

```
##
##      proportion power calculation for binomial distribution (arcsine transformation)
##
##               h = 0.4115168
##               n = 123.4389
##       sig.level = 0.001
##           power = 0.9
##     alternative = two.sided
```

The answer is that $n = 124$ would give power of 90% in this setting.

We can also ask values for several parameter values at a time. Let's compute power at three significance levels 0.05, 0.001 and 1e-8.

```r
#Compute power for three significance levels at once
pwr.p.test(ES.h(0.5,0.7), sig.level = c(0.05, 0.001, 1e-8), n = 100)
```

```
##
##      proportion power calculation for binomial distribution (arcsine transformation)
##
##               h = 0.4115168
##               n = 100
##       sig.level = 5e-02, 1e-03, 1e-08
##           power = 0.98442708, 0.79521249, 0.05309469
##     alternative = two.sided
```

We see that we have almost full power (98%) at significance level 0.05, but little power (5%) at significance level 1e-8.

Ingredients of statistical power

One-sample t-test power with `pwr.t.test()` Let's consider continuous data. We have a biomarker whose mean value in the population studied (e.g. men aged 40-50 years) is 6.7 (sd = 1.0). We want to evaluate whether this biomarker is elevated in a particular subset of men (e.g. smokers). What is the power to detect 0.5 standard deviation unit difference from the population mean at the significance level of 0.01 if we had collected 20, 50 or 100 individuals from the target population?

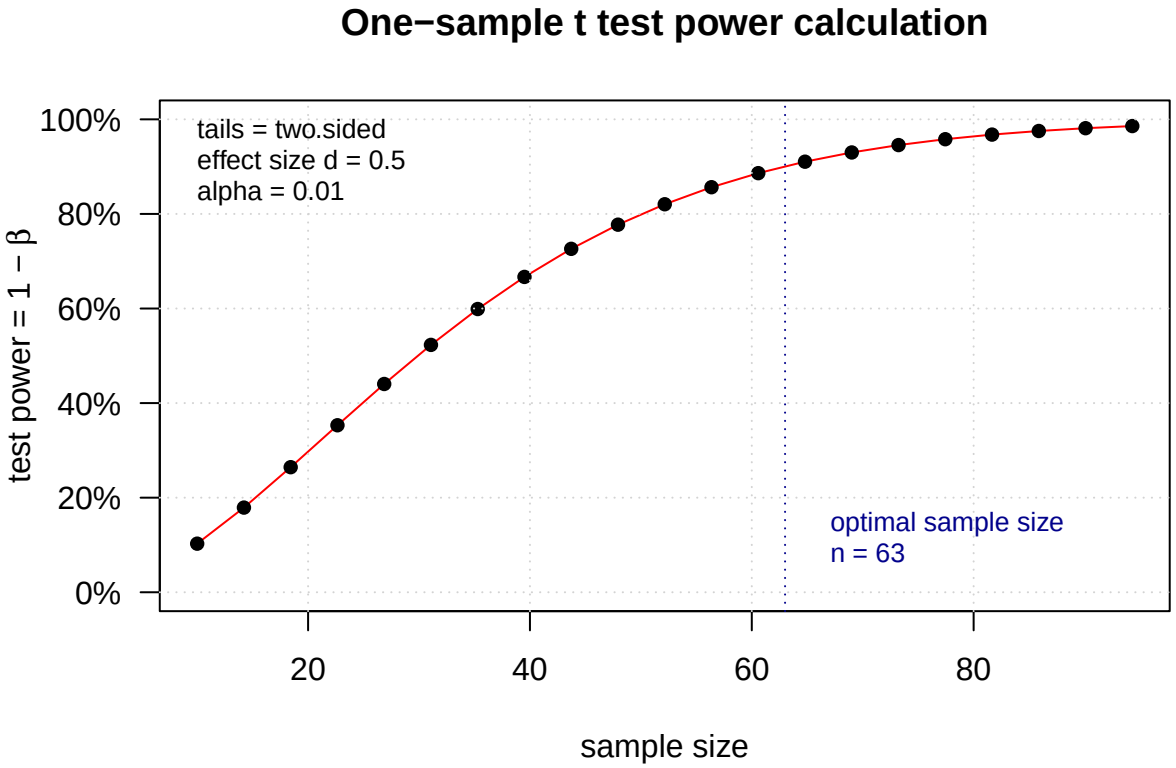
```
#We assume that SD in the target population is the same as in the general population.
# (While not necessarily true, but how could we know otherwise before collecting data.)
#Effect size for pwr.t.test is given as the difference in the means divided by
# the standard deviation that is assumed the same in both groups
# type="one.sample" means that we collect one sample and compare that to a KNOWN mean value.
pwr.t.test(d = 0.5/1.0, sig.level = 0.01, n = c(20, 50, 100),
           type = "one.sample", alternative = "two.sided")
```

```
##
##      One-sample t test power calculation
##
##               n = 20, 50, 100
##               d = 0.5
##       sig.level = 0.01
##           power = 0.2973461, 0.7993369, 0.9903473
##     alternative = two.sided
```

So when both the effect size (difference between the means of the two populations) and the significance level (here 0.01) are kept fixed, we see that as n grows, it is easier to detect that the subpopulation is different from the overall population with the statistical significance required.

We can use `pwr` package to plot a figure of the sample size and power by applying `plot.power.htest()` to the output of `pwr` functions.

```
plot.power.htest(pwr.t.test(d = 0.5/1.0, sig.level = 0.01, power = 0.9,
                            type = "one.sample", alternative="two.sided") )
```



Here the "optimal sample size" corresponds to the value of 90% given above in the function call.

If we keep n and the significance level fixed and increase the effect (the difference between the means of the populations), then power will increase because larger effects will generate data sets that look more and more extreme under the null, and hence will more easily lead to smaller P-values and more significant results than smaller effects.

```
pwr.t.test(d = c(0.5, 1.0), sig.level = 0.01, n = 20,
           type = "one.sample", alternative = "two.sided")
```

```
##
##      One-sample t test power calculation
##
##               n = 20
##               d = 0.5, 1.0
##       sig.level = 0.01
##           power = 0.2973461, 0.9324954
##     alternative = two.sided
```

Finally, if we keep n and the effect size fixed and ask for more and more stringent statistical significance, that is, results that would be more and more unlikely to appear under the null hypothesis, then power will decrease because we will consider only more and more extreme observations as being statistically significant.

```
pwr.t.test(d = 1.0, sig.level = c(0.01, 1e-6), n = 20,
           type = "one.sample", alternative = "two.sided")
```

```
##
##      One-sample t test power calculation
##
```

```
##               n = 20
##               d = 1
##       sig.level = 1e-02, 1e-06
##           power = 0.93249537, 0.04705335
##     alternative = two.sided
```

Examples of power calculations with pwr package

Let's go through some settings that `pwr` package can handle. https://cran.r-project.org/web/packages/pwr/vignettes/pwr-vignette.html

Two sample proportion test with `pwr.2p.test()` We expect that a new treatment might reduce the proportion of recurrent infections from about 20% (which is the current rate) to about 10% in a specific hospitalized group of individuals. How large a randomised trial should we run in order to have good power to detect this difference at a significance level of 0.05? (Note that here we do not expect 20% to be the exact value but we will estimate the proportion also in the placebo group. This is a different scenario from an earlier one-sample proportion test that compared the data against a fixed null value of 50% using `pwr.p.test`.)

```
pwr.2p.test(h = ES.h(0.2, 0.1), power = 0.90, sig.level = 0.05)
```

```
##
##      Difference of proportion power calculation for binomial distribution (arcsine transformation)
##
##               h = 0.2837941
##               n = 260.9272
##       sig.level = 0.05
##           power = 0.9
##     alternative = two.sided
##
## NOTE: same sample sizes
```

So we would need about 261 individuals in both the treatment and in the placebo group.

What if we had a fixed size of the treatment group of n1 = 230 set by the available resources, but could collect a larger placebo group. How large would the placebo group need to be for 90% power at significance level of 0.05?

```
pwr.2p2n.test(h = ES.h(0.2, 0.1), n1 = 230, power = 0.90, sig.level = 0.05)
```

```
##
##      difference of proportion power calculation for binomial distribution (arcsine transformation)
##
##               h = 0.2837941
##              n1 = 230
##              n2 = 301.4638
##       sig.level = 0.05
##           power = 0.9
##     alternative = two.sided
##
## NOTE: different sample sizes
```

We would need about n2 = 302 individuals in the placebo group.

Chi-square test for contingency table with `pwr.chisq.test()` Suppose that patients are treated with certain therapy and the outcome is recorded as Good, Satisfactory or Bad. It is observed that about 20% of people fall into Bad category and about 40% to Good category. MD expects that the treatment works better for men than for women and assumes that the proportion of men in Bad is 30% while for women it is only 10%. However, the doctor expects that the Good category seems similar in both sexes. How large a sample (with equal number of men and women) would one need to see this effect at significance level 0.01 using a Chi-square test for a 2x3 table?

```
#Let's generate 2x3 matrix of probabilities for the alternative hypothesis.

p.alt = matrix(c(0.5*0.4, 0.5*(1-0.1-0.4), 0.5*0.1, #1st row is for women
                 0.5*0.4, 0.5*(1-0.3-0.4), 0.5*0.3),
                 dimnames = list(c("M","F"), c("Good","Satisf","Bad")),
                 byrow = TRUE, ncol = 3, nrow = 2)
p.alt
```

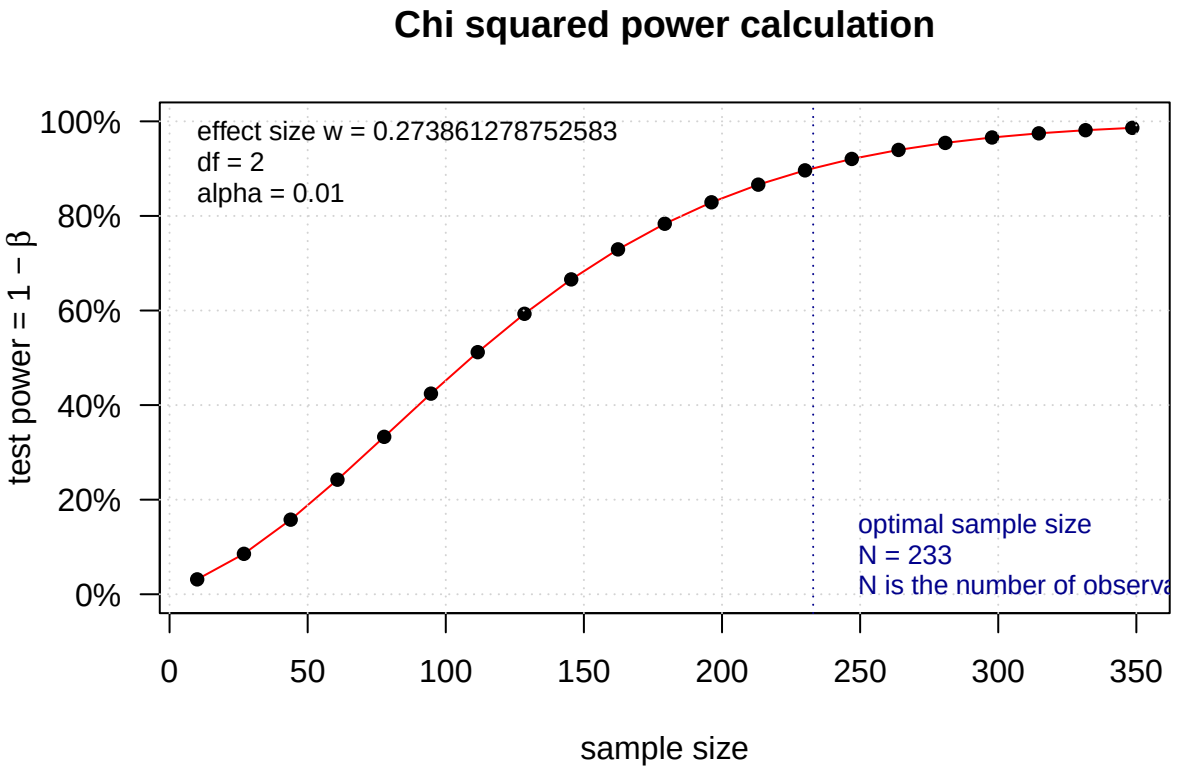
```
##   Good Satisf  Bad
## M  0.2   0.25 0.05
## F  0.2   0.15 0.15
```

```
# Effect size for chi-square test is given by ES.w2 function applied to p.alt.
# Degrees of freedom of the chi-square test is (Rows-1)x(Cols-1), here (2-1)x(3-1)
pwr.chisq.test(ES.w2(p.alt), df=(2-1)*(3-1), sig.level = 0.01, power = 0.90)
```

```
##
##      Chi squared power calculation
##
##               w = 0.2738613
##               N = 232.3559
##              df = 2
##       sig.level = 0.01
##           power = 0.9
##
## NOTE: N is the number of observations
```

We would need about 240 individuals, 120 males and 120 females. Let's see the power curve.

```
plot.power.htest(pwr.chisq.test(ES.w2(p.alt), df = (3-1)*(2-1), sig.level = 0.01, power = 0.90))
```



One sample t-test with `pwr.t.test( ,type = "one.sample")` We want to test whether a target population treated with medication M shows a decrease in risk factor R. Suppose that the mean in the general population is 4.1 (sd 0.8) and we measure a group treated with M 12 months after starting the therapy. How large the group needs to be in order to have 90% power to find a difference in mean of 0.3 at 2-sided significance level of 0.05?

```
#NOTE: use "one.sample" to compare a target population to a fixed reference value (here mean of 4.1)
#      and give the effect size parameter d in units of SD of the general population (here 0.8)
pwr.t.test(d = 0.3 / 0.8, sig.level = 0.05, alternative = "two.sided",
           power = 0.9, type = "one.sample")
```

```
##
##      One-sample t test power calculation
##
##               n = 76.66599
##               d = 0.375
##       sig.level = 0.05
##           power = 0.9
##     alternative = two.sided
```

Two sample t-test with equal sample sizes with `pwr.t.test(, type = "two.sample")` We do the same comparison but collect equal sized groups from the general population and from the treated population. How large groups do we need?

```
#NOTE: use "two.sample"" to compare groups from two populations
pwr.t.test(d = 0.3 / 0.8, sig.level = 0.05, alternative = "two.sided",
           power = 0.9, type = "two.sample")
```

```
##
##      Two-sample t test power calculation
##
##               n = 150.4057
##               d = 0.375
##       sig.level = 0.05
##           power = 0.9
##     alternative = two.sided
##
## NOTE: n is number in *each* group
```

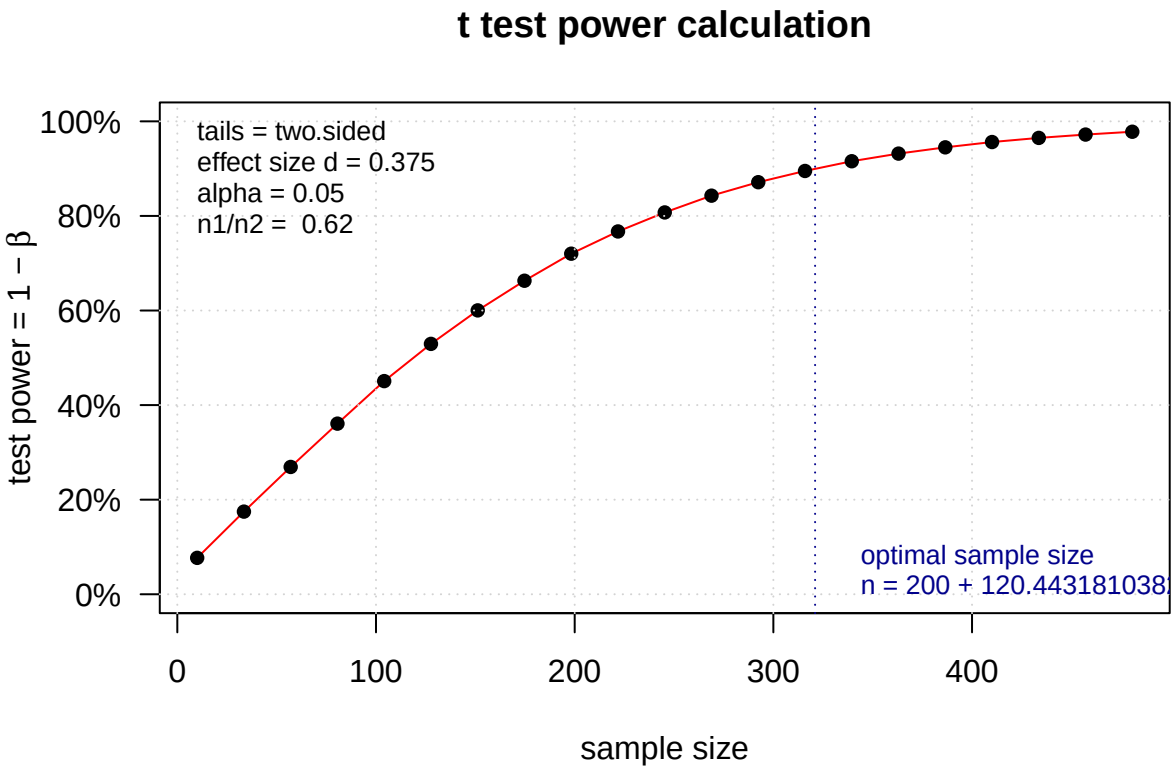
Note how we need double the sample size in each group compared to the one-sample test above. This is because now we need to estimate means of two populations and they both come with some uncertainty that further accumulates in the calculation of the difference between the populations. Hence, we need larger sample sizes in this case than when we compared an estimated mean of one population against a fixed reference value.

Two sample t-test with unequal sample sizes with `pwr.t2n.test()` What if we had a fixed set of 200 individuals from the general population measured and we need to collect a sample from the treatment population. How large a sample?

```
#NOTE: We use "pwr.t2n.test to have different n in the two samples
pwr.t2n.test(d = 0.3 / 0.8, sig.level = 0.05, alternative = "two.sided", power = 0.9, n1 = 200)
```

```
##
##      t test power calculation
##
##              n1 = 200
##              n2 = 120.4432
##               d = 0.375
##       sig.level = 0.05
##           power = 0.9
##     alternative = two.sided
```

```
plot.power.htest(
  pwr.t2n.test(d = 0.3 / 0.8, sig.level = 0.05, alternative = "two.sided", power = 0.9, n1 = 200))
```



Example 5.3. *Selective laser trabeculoplasty versus eye drops for first-line treatment of ocular hypertension and glaucoma (LiGHT): a multicentre randomised controlled trial* in Lancet 2019 compares two treatments (laser trabeculoplasty and eye drops) for patients with open angle glaucoma or ocular hypertension and no ocular comorbidities. The primary outcome was health-related quality of life at 3 years, assessed by EQ-5D. They write: "We calculated that a sample size of 718 patients was needed to detect a difference of 0.05 in EQ-5D between the two groups using a two sample t test at the 5% significance level with 90% power, assuming a common standard deviation of 0.19 and 15% attrition."

Let's see if we agree. Here the mean difference should be input in the units of SD and is $d = 0.05/0.19$.

```
pwr.t.test(d = 0.05/0.19, power = 0.9, type = "two.sample",
           alternative = "two.sided", sig.level = 0.05)
```

```
##
##      Two-sample t test power calculation
##
##               n = 304.4178
##               d = 0.2631579
##       sig.level = 0.05
##           power = 0.9
##     alternative = two.sided
##
## NOTE: n is number in *each* group
```

Thus, each sample should have 305 individuals and hence, in total, we would need $2 \cdot 305 = 610$ individuals. If we take into account that 15% of the recruited individuals may leave the study (15% attrition rate), then we need to recruit even a larger sample n for which $0.85 \cdot n = 610$. Thus, we need

```r
ceiling(610 / 0.85) #ceiling function rounds up the values to next integer
```

```
## [1] 718
```

individuals, just like they reported.

Power in designing an experiment

If the experiment does not have enough power to answer the question of interest, then we are unlikely to learn much from it. And even worse, if we do not understand that a reason for our test not reaching statistical significance may be small power of the study, then we may wrongly conclude that it has been "statistically" shown that the effect does not exist (see below). We should avoid designing underpowered studies.

Power when interpreting the results

In a cohort of 200 female apendicitis cases a new scoring system was found to predict the severity of the condition: difference between the means of the groups of severe and benign cases were 10 (95%CI: 5.2,. . . ,14.0) with a P-value of 0.001. You collected 30 male cases and the corresponding values were 7 (-5.0,. . . ,20.4) with $P = 0.56$. Does this mean that the apendicitis scoring system works well for women but not for men because in women the difference was statistically significant at level 0.001 but in men it was not significant even at level 0.05?

If our experiment is underpowered to answer the question of interest, then a negative result (the one that does not find a statistically significant difference between groups/treatments) does NOT prove that there is no difference. "Absence of evidence is not evidence of absence." http://www.bmj.com/content/311/7003/485.full

If we have designed an experiment with high power to detect an effect, but still we don't see a statistically significant effect, then we can conclude that the effect of **that size** does probably not exist. However, it is still possible that some smaller effects may exist.

If we have really large studies, we can find statistically significant effects between almost any two populations. The more relevant question is that which sizes of effects have any practical importance. For example, even if we can show by using very large samples that the prevalence of MS-disease in people born in April (say risk of 11/10000) is statistically significantly higher than those born in October (say risk of 10/10000) this does not have much practical importance since the increase in absolute risk is tiny. Scientifically though, such observations may be interesting and open up new avenues for understanding the disease.