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LETTER TO THE EDITOR

Inclusive use of effect size conversion and Bayes factor in intensive care medicine research☆

Uso inclusivo de la conversión del tamaño de efecto y del factor Bayes en la investigación de medicina intensiva

Dear Editor:

On 26 September 2020, this journal published an important article that reported on the existence of a series of statistically significant associations ($P < .05$) between different genetic polymorphisms of the human leukocyte antigen (HLA) system and mortality due to COVID-19 in 72 patients,[1] one of which included the HLA-A*11 gene, based on measurement of the odds ratio (OR = 7.693).

The replication of clinical investigations based on significance tests is advised. This can be done through Bayesian inference, since it allows us to reanalyze the significant finding reported by Lorente et al.,[1] where the Bayes factor (BF) method is referred to as the probability of the data under one hypothesis in relation to the other hypothesis (null hypothesis versus alternative hypothesis).[2,3] In other words, the BF estimates quantification of the strength of proof on which the data support both hypotheses in contrasting them, beyond the dichotomic interpretation or rejection or acceptance of the null hypothesis.[2,3] The statistical replication of significant findings with the BF allows us to strengthen the practical credibility of articles in the field of Intensive Care Medicine (experimental research, clinical trials, interventions and treatments). This is required when Bayesian inference reports conclusive or greater level evidence ($BF_{10} > 10$), based on Jeffrey's classification scale[4] for BF: weak, moderate, strong, very strong and extreme (Table 1).

The aim of the present letter is to report an example of Bayesian reanalysis to define the level of evidence of statistical hypotheses. Accordingly, consideration was made of the sample size and conversion of OR to correlation effect size (r) through an online calculator,[5] where the conversion value was r = 0.49. This method considers two interpretations: BF_{10} (in favor of the alternative hypothesis) and BF_{01} (in favor of the null hypothesis), with a credibility interval of 95%. The results obtained for BF are: $BF_{10} = 1.690$ and $BF_{01} = 0.0006$, with 95%CI: 0.284–0.64, which warrants the significant finding reported by Lorente et al.,[1] with extreme evidence in favor of the alternative hypothesis (correlation). This allows us to infer that the rest of statistical associations of greater magnitude between the HLA genes and mortality also exhibit extreme evidence – thus contributing greater credibility to the clinical conclusions drawn in the mentioned study.

Table 1 Bayes factor quantifiable interpretation values.

>100	Extreme	Alternative hypothesis
30 + 100	Very strong	Alternative hypothesis
10 + 30	Strong	Alternative hypothesis
3.1–10	Moderate	Alternative hypothesis
1.1–3	Weak	Alternative hypothesis
1	0	No evidence
0.3–0.99	Weak	Null hypothesis
0.29–0.1	Moderate	Null hypothesis
0.09–0.03	Strong	Null hypothesis
0.03–0.01	Very strong	Null hypothesis
<0.01	Extreme	Null hypothesis

Note: Proprietary table based on Jeffrey's classification scale.[4]

In conclusion, the inclusive use of effect size conversion and the BF is a great methodological contribution that has practical implications for medical decision making, based on the confirmation of results that are effectively conclusive and of greater relevance in the context of COVID-19.

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Validation of medical researchs☆

Validación de las investigaciones médicas

Dear Editor,

We have read the letter «Inclusive use of effect size conversion and Bayes factor in Intensive Care Medicine research»,[1] referred to our article recently published in MEDICINA INTENSIVA, entitled: «HLA genetic polymorphisms and prognosis of patients with COVID-19», with great interest.[2]

Our study involved 72 patients with COVID-19 (10 deceased and 62 surviving after 30 days), and reported a statistically significant association between different genetic polymorphisms of the human leukocyte antigen (HLA) system and mortality due to COVID-19 in the regression analysis. One of the mentioned alleles was HLA-A*11.

The comparison of deceased patients and survivors identified a statistical tendency ($p = 0.051$) towards a greater presence of the HLA-A*11 allele among the patients that died (3/30 [30%]) versus the survivors (4/62 [6.5%]). However, the deceased individuals presented higher APACHE-II ($p < 0.001$) and SOFA scores ($p = 0.001$) than the survivors. The regression analysis found the presence of the HLA-A*11 allele to be associated to increased mortality controlling for SOFA (OR: 7.693; 95%CI: 1.063–55.650; $p = 0.04$) or APACHE-II (OR: 11.858; 95%CI: 1.524–92.273; $p = 0.02$).

We admitted that our study had limitations, including the fact that we only entered two variables in each regression model, due to the small number of deceased patients in our study, which precluded the inclusion of several variables.[3] Nevertheless, we feel that the strengths of the study were the fact that the presence of the HLA-A*11 allele was associated to mortality after controlling for two patient severity scores (SOFA or APACHE-II), and that the presence of this allele has previously been associated to a poor outcome in the context of other infectious diseases.[4,5]

We agree with the methodological reflection of Ramos-Vera, recommending the confirmation of clinical research in order to validate the results obtained and strengthen their practical credibility. As commented by Ramos-Vera, the option of using Bayesian inference offers a very good approach to the control of error in estimations. Moreover, we are happy to know that the Bayesian analysis made by Ramos-Vera to define the level of evidence of our study using the Bayes factor (BF) method found the results referred to FB10 (in favor of the alternative hypothesis) and FB01 (in favor of the null hypothesis) to indicate extreme evidence of our findings. Nevertheless, we recommend the validation of observational or experimental results to be made using replication with samples external to the study. We therefore consider that it would be interesting to obtain findings similar to our own in future samples involving different COVID-19 patients, in order to determine whether the findings are stable, reducing the uncertainty of possible type 1 errors.

In conclusion, we agree with Ramos-Vera that the confirmation of clinical research is necessary (based on external samples or Bayesian inference) in order to validate the results obtained and strengthen their practical credibility.

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