BayesianAlpha

Introduction

In a clinical trial, the traditional setup is: you estimate the parameters of interest (for example, the treatment effect size), choose your type I error rate α and power - $1-\beta$ - from which you can estimate the sample size needed to show there is a statistical significance between groups (if one exists). The trial is then conducted according to this calculated sample size and the results are analysed to test for statistical significance at the nominated α level from the trial setup.

However, experimenters may want to look at the data before the conclusion of the trial. There are various different reasons for this, including considerations around safety and ethics. When experimenters look at the data before the conclusion of a trial, this is called an **interim analysis**. At an interim analysis, there are different decisions the experimenters can take. If they feel the treatment is no better than the control then they can decide to stop the trial here. This is called *stopping for futility* and it is used because it is unethical to continue to subject patients to a treatment that is no better than the control. If the trial stops early then the trial unit can save time, resources and money by not continuing with a trial that is not beneficial to continue. Another decision is to increase the sample size of the trial, this is done in situations where the treatment effect is showing to be working, but maybe the effect is not quite as large as they had thought when planning the trial. As a result, the trial is now underpowered and will not be statistically significant with the current sample size. Another decision is to keep the sample size the same as original - this can be due to two reasons. Talk etc. The last decision they can make is to stop the trial due to the treatment effect being greater than they had planned for and therefore the data is statically significant - this is called *stopping for efficacy*.

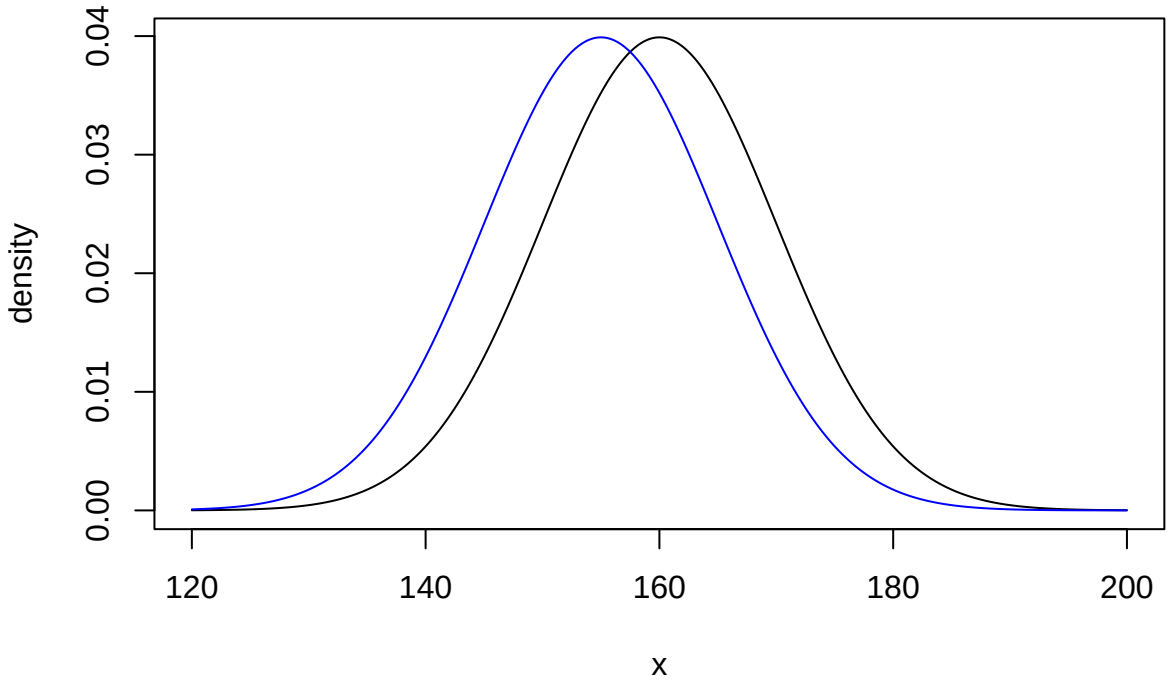
I will only focus on stopping for efficacy here.

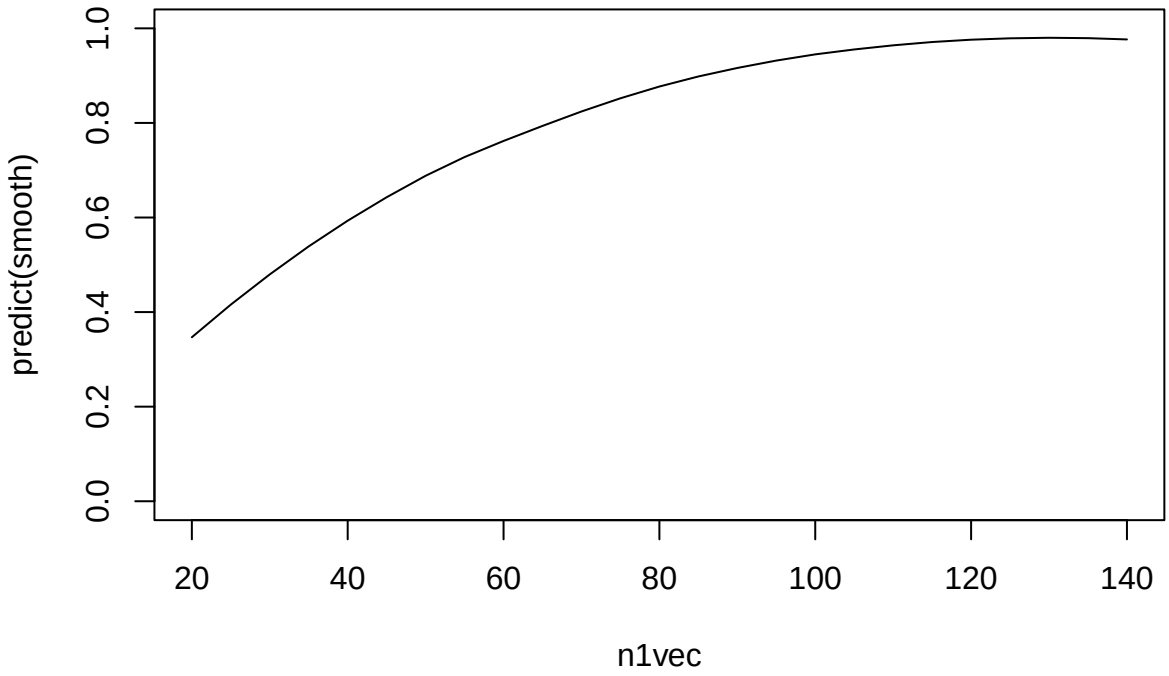
An example

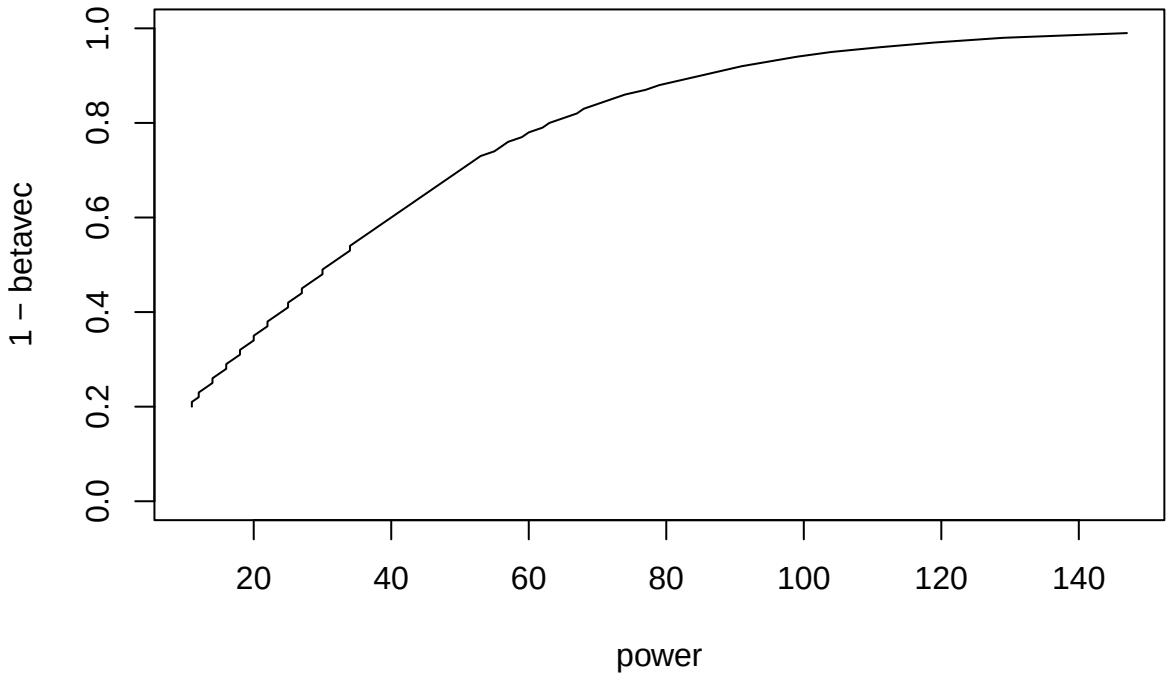
Imagine we are performing a clinical trial for a drug that is said to reduce systolic blood pressure in morbidly obese patients. We will measure the systolic blood pressure of patients after a month (28 days) of taking this drug every day. After discussion with the clinicians, they decide that the minimum clinically relevant difference is 5mmHg. We know that the endpoint will be Normally distributed, and we will assume equal variance for simplicity, so we can calculate the sample size required using this information.

We suppose that $\sigma^2 = 10$

```
x <- seq(120, 200, by=0.01)
control <- dnorm(x, 160, sd = 10)
plot(x,control, type="l", ylab="density")
treatment <- dnorm(x, 155, sd =10)
lines(x, treatment, col="blue")
```


density
0.00
0.01
0.02
0.03
0.04
120
140
160
180
200
x


predict(smooth)
0.0
0.2
0.4
0.6
0.8
1.0
20
40
60
80
100
120
140
n1vec


1 – betavec
0.0
0.2
0.4
0.6
0.8
1.0
20
40
60
80
100
120
140
power