# Once a prior has been derived, assurance can be calculated in different ways

- Analytic calculation for simpler cases
- Simulation approach for more complex cases

# Assurance – calculation for simple case

## The prior predictive distribution

Suppose that the prior distribution for the effect $\delta = \mu_1 - \mu_0$ has the conjugate normal form $\delta \sim N(\mu_\delta, \sigma_\delta)$

We previously discussed that $\bar{y}_1 - \bar{y}_0 \,|\delta, \tau \sim N(\delta, \tau)$, with $\tau = \sqrt{\frac{\sigma_1^2}{n_1} + \frac{\sigma_0^2}{n_0}}$

Equivalently $\bar{y}_1 - \bar{y}_0 = \delta + \tau Z$ with $Z \sim N(0,1)$

The unconditional (prior predictive) distribution for $\bar{y}_1 - \bar{y}_0$ has mean

$$E(\delta + \tau Z) = E(\delta) = \mu_\delta$$

and variance

$$Var(\delta + \tau Z) = Var(\delta) + Var(\tau Z) = \sigma_\delta^2 + \tau^2$$

In short, unconditionally

$$\bar{y}_1 - \bar{y}_0 \sim N(\mu_\delta, \sqrt{\sigma_\delta^2 + \tau^2})$$

See: O'Hagan, A., Stevens, J. W., & Campbell, M. J. (2005). Assurance in clinical trial design. *Pharmaceutical Statistics*, *4*(3), 187–201.

# Assurance – calculation for simple case

## One-sided superiority trial with significance as success criterion

Assurance gives the PoS before having collected any data

Success in this simplest case is defined as observing a one-sided p-value below the significance level α, or equivalently, observing $\bar{y}_1 - \bar{y}_0 > Z_{1-\alpha}\tau$

Assurance can be calculated as follows:

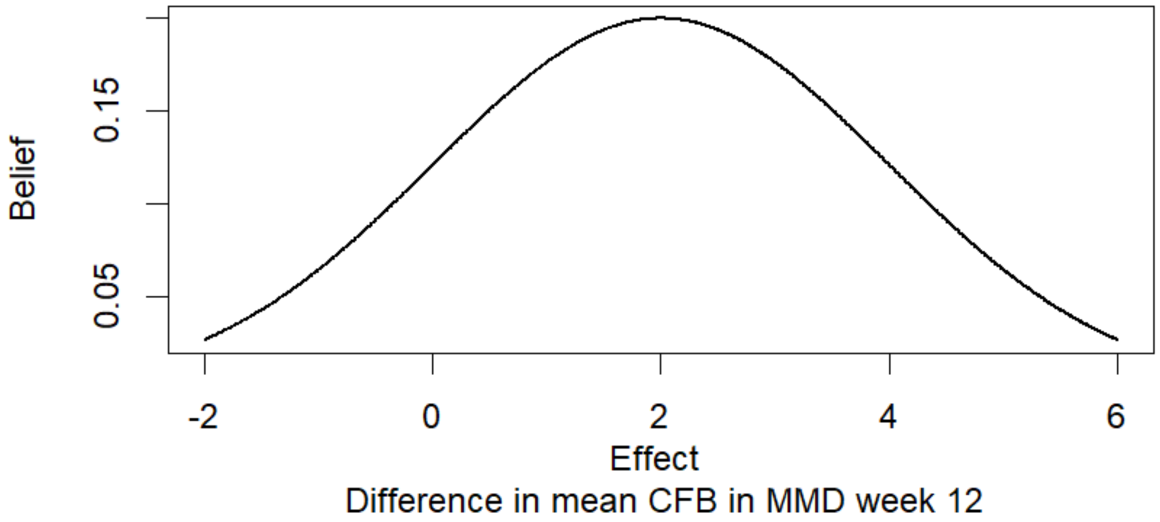
$$P[\bar{y}_1 - \bar{y}_0 > z_{1-\alpha}\tau] = \Phi\left(\frac{-Z_{1-\alpha}\tau + \mu_\delta}{\sqrt{\sigma_\delta^2 + \tau^2}}\right)$$

See: O'Hagan, A., Stevens, J. W., & Campbell, M. J. (2005). Assurance in clinical trial design. *Pharmaceutical Statistics*, *4*(3), 187–201.

FERRING PHARMACEUTICALS

# Exercise 2 – calculate assurance for the confirmatory trial

Use a normal distribution with mean 2 and standard deviation 2 as prior




**Coding tip:** use the apply function to quickly obtain the value of a function for a sequence of input values

```
n <- seq(0,1000,1)
dim(n) <- c(1,length(n))
results <- apply(n,2,yourfunction,...) where you can use ...
to give further arguments to yourfunction
```

1. Create a plot with sample size on the x-axis and PoS on the y-axis. Include one curve displaying power as a function of the sample size and one curve displaying assurance as a function of sample size. **Hint:** *first create R functions that return power and assurance as a function of sample size using formulas from Slides 31 and 13 (if you need help, see last slide in this presentation).*
2. What is the assurance for the sample size you calculated in Exercise 1? Would you choose a different sample size based on assurance?
3. What is the upper bound for assurance for this example? What is the interpretation of this upper bound?

# Success criteria

## A p-value alone for a null hypothesis of no effect is rarely sufficient

The null hypothesis will be rejected if p<0.025 or equivalently if $\bar{y}_1 - \bar{y}_0 > Z_{1-\alpha}\tau$

For our confirmatory study, what is the smallest observed effect $\bar{y}_1 - \bar{y}_0$ that would lead us to reject the null hypothesis for a sample size of 222/arm and a common standard deviation of 6.5?