

The choice of the first maximum at -2.25) over the second at 2.7 is based on the following 3 considerations.

1. The p-value at 2.7 never reaches 1.0 suggesting there is no solution to the implied RPSFTM estimating equation at 2.7. Of course, another possibility is that our grid was not fine enough and we missed the value of  $\psi$  where it obtained the value 1 or the p-value was never 1 because of the discontinuity of the estimating function in  $\psi$ .

2. If rather than looking at p-values we had looked at Z-scores it is well known that in a neighborhood of the true  $\psi^*$ ,  $Z(\psi) = (\psi - \hat{\psi}) / se(\hat{\psi})$  so  $Z(\hat{\psi}) = 0$ , at least in large samples.

Thus  $Z'(\psi) = 1/se(\hat{\psi})$

Now the 2 sided signed p-value on our graph is

$$p(\psi) = 1 - 2\Phi(Z(\psi))$$

when  $Z(\psi) \geq 0$   
and

$$1 - 2\Phi(-Z(\psi))$$

otherwise, where  $\Phi$  and  $\phi$  are the CDF and density of a  $N(0, 1)$  random variable.

Thus, when  $Z(\psi) \geq 0$ , to second order

$$\begin{aligned} p(\psi) &= p(\hat{\psi}) - 2\phi(Z(\hat{\psi})) (\psi - \hat{\psi}) / se(\hat{\psi}) \\ &= 1 - (\psi - \hat{\psi}) 2(2\pi)^{-1/2} / se(\hat{\psi}) \end{aligned}$$

since  $\phi'(0) = 0$ .

Thus  $p(\psi)$  is locally linear in  $|\psi - \hat{\psi}|$  with slope  $-2(2\pi)^{-1/2} / se(\hat{\psi})$  when  $\psi - \hat{\psi} > 0$

and slope  $2(2\pi)^{-1/2} / se(\hat{\psi})$  when  $\psi - \hat{\psi} < 0$

Thus we can use the empirical slope to estimate  $se(\hat{\psi})$ .

When we do so, we get  $se(\hat{\psi})$  at  $\hat{\psi} = 2.7$  is approximately  $\frac{2}{2.8} (.399)$ , while at  $\hat{\psi} = -2.25$ ,  $se(\hat{\psi})$  is approximately  $2(.399)$ .

Since (i) the uncertainty should increase with the absolute value of  $\psi$  due to more artificial censoring and (ii) a value  $\frac{2}{2.8} (.399)$  seems quite incompatible with our bootstrap estimates of uncertainty, we conclude that  $\hat{\psi} = 2.7$  is unlikely to be near the true  $\psi^*$ . This is further confirmed by the slopes of the p-values to the left and to the right of  $\hat{\psi} = 2.7$  having quite different absolute values.

3. The estimate of 2.7 implies that a continuous dose of the drug reduces survival by 14.9 times, a biologically implausible value that also has small uncertainty if our above estimate of the standard error is correct (reflecting the sharpness of the p-value peak.)

The estimate -2.25 implies that a continuous dose of drug increases survival by 9.49 times, also a biologically implausible value although less implausible. In addition the estimate is consistent with biologically plausible values because the standard error at -2.25 is larger ( reflecting a wider p-value peak).