

# Bayesian Clinical Trials

## Case study

## Example

Osteosarcoma is the most common malignant bone tumor in children and young adults and prognosis after its recurrence is poor.

There is a need to identify novel effective agents and these agents are usually evaluated initially in patients with relapsed osteosarcoma.

Consider the design of a controlled phase II B trial to compare two different treatment, say A and B, with (dichotomized) response measured according to RECIST criteria as outcome.

What sample size is needed to provide sufficient information to specify the true difference in response rates to within a total interval width of 20 percentage points?

# Evidence

Phase II Study	Treatment	Sample Size	Responses (%)	95% CI
1	A	26	5 (19)	22;53
2	B	37	14 (37)	
3	A	14	4 (28.5)	

Assume a pooled estimate for Treatment A:  $\frac{9}{40} = 22.5$

Assume an estimate for Treatment B:  $\frac{14}{37} = 38.0$

## Frequentist Sample size (per group) by $I$ and $(1 - \alpha)$

If we consider not only the estimates but also uncertainty, for example the upper and lower limit of the 95% confidence interval, we can get different sample sizes:

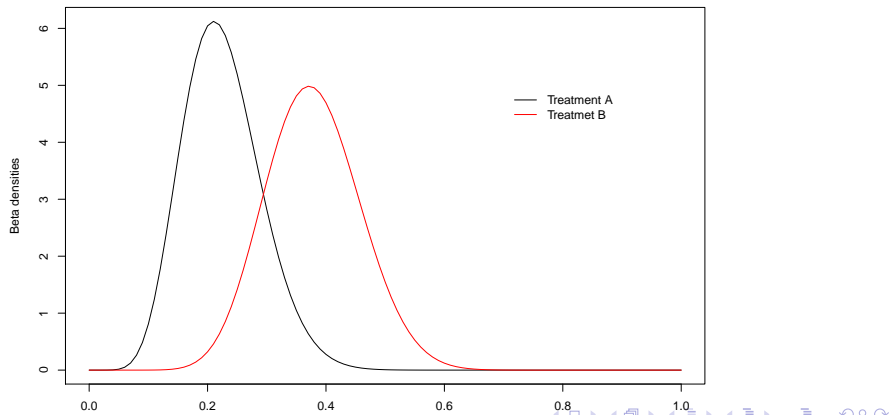
```
library(SampleSizeProportions)
```

```
##                                theta
##                                -0.01  0.02  0.15  0.3
##-----
## length= 0.2      134      141      159      164
## length= 0.21     122      128      144      149
## length= 0.22     111      116      132      136
## length= 0.24      94       98      111      114
## length= 0.25      86       90      102      105
```

Which is best?

# Priors

- ▶ For Treatment A we can assume that 0.225 is the mean of a Beta distribution:  $Beta(c_1 = 9, d_1 = 31)$
- ▶ For Treatment B we can assume that 0.38 is the mean of a Beta distribution:  $Beta(c_2 = 14, d_2 = 23)$



# SampleSizeProportions package

SampleSizeProportions implements a set of functions for calculating required sample sizes for

- ▶ Average Length Criterion (ALC)
- ▶ Average Coverage Criterion (ACC)
- ▶ Worst Outcome Criterion (WOC)

in the context of binomial observations.

```
library(SampleSizeProportions)
```

## Bayesian Sample size (per group) by $I$ and $(1 - \alpha)$

##		lev= 0.9	lev= 0.95	lev= 0.99
##		ACC	ACC	ACC
##	length= 0.2	70	116	229
##	length= 0.22	51	89	182
##	length= 0.25	31	60	132
##		-	-	-
##		ALC	ALC	ALC
##	length= 0.2	70	115	225
##	length= 0.22	51	89	180
##	length= 0.25	31	60	130
##		-	-	-
##		WOC	WOC	WOC
##	length= 0.2	96	153	292
##	length= 0.22	73	120	234
##	length= 0.25	48	84	172