Bayesian Statistical Inference in ANESTHESIOLOGY

In this issue of Anesthesiology, Kant et al.\(^1\) demonstrate the application of the Continual Reassessment Method in the estimation of the \(ED_{95}\) for bupivacaine. The article is not only of clinical interest, but also serves to illustrate the utility of a formal Bayesian statistical analysis. In the field of statistics, the use of such a Bayesian approach to evaluate scientific evidence is becoming increasingly popular. For example, in the 23 leading statistical journals, the proportion of articles which could be identified using either “Bayes” or “Bayesian” search terms, increased from 11% in 1995 to 32% in 2000.\(^2\) Since that time, improvements in the available software to conduct the analyses have, no doubt, encouraged the use of Bayesian methods to increase even further.

The field of Anesthesiology has a long history of using Bayesian principles in engineering or technical applications, but such approaches have not often been used in clinical studies. Although lagging well-behind statistical journals in terms of the number of studies applying formalized Bayesian inference, numerous studies using or discussing a Bayesian approach to statistical inference have been published in ANESTHESIOLOGY. Dating back to 1988, Maitre and Staniski\(^3\) published what appears to be the first use of Bayesian inference in the Journal: a prediction study of intraoperative plasma concentrations of alfentanil. Since that time, an increasing number of statistical procedures have either relied on some aspects of the Bayesian approach to estimate probability or used a formalized Bayesian system to update prior knowledge for incorporating novel information. As a few examples, several very recent studies have featured comparisons estimated using Bayesian methods,\(^4,5\) two meta-analyses have been published in the Journal using Bayesian methods,\(^6,7\) and the Journal now regularly publishes high-quality pharmacokinetic studies that rely on some part of this approach to analysis.\(^8,9\)

Because of its logical consistency and ever-improving software, we anticipate that the popularity of the Bayesian approach for conducting statistical analysis will grow immensely in the Journal over the next several years. However, because the approach is still novel to many analysts and many of our readers, authors must take care to adequately describe and report the results of such studies. Our goal of this editorial is to articulate the reporting elements that are required to adequately communicate the results of a Bayesian analysis to the readers of ANESTHESIOLOGY. Because of its excellence in reporting, the study reported by Kant et al.\(^1\) serves as an exemplary model for illustrating both the benefits of using this approach and how it is best reported.

The vast majority of published articles in ANESTHESIOLOGY rely on the “frequentist” approach to statistical inference. This approach is familiar to most readers and consists of answering the question: “if the null hypothesis is true, how frequently would we expect to obtain this result (or a result more extreme than this one)?” Answering this question involves the execution of a statistical analysis that can be reported either using the best practices outlined in the guidelines to authors or those highlighted in several past editorials.\(^10,11\)

In contrast to the frequentist approach, a Bayesian approach answers the question: “considering our prior beliefs (about a hypothesis, a parameter, etc.), what should our new beliefs be given the collected data?”

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an updated belief system (posterior distribution). Although the intricacies of Bayesian analysis are beyond the scope of this editorial, many detailed discussions are available, including an elegant treatise published in this Journal.

Reporting a Bayesian analysis requires careful consideration of the unique elements of this type of analysis. Many of the reporting elements may not be immediately familiar to analysts trained in the classical frequentist approach. At the time of writing this article, three different reporting guidelines have been offered to assist analysts in reporting their results; these include BayesWatch, BaSiS*, and the more recent, Reporting Of Bayes Used in clinical StUdies (ROBUST) guidelines. Although any of these guidelines could be used to elegantly report the results of a study based on Bayesian inference, this editorial recommends the use of the ROBUST guidelines when reporting a clinical study, such as the one conducted by Kant et al. In what follows, each of the elements of the ROBUST guidelines is presented in the context of how they were addressed in the study by Kant et al. Following these guidelines for all submissions of this type will help ensure that our research community best leverages the benefits of Bayesian statistical analysis.

Prior Distribution

Specified
Because of their crucial importance in estimating the parameters of interest using Bayes theorem, the prior probabilities (e.g., distributions, point estimates) must be reported to the reader. Kant et al. clearly reported that they used an exponential unit in prior analysis. The authors’ prior beliefs about the probability of a failed block then corresponded to 0.5, 0.25, 0.10, 0.05, 0.02, and 0.01 for the respective dose levels of 12, 15, 18, 21, 24, and 27 ml of bupivacaine.

Justified
Because prior beliefs are subjective (i.e., they could rationally differ among individuals) and because they can impact the inferences generated in the analysis, it is important to explicitly justify how the system of beliefs was quantified for the analysis. Kant et al. state that their considerations were based on referenced prior dose-finding studies and clinical judgment.

Sensitivity Analysis
Even thoughtful specification of a prior distribution might leave a skeptical reader wondering: “how might the results have been different if a different set of prior beliefs had been considered?” For this reason, consideration and reporting of how alternate prior belief systems impacted the findings is a very good practice. Kant et al. did not perform a formal sensitivity analysis, but used sequential estimates where the posterior of the previous cohort informed the prior of the next cohort. In this way, the original priors were replaced at each step in light of updated information.

Analysis

Statistical Model
To allow evaluation, the statistical model used to describe the new information must be reported to the reader. As in any statistical analysis, the choice of the model form has important implications, therefore care should be taken to describe the model that is used to characterize the data. Kant et al. report a power model to predict the probability of block failure conditional on dose.

Analytical Technique
The actual conduct of the analysis, including iterative design, estimation details, or any other detail required to allow replication of the model, must be provided. Although not required by the ROBUST guidelines, the software used to conduct the analyses, convergence statistics, and details on the estimation runs are all good reporting practices. Kant et al. have provided a wealth of information in their study including the software, nature of the starting dose, the iterative cohort design, and the stopping rules for the analysis.

Results

Central Tendency
The posterior distribution is essential for interpreting the findings of the analysis, therefore characterizing this distribution using appropriate aspects of central tendency is a good reporting practice. Analyses will widely differ in terms of the nature of the posterior probability distributions, and the descriptive statistics used to represent these distributions should be ones relevant to the distribution and goal of the analysis. Kant et al. do not explicitly provide such a summary statistic (they provide one-point estimate within this distribution), but thoroughly report all of the posterior probabilities by dose range and cohort.

SD or Credible Interval
Given the importance of the posterior, the variability in the posterior distribution, particularly for any parameter(s) of interest, must be reported. Often this will involve reporting the probability coverage for some specified range of the posterior (i.e., the credibility interval), providing an important aspect of interpretation. Kant et al. were specifically interested in the fifth percentile of the final posterior distribution of the dose-failure relationship, and they report the range of doses (24–28 ml) that fell into this 95% credibility interval.

Application in Anesthesiology
There are many benefits associated with using the Bayesian approach, but we shall consider only three. The first group of these relate to how the results of such analyses are interpreted. Bayesian methods condition on the collected

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data to make inferences about parameters and hypotheses, whereas frequentist methods condition on some null hypothesis to make inferences about the plausibility of the data.\textsuperscript{19} Using a Bayesian approach allows a simple interpretation of a hypothesis test (e.g., there is a 95\% chance that the two groups differ) versus the well-known difficulties in interpreting frequentist inferences (e.g., assuming the two groups do not differ, there is less than a 5\% chance that these results [or those more extreme] would have been observed). A second benefit of using a Bayesian approach is the thorough consideration of prior information or expectation in the analysis. By considering a prior probability in the calculation, prior work can be readily considered in the current calculation. Kant \textit{et al.}\textsuperscript{1} nicely demonstrate this advantage when using the Continual Reassessment Method to continually update estimates using just previously collected data. The use of prior probabilities can also be useful to scrutinize extremely surprising findings. The prior probability of observing surprising findings can be postulated, discussed, fought over, and then combined with the data to estimate a posterior distribution that reflects a rational new belief under a range of prior beliefs. A third benefit of a Bayesian approach is in applications where the collected data are not samples or are otherwise not repeatable. Frequentist inference is based on the thought experiment of repeated random sampling from a population (i.e., probability as relative frequency). For applications where repeated sampling would produce the same sample, frequentist estimates of uncertainty become inappropriate, and Bayesian approaches are more conceptually sound.

There are also a host of objections and challenges in using Bayesian analysis, but we will not consider any of these here (for an interesting discussion, see the paper by Gelman).\textsuperscript{20} Of note is that this editorial does not recommend a Bayesian approach to analysis but instead emphasizes good reporting practices for communicating the results of a Bayesian inference when one is conducted. Relevant submissions to the Journal will be reviewed in accordance with the ROBUST guidelines, and the authors will be required to report these elements in all submissions of this type. Doing so will ensure that our readership will have an access to the important elements that are required for interpreting such an approach, and will ensure that our research community maximally benefits from this new era of scientific inference.

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