Lecture 12: Normal Means & Multiple Testing

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October 18

Normal Means Model

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- $H_{0i} : \mu_i = 0$ versus $H_{1i} : \mu_i \neq 0$

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Multiple Testing

- $H_{0i} : \mu_i = 0$ versus $H_{1i} : \mu_i \neq 0$
- n hypotheses that may potentially be closely related, e.g. H_{01} no difference in expression gene i between cases and controls, for n genes

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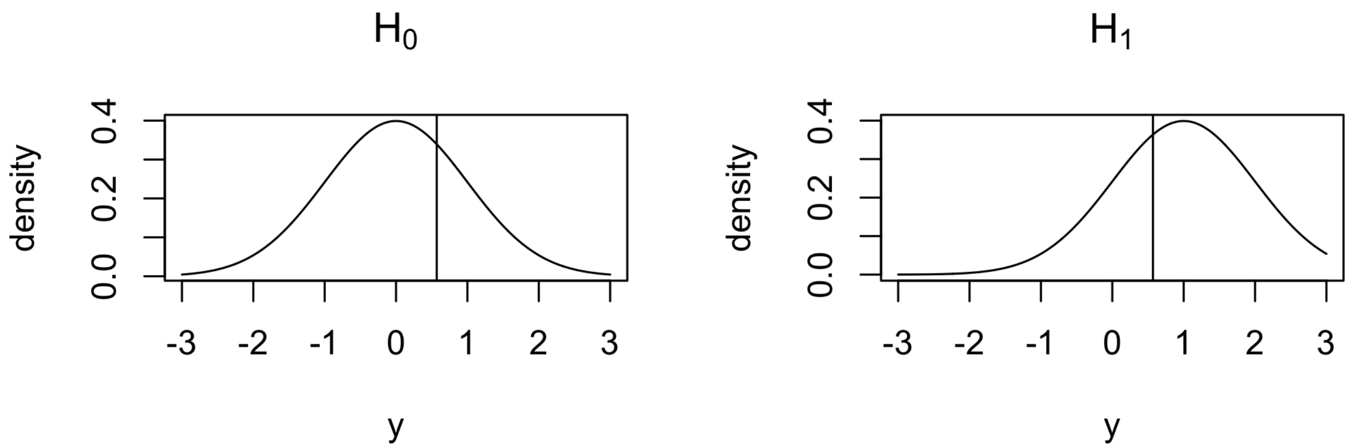
Limitations?

- overall lots of type I errors potentially in testing over and over again
- α is the probabibility of making a type I error in an individual test, but not the probability of the family-wise type 1 error, e.g the probability of making at least one type 1 error in the n tests)

Power

- very low power (high type II error rate) because we have a single observation per hypothesis



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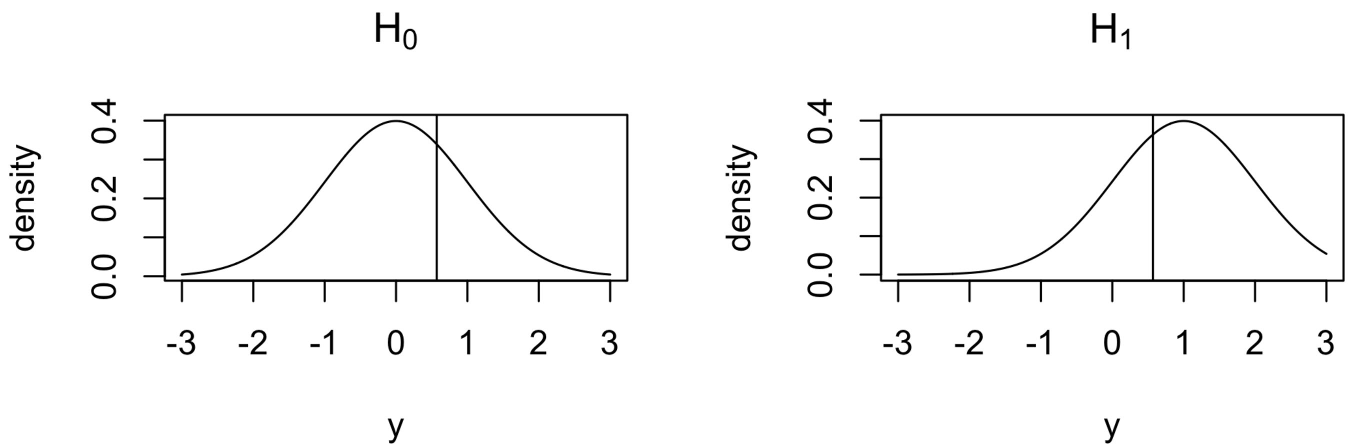

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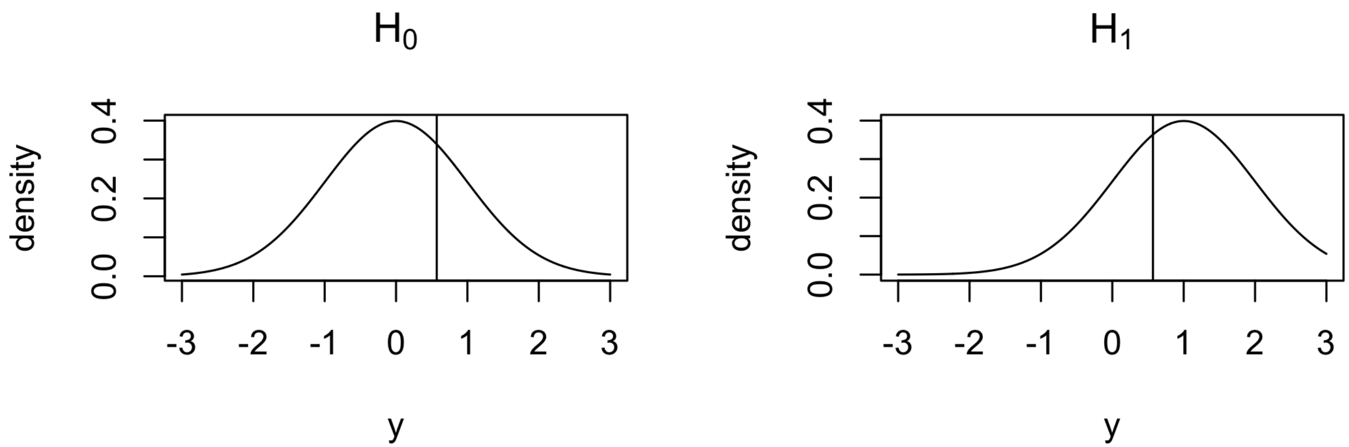

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- low power may actually lead to very few type I errors even in multiple testing but often still lots of type I and type II errors

Strategy Ib

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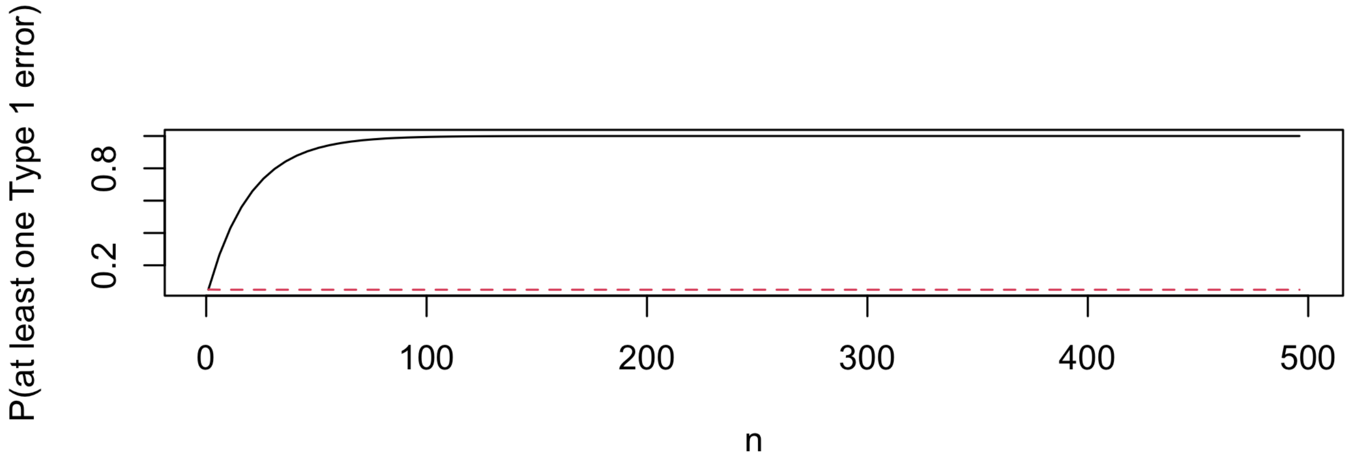
- Probability of at least one Type I error if tests are independent

$$1 - \Pr(\text{ } 0 \text{ Type I errors in } n \text{ tests}) = 1 - (1-\alpha)^n$$



- to control the increase in Type I errors with n we may need to decrease the α threshold with n

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- in the extremely low power setting, probably very few tests exceed the new threshhold (conservative)

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- Borrow strength!

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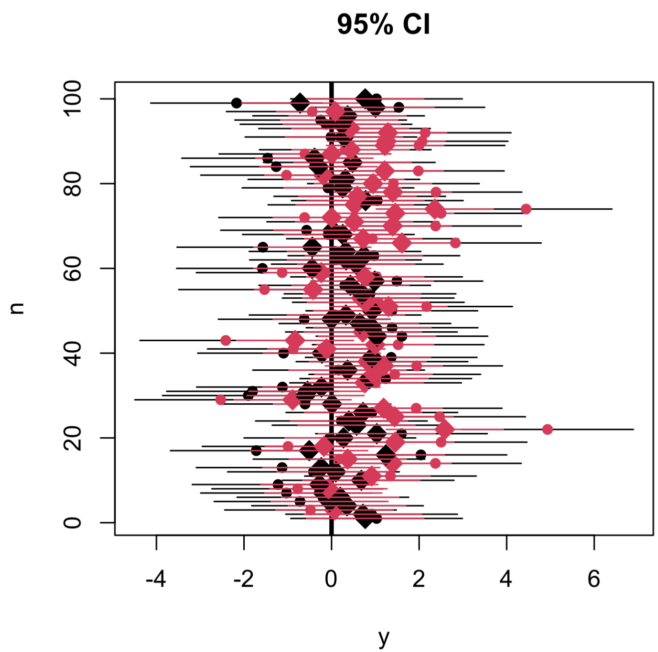

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- when σ^2_μ is small credible intervals are much narrower than with MLE

Hypothetical Setting

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Does throwing in more nulls lead to more Type I errors?

- what happens to $\hat{\mu}$ and $\hat{\sigma}^2_\mu$?
- what happens to the credible intervals?

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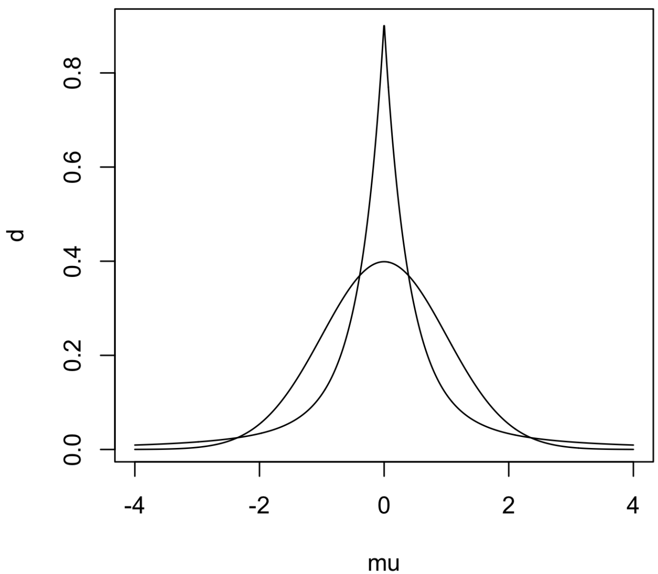

Local-Global Scale Mixtures of Normals

Local scale

$$\begin{aligned} \mu_i \mid \lambda_i, \tau &\sim N(0, \lambda_i \tau) \\ \lambda_i &\sim f \qquad \text{local-scale} \\ \tau &\sim h \qquad \text{global-scale} \end{aligned}$$

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- Includes:
  - horseshoe
  - generalized double pareto
  - Dirichlet Laplace

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- allows formal Bayes multiple testing $H_{0i} : \mu = 0$
- $\pi_0 = \Pr(H_{0i} \text{ is true})$ another unknown to learn from the data; provides automatic adjustment for multiple testing error!