Journal of Data Science 23 (1), 59–61
January 2025
DOI: 10.6339/25-JDS1161E
Discussion

Discussion of "Power Priors for Leveraging Historical Data: Looking Back and Looking Forward"☆

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Congratulations to Minghui Chen and collaborators for this nice article that provides a comprehensive exploration of power priors that is an essential class of informative priors designed to integrate historical data into data analyses at hand. This framework is particularly relevant in diverse fields such as clinical trials, genetics, and healthcare, where the use of prior information can improve statistical efficiency and decision making. By focusing on foundational models like binomial regression and normal linear regression, the authors offer a systematic overview of power priors, highlighting their flexibility and applicability. The use of real-world datasets as examples demonstrates the practical utility of these methods to address complex domain-specific challenges. The discussion aimed at theoretical developments, applied examples, and software tools outlined in the paper. Future directions are also discussed for advancing the use of power priors in research and practice.

My question in this discussion note concerns a particular example that I encountered in a consulting project a few years back on drug discovery for migrant headache (Xie et al., 2013). We encountered a so-called *discrepant (or outlying) posterior phenomenon*. I wondered whether the development of power priors can provide a solution to the particular clinical study example in Xie et al. (2013), where we did have incomplete historical information to fully specify our prior distribution.

A Binomial Clinical Trial The phenomenon of outlying (or discrepant) posterior distributions, as described in Xie et al. (2013), arises in certain Bayesian analyses involving multiple parameters. Although the phenomenon is commonly seen and may also be somewhat explained by Simpson's paradox (Xie and Singh, 2013; Robert, 2013; Xie, 2013; Chen et al., 2020), we first noticed this phenomenon is in the context of a binomial clinical trial designed to study treatments for migrant headache by Ortho-McNeil Janssen Scientific Affairs (OMJSA) LLC.

In the OMJSA trial, two treatment groups were compared: [A]: consisting of n_1 subjects receiving two drugs (topiramate and almotriptan); [B]: consisting of n_0 subjects receiving one drug (almotriptan). The responses are binary, modeled as

$$X_{1i} \sim \text{Bernoulli}(p_1) \quad \text{and} \quad X_{0j} \sim \text{Bernoulli}(p_0),$$

where p_1 and p_0 represent the probabilities of improvement (measured on certain endpoints, e.g., achieving pain relief at 2 hours, etc.) in the respective groups. Prior to conducting the clinical trial, expert opinions on the improvement difference ($\delta = p_1 - p_0$) were solicited from 11 experts, following established designs of Parmar et al. (1994); Spiegelhalter et al. (1994).

The goal of the study was to incorporate these expert opinions alongside the clinical data to estimate δ. Additionally, historical data of previous clinical trials on the single drug almotriptan

☆Main article: https://doi.org/10.6339/24-JDS1161.
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are available (e.g., from FDA database) and they provide prior information about p_0. Here, two marginal prior distributions, the prior distribution of $\delta = p_1 - p_0$ from experts and the prior distribution of p_0 from historical trials, are available. However, almotriptan are used in both arms, p_0 and p_1 are not independent but we do not have any prior information on the dependence of p_0 and p_1. The information in the two marginal prior distributions is not enough to fully specify the joint prior distribution of (p_0, p_1) or (p_0, δ).

Discrepant Posterior Phenomenon Through approximations, Spiegelhalter et al. (1994, pp. 360–361) outlined a univariate Bayesian approach that directly models $\delta = p_1 - p_0$ (and ignores other model parameters). However, there is a theoretical flaw in this univariate Bayesian approach. This approach does not align with Bayesian theory because the conditional density $f(\text{data} \mid \delta)$ is not defined for a binomial trial, making it impossible to apply Bayes' formula. This limitation reflects the broader critique that Bayesian methods struggle with the "division of labor" concept, as discussed by Efron (1986) and Wasserman (2008). See also discussions in Xie et al. (2013), Xie and Singh (2013), and Xie (2013).

In contrast, a full Bayesian approach that jointly models (p_0, p_1) offers a more comprehensive and theoretically sound solution. However, this approach is not without issues: In certain situations, it can lead to a paradoxical *discrepant posterior phenomenon*, where the marginal posterior of δ contradicts both the data evidence and the marginal prior of δ. In particular, in the OMJSA clinical trial, as stated in Xie et al. (2013, p. 360), "if we use the means as our point estimators, we would report from Figure 4(c) that the experts suggest about 15.9% improvement and the clinical evidence suggests about 10.3% improvement but, incorporating them together, the overall estimator of the treatment effect is 20.1%, which is bigger than either that reported by the experts or that suggested by the clinical data. This result is certainly not easy to explain to clinicians or general practitioners of statistics." This counterintuitive phenomenon can happen in many Bayesian analyses involving the joint distribution of multiple parameters (cf., e.g., Xie and Singh, 2013; Xie, 2013; Chen et al., 2020). It highlights the necessity of sensitivity analysis and challenges the interpretation of Bayesian results as purely data-driven, especially in scenarios where prior assumptions heavily influence conclusions.

Potential of Power Prior for OMSJSA Trial I think the power prior framework described in the current article by Chen et al. (2025) may be more flexible than the family of priors considered in Xie et al. (2013). Although I do not expect the power prior framework to fully address the discrepant posterior phenomenon, I am curious how power priors can be used to analyze this OMJSA migrant headache trial and whether using the power prior can mitigate the counterintuitive phenomenon presented in Xie et al. (2013).

Funding

The author's work was partially supported by NSF-DMS2319260, NSF-DMS2311064, and NIH-1R01GM157610.

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