Assurance with unknown variance

Let's consider the same framework as discussed so far, but with unknown variance σ^2 that is equal for both groups ($\sigma = \sigma_0 = \sigma_1$)

In this case we typically base our test on the t-distribution rather than the normal distribution, i.e. we reject the null hypothesis if

$$\bar{y}_1 - \bar{y}_0 > t_{1-\alpha,2n-2}\hat{\sigma}\sqrt{\frac{2}{n}},$$

with $\hat{\sigma}^2 = \frac{\sum_{i=0}^{1}\sum_{j=1}^{n_i}(y_{ij}-\bar{y}_i)^2}{2n-2}$ the estimate of the variance and $t_{1-\alpha,2n-2}$ the *1-α* percentile of the *t*-distribution with *2n-2* degrees of freedom.

Since we do now not know σ, we may also wish to define a prior on σ.

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

For the case of unknown sigma (or complex success criteria) a simulation approach can be used to calculate assurance

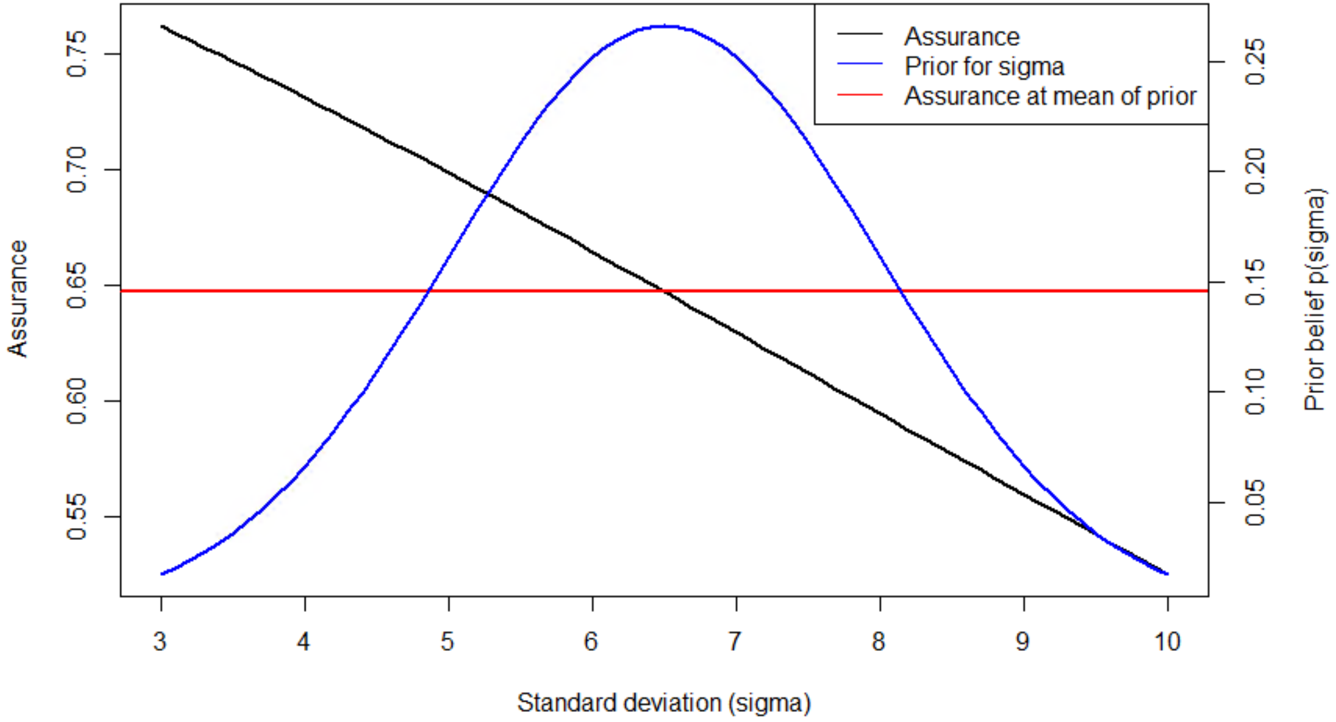
1. Set counters *I* = *P* = *0*. Set required number of simulations *N*.
2. Sample δ and σ from their joint prior distribution.
3. Sample an observed effect $\bar{y}_1 - \bar{y}_0 \sim N(\delta, \tau)$ and an estimated standard deviation using $(2n - 2)\hat{\sigma}^2/\sigma^2 \sim \chi^2_{2n-2}$.
4. Increment *P* if $\bar{y}_1 - \bar{y}_0 > t_{1-\alpha,2n-2}\hat{\sigma}\sqrt{\frac{2}{n}}$.
5. Increment *I*. If *I* < *N*, go to step 2.
6. Estimate assurance by *P/N*

FERRING PHARMACEUTICALS

A comment on priors on the standard deviation

Both in my own experience and that of Walley et al (2015) a prior on σ does not affect assurance in a relevant manner compared to calculating assurance based on the mean of the prior for σ

This finding is due to the assurance value changing almost linearly over the credible range for σ, which when combined with an approximately symmetrical prior distribution results in the marginal assurance value almost being equal to the assurance at the prior mean for σ.



Walley, R. J., Smith, C. L., Gale, J. D., & Woodward, P. (2015). Advantages of a wholly Bayesian approach to assessing efficacy in early drug development: A case study. *Pharmaceutical Statistics*, *14*(3), 205–215. https://doi.org/10.1002/pst.1675