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LETTER

COVID-19 encephalopathy, Bayes rule, and a plea for case–control studies

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We are interested in investigating encephalopathy rates in COVID-19 with the Bayes rule, a more intuitive way to understand and communicate risks and associations than *P*-values. Like in classical statistics, Bayes cannot help much with low numbers from individual case series. Liotta and coauthors provided a sample size large enough to make more robust estimations than any other research we have seen.[1] They found a substantial association between encephalopathy and greater morbidity in COVID-19. This association does not prove causality: the most likely cause of encephalopathy in COVID-19 is multifactorial, and the press has accurately interpreted this information.[2]

We replicated selected outcomes from their study using the Bayesian A/B test for summary statistics in Jeffrey's Amazing Software Package (JASP).[3] The test can monitor and update the evidence for or against an association between two variables of interest. Beyond *p*-values, Bayes factors (BF) quantitatively measure the evidence after seeing the data. Even better, by estimating the median with a 95% credible interval (95% CrI) of the posterior probability

Table 1. Selected outcomes and association with COVID-19 encephalopathy.

	COVID-19 (n = 509)				
	Encephalopathy (n = 162)	No encephalopathy (n = 347)	BF[1]	Posterior probability median, (95% CrI)[2]	P[3]
Male[4]	101	180	4	0.6(0.5–0.7)	0.034
History Neurological disorder	55	79	12	0.6(0.5–0.7)	0.01
Cancer	32	29	236	0.7(0.6–0.8)	<0.001
CVD	21	18	39.5	0.7(0.6–0.8)	0.004
CKD	27	29	19.3	0.7(0.5–0.8)	0.008
COVID-19 severity	49	113	109	0.97(0.94–0.98)	<0.001
30-day mortality	35	11	18.7	0.86(0.78–0.92)	<0.001

COVID-19, Coronavirus disease 2019; BF, Bayes factor; 95% CrI, 95% credible interval; CVD, cerebrovascular disease; CKD, Chronic kidney disease.
[1]Bayes factors quantify evidence on a continuous scale around 1, the point of no difference between two groups, ideas, or hypotheses. BF between 0.3 and 3 provide no evidence at all, whereas BF > 3 or < 0.3 provide increasingly strong evidence[4]. For very high BF such as in disease severity and mortality, we used the logarithmic (log) BF.
[2]The result of combining the prior probability (see text) and the BF after seeing the data from Liotta and coauthors, in direct probability terms after rolling back from log-odds ratios. We can use this probability to quantify the risk of encephalopathy instead of statistical significance, which conveys little practical information to clinicians and patients. For example, a man with COVID-19 has a probability of 0.6 (60%) of developing encephalopathy at any point during the acute infection; this risk could be as low as 0.5 (indicating the same risk as women) or as high as 0.7, with 95% certainty that the true probability is in the interval.
[3]*P*-value from the article by Liotta and coauthors.
[4]By comparing men with encephalopathy (101/281) and women (61/228).

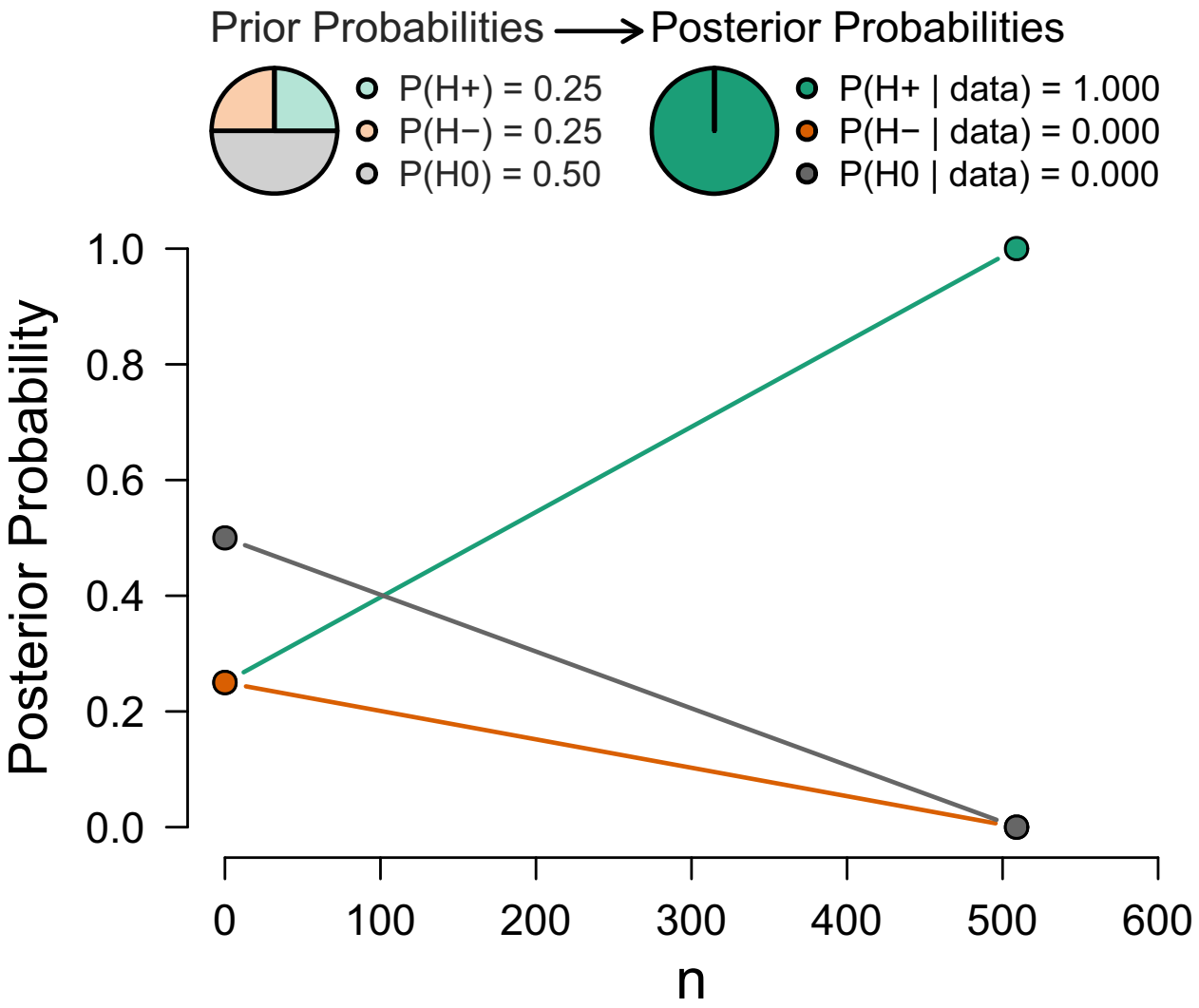

Figure 1. Upper panel: the left probability wheel shows the distribution of probabilities of no difference P(H_0), and a difference P(H +-) in encephalopathy by COVID-19 severity. The right probability wheel is the change of these probabilities after the Bayes rule (posterior). Lower panel: the sequential analysis plots how the probabilities increase with more observations.

distribution, we can communicate results in real probability terms, something classical statistics cannot do.

We specified a weakly informative prior (N ~0,1) based on level VI evidence on COVID-19-related encephalopathy. All the computations with notes are accessible at the Open Science Framework portal (osf.io/p94u8/). A summary of the results is in Table 1, and Figure 1 will help readers to visualize the effect of disease severity on encephalopathy within a Bayesian framework.

We believe that these probabilities are overestimates because we worked with descriptive data from a single study. As an example, in our model, the probability that a patient with severe COVID-19 will be encephalopathic was 97%, which tallies well into the odds ratio of 131 by Liotta and coauthors in their adjusted regression model. A case–control design will recalibrate these results to a less impressive but more accurate figure. COVID-19 suspect cases admitted during the same period with a negative test result are acceptable as controls, understanding the limits of test accuracy. We should view rates, risks, and effect sizes from case series of COVID-19 with plenty of caution.

References

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