Absence of Evidence and Evidence of Absence in the FLASH Trial: A Bayesian Reanalysis

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The multicenter FLASH trial¹ concluded that “Among patients at risk of postoperative kidney injury undergoing major abdominal surgery, use of HES [hydroxyethyl starch] for volume replacement therapy compared with 0.9% saline resulted in no significant difference in a composite outcome of death or major postoperative complications within 14 days after surgery.” Indeed, the results were opposite to those expected: death or major complications were *more* prevalent in the HES group (139 of 389 patients: 35.7%) than in the saline group (125 of 386 patients: 32.4%). An associated editorial² pointed out that “absence of evidence is not evidence of absence” and concluded that “The results of the FLASH trial corroborate the detrimental kidney effects of HES” suggested by recent meta-analyses.

Here we quantify the degree to which the data from the FLASH trial, considered in isolation, undercut the hypothesis that HES improves the primary outcome. We conducted Bayesian logistic regression^{3,4} and considered three rival models. First, under H_0 , (i.e., HES is ineffective) the log odds ratio equals $\psi=0$; second, under the positive-effect model H_+ (i.e., HES helps, the authors’ hypothesis), ψ is assigned a positive-only normal prior distribution $N_+(\mu, \sigma)$; third, under the negative-effect model H_- (i.e., HES harms, the hypothesis suggested by recent meta-analyses), ψ is assigned a negative-only normal prior distribution $N_-(\mu, \sigma)$.

A default analysis (i.e., $\mu=0$, $\sigma=1$) shows that H_0 receives the most support from the data; however, the data are only about 2.41 times more likely under H_0 than under H_- , a level of evidence that has been termed “not worth more than a bare mention”.⁵ In contrast, the data are about 12.30 times more likely to occur under H_0 than under H_+ , a level of evidence that has been termed “strong”.⁵ If the three rival models were deemed equally plausible a priori (i.e., each 0.33), the corresponding posterior model probabilities for H_0 , H_- , and H_+ would be 0.67, 0.28, and 0.05, respectively.

In sum, the data from the FLASH trial mainly act to increase the plausibility that HES is ineffective, and decrease the plausibility that HES is helpful. These analysis, easily conducted in JASP (jasp-stats.org) or R (<https://CRAN.R-project.org/package=abtest>) arguably provide a more detailed perspective that supplements the statement that the results showed “no significant difference”.

References

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