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Letter to the Editor

RE: "SHOULD META-ANALYSES OF INTERVENTIONS INCLUDE OBSERVATIONAL STUDIES IN ADDITION TO RANDOMIZED CONTROLLED TRIALS? A CRITICAL EXAMINATION OF UNDERLYING PRINCIPLES"

In their recent article, Shrier et al. (1) considered a 95% confidence interval as being one with a 95% probability that a population parameter is included in the interval and a 5% probability that it will lie outside the interval. We wish to clarify some aspects of confidence intervals' interpretation. A simple example illustrates our points.

Let us consider a group of 20 patients who receive a new treatment. Only 6 fail to respond to the treatment. Let π be the population proportion of possible patients who would not respond to the treatment. π is the parameter of interest; its true unknown value is the quantity to be estimated. Considering the Bernoulli process, the likelihood is $\pi^6(1 - \pi)^{14}$ for $0 < \pi < 1$. We calculate an exact interval with 90% confidence (2) that happens to be nonsymmetric around 6/20: (0.175, 0.505). This may be the smallest (most precise) 90% confidence interval for the observation "6 out of 20." The correct interpretation of the information that π is in this interval with 90% confidence is as follows: If we could repeat this procedure over a large number of samples of size 20, the true unknown value of π would be contained in 90% of the intervals; hence, we are confident that our particular interval, (0.175, 0.505), contains the true value of π. Note that we never use the term *probability*, since this interpretation is actually a frequentist one. The evaluation is based on samples that could have been observed but were not. Note also that since π is not a random quantity in the frequentist environment, π belongs (or not) to the interval without any probability attached to the statement. This is the reason to speak about confidence, not probability.

Alternatively, to build Bayesian credible intervals (2, 3), consider a uniform prior in (0;1). This corresponds to normalizing the likelihood function, producing a beta posterior with, for example, $\alpha = 7$ and $\beta = 15$. The 90% credible interval, the smallest interval with a posterior probability of 0.9, is (0.165, 0.483). This interval contains π with a posterior probability of 0.9. In fact, this is the smallest interval that has 90% of the area under the likelihood function. This interval is a bit narrower than the confidence interval presented previously.

We have shown that if one decides to use probabilities to replace confidences, the construction of the intervals is completely different than the usual method.

In other words, Shrier et al.'s interpretation of the 95% confidence interval given on page 1204 of their article (1) and in their Appendix was technically incorrect. Rather than providing 95% confidence that the true value of the population parameter lies within the interval, the correct interpretation is that with the performance of equivalent studies, 95% of the observed confidence intervals would cover the true value of the parameter—a subtle but important difference, since population parameters are not random quantities and therefore probability statements should not be attached to them. Only in the Bayesian framework, which was not considered by Shrier et al., are parameters treated as random variables.

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Carlos Pereira[1] and Euclides Castilho[2] (e-mail: cadebp@gmail.com)
[1] *Department of Statistics, Institute of Mathematics and Statistics, University of Sao Paulo, Rua do Matão, 1010, Cidade Universitária, CEP 05508-090, Sao Paulo, Brazil*
[2] *Department of Preventive Medicine, School of Medicine, University of Sao Paulo, Avenida Dr. Arnaldo, 455, Cerqueira César, CEP 01246-903, Sao Paulo, Brazil*

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