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Bayesian prediction modeling for two-stage experimental trials for Poisson or Gamma distributed data

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We consider Bayesian prediction modeling to evaluate a satisfaction index after a first phase of experiment in order to decide to stop or continue at the second stage. We apply this method to Poisson and Gamma distributed outcomes in many fields such as reliability or survival analysis for early termination due to either futility or efficacy. We look at two kinds of decisions making: an hybrid Bayesian-frequentist or a full Bayesian approach.

keywords: Bayesian predictive distribution; satisfaction indices; two-stage sequential analysis; experimental trials; Poisson and Gamma outcomes.

1 Introduction

Bayesian design of experiments can be considered as a natural combination of prediction and decision-making, in that the investigators seek the best design to achieve a targeted goals, based on prior or updated knowledge. They are currently interested because of their potential to save time and resources, as well as to reduce the number of adverse events Spiegelhalter et al. (1995), Hand et al. (2016). Bayesian predictive procedure plays a crucial role in different areas of applied statistics, epidemiology, reliability and survival analysis in the aim of developing an adaptive design. More generally, these Bayesian predictive procedures about future observations give to the researcher an accurate method to evaluate the chances that the experiment will end up showing a conclusive

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result, or on the contrary a non-conclusive result Djeridi and Merabet, (2019). They are particularly adapted to sequential designs where interim analysis may provide grounds for terminating the study-effectively by reducing costs moreover it may benefit the general patient population by allowing early dissemination of its findings. Group sequential methods provide a mean to balance the ethical and financial advantages of stopping a study early against the risk of an incorrect conclusion Chow et al. (2011). Decision-theoretic approaches to design of trials take into account the finite number of future patients for whom the trial results will be definitive Shih and Lavori, (2013). In applied work, Gamma distributions give useful representations of many physical situations. For instance, they have been used to make realistic adjustments to exponential distributions in representing life times Nadarajah, (1973). Furthermore, Gamma outcomes have an extensive implementation in various fields: in hydrology, finance medical science, psychology and reliability. One can find other examples with Poisson and Gamma data in Bakhshi ,(2011), Hamada et al. (2008), Lakshmi and Vaidyanathan, (2015), Anisimov, (2008) and Zaslavsky, (2010).

In our paper we exploit Bayesian predictive distribution for Poisson and Gamma distribution in experimental clinical trials with count data as outcome. The Poisson distribution is a natural and commonly used model. For example, Hand et al. (2016) employ count data in single-arm studies as the primary endpoint to demonstrate the effectiveness of commercial preparations of intravenous immunoglobulin (IGIV) for preventing serious acute bacterial Infections in patients with primary immunodeficiency .

The main aim of this paper is to propose a procedure based on the concept of index of satisfaction related to hypothesis testing which is a function of the p-value or the probability of observing a result as extreme or more extreme than the perceived result under the null hypothesis. Given the available data, we calculate a predicted satisfaction index conditioning to the previous observations to achieve successful results at the end of trial Merabet, (2013). We consider the case of a two-stage procedure with Poisson or Gamma distributed data that allows for early termination owing to either futility or extreme efficacy.

This paper is organized as follows: In Section 2, we study background information on statistical inference for two stage sequential designs; we discuss both frequentist and bayesian indexes, we also provide prediction of satisfaction index and stopping rules. We describe our two-stage designs for Poisson and Gamma outcomes in Section 3. A simulation results is given in Section 4. In Section 5, we test the relevance of the Poisson model on real count data. We make a conclusion in Section 6. In the Appendix, we explain the effective sample size of a prior distribution for our Gamma-Poisson and Gamma-Gamma models.

2 Two-stage design

2.1 Statistical inference for two stage experimental design

In recent years, the concept of two-stage design has led to the development of group sequential designs, where there is a set of available experiments which may be conducted.

After each stage, if the decision is made to continue or not the experiment, and if it is the case, to build a new design for the next case. Since some experiments may be more "informative" than others, there is a potential saving in using decision rules which choose experiments rather than using decision rules which typically take one experiment of each type Blot and Meeter, (1973).

In sequential experimental design, we sequentially choose an experiment to be performed and observe the outcome. We consider here two stage experimental designs and we denote by $x \in X$ and $y \in Y$ the results of each experiment, that are assumed to be independent. The distributions of x and y depend on a common parameter $\theta \in \Theta$. We propose a satisfaction index based on both the first and the second phase of the experiment Merabet et al. (2017). This experiment is used to establish the final conclusion on the study and determine the user's satisfaction, denoted $\varphi(z)$. In our study, the prediction is carried out in a Bayesian context; that is, based on the choice of a prior probability on Θ .

Since satisfaction indexes are essential to the study of both frequentist and bayesian test, we consider both a hybrid frequentist-bayesian approach and a fully bayesian approach. Those indexes are used as a stopping rule for designing phase II clinical trials.

2.1.1 Frequentist index

We define the frequentist satisfaction index in classical test as a measure of the degree of satisfaction with a given result.

We want to test the null hypothesis $H_0 : \theta \in \Theta_0$ vs $H_1 : \theta \in \Theta \setminus \Theta_0$ on the parameter θ . The rejection region R^α of the usual frequentist test at level α is defined by:

$$R^\alpha = \{z ; p(z) \leq \alpha\}$$

where $p(z)$ is the p-value of the test.

A basic satisfaction index is defined by:

$$\varphi_0(z) = 1_{R^\alpha}(z) \tag{1}$$

where $1_A(z) = 1$ if $z \in A$ and 0 otherwise.

The index $\varphi_0(z)$ has a form that express a satisfaction "all or nothing". However, it is interesting to take into account the level at which the result appears significant. It thus appears natural to consider satisfaction indexes that are null if a significant effect is not detected, and in the opposite case as an increasing function of the classical indicator of significance which is the p-value Saville et al. (2014). For this purpose the p-value is regarded as a measure of credibility to be attached to the null hypothesis that practitioners often use to answer several criticisms and disadvantages of the Neyman Pearson approach. Therefore, we propose a satisfaction index, considered as improved for its interest in the concept of predicting satisfaction and defined as a decreasing function of the conclusive measure p after the processing of the data in the following manner:

$$\varphi(z) = \begin{cases} 0 & \text{if } p(z) \geq \alpha \\ 1 - p(z) & \text{otherwise} \end{cases} \quad (2)$$

2.1.2 Bayesian index

In a Bayesian context, let $\Pi(\Theta|z)$ be the posterior probability given the observation z . It is conventional in Bayesian statistics to treat the situation test of Θ_0 against Θ_1 by providing $\Pi(\Theta_1|z)$. We denote \tilde{R}^α the rejection region of the Bayesian test at level α defined by:

$$\tilde{R}^\alpha = \{z; \Pi(\Theta_1|z) \geq 1 - \alpha\}$$

Similarly to the frequentist approach, we consider the two satisfaction indexes:

$$\tilde{\varphi}_0(z) = 1_{\tilde{R}^\alpha}(z) \quad (3)$$

and

$$\tilde{\varphi}(z) = \begin{cases} 0 & \text{if } z \notin \tilde{R}^\alpha \\ \Pi(\Theta_1|z) & \text{if } z \in \tilde{R}^\alpha \end{cases} \quad (4)$$

2.2 Prevision of satisfaction index and stopping rules

The claim of efficacy rules or treatment benefit can be based either on Bayesian posterior distributions (fully Bayesian) or frequentist criteria such as p-values (hybrid Bayesian-frequentist), see Saville et al. (2014). The main matters to focus on are the eligible reasons either to stop or to carry on a study. Reasons for stopping may include Todd et al. (2011):

- The experimental treatment is evidently worse than the control
- The experimental treatment is already evidently better
- The chances of showing that the experimental treatment is better are little.

The continuing may include the following reasons:

- A moderate advantage of the experimental treatment is likely and it is desired to assess the magnitude carefully
- The event rate is low and more patients are needed to reach a given power.

Numerous authors have been strong and consistent in advocating the use of predictive probabilities to make decisions based on accumulating experimental trial data. In the logic of the introduction of the satisfaction index, it is natural to characterize the value of the test procedure instead of the power function, a prediction index, that is the mathematical anticipation with respect to the predictive probability on the complete data conditioned by the result of the first stage Merabet, (2013), where a two-step experiment must be conducted:

- A first result x , determines whether or not we continue the experiment,
- If the experimenter is highly satisfied and we effectively continue the experiment, then the final test is based on the result of both stage z rather than only the result y of the second stage.

Let $p(z|x)$ be the predictive probability of $z = (x, y)$ after the first stage, i.e. conditionally on x . The predicted value of the index φ is defined by:

$$\eta(x) = E(\varphi(z)|x) = \int \varphi(z)p(z|x)dx \quad (5)$$

The predicted index $\eta(x)$ generalizes the power of the test in the dialectic of the index of satisfaction. The practitioner decide a predicted index above which the experiment is carried on. In a purely Bayesian viewpoint, the predicted index is:

$$\tilde{\eta}(x) = E(\tilde{\varphi}(z)|x) = \int \tilde{\varphi}(z)p(z|x)dx \quad (6)$$

3 Two-stage Design for Poisson and Gamma outcomes

3.1 A Bayesian two-stage strategy for Poisson outcome

In experimental clinical trials using count data of rare events, the Poisson distribution is a natural and commonly-used model. One of the essential goals of most Phase II clinical studies is to decide whether to continue with a large-scale randomized Phase III trial or to reconsider or abandon the therapy because of an absence of efficacy or evaluate toxicity Stallard, (1998). If a treatment may yield inferior results than expected, some Phase II studies use a two-stage design to allow for early termination. We consider the case of a Phase II trial whose primary endpoint is the number of events observed over a fixed period of time, where this count has a Poisson distribution Hand et al. (2016). We also presume that the events considered here show a negative outcome for patients, and, thus, a huge number of events indicate an absence of efficacy. Hence, the two-stage design for Poisson data is as follows.

Let n_1 and n_2 be the number of subjects included in the first and second stage and $n = n_1 + n_2$. Let x_j , resp. y_j , be the number of occurrences of the events of interest for the j th subject at the first, resp. the second, stage during a period of time t_{1j} , resp. t_{2j} . We assume that x_i and y_j are independent and Poisson distributed with parameter $\theta \times t_{1j}$ and $\theta \times t_{2j}$. Let $x = \sum_{j=1}^{n_1} x_j$ and $y = \sum_{j=1}^{n_2} y_j$ be the total number of observed events over the first and second stage and $t_i = \sum_{i=1}^{n_i} t_{ij}$, $i = 1, 2$. We define here $z = x + y$ as the number of events over the two stages and $t = t_1 + t_2$. Let s and s_1 be pre-specified thresholds such that

1. If $x \geq s_1$, then the trial is stopped for lack of efficacy;
2. otherwise, the phase II trial continues to the second stage,

If the trial continue to the second stage, n_2 patients are enrolled and

1. If $z \geq s$, then the development is stopped for lack of efficacy;
2. otherwise, the Phase II trial continues to a Phase III trial,

In another meaning, on the basis of the accumulated data at stage 1, one can stop the trial because of lack of convincing efficiency. This occurs when the predicted satisfaction index is less than a specified threshold. Otherwise the experiment goes on. More rarely, a trial may be stop for strong evidence of efficacy, that is when the predicted satisfaction index is larger that a given threshold. Early stopping means ensures that resources are not wasted and, in case of evidence of efficacy, allow a faster development.

In Bayesian modeling, the choice of a prior distribution is crucial because it has potentially a large influence on the posterior density, especially when the collected observed counts of interest are small. Researchers attempt to find a prior distribution that summarizes available information and accurately reflects uncertainty. In the posterior analysis, we usually desire that the likelihood dominates and, therefore, encourage the use of a relatively non-informative prior. Here, we use a conjugate gamma family of prior for θ with parameter (a, b) Hand et al. (2016).

Let $x \sim Poisson(t_1\theta)$ with probability function

$$f(x|t_1, \theta) = \frac{(t_1\theta)^x}{x!} \exp[-t_1 \theta], \quad x = 0, 1, 2, \dots \quad (7)$$

The posterior distribution $\pi(\theta|x, t_1)$ is a gamma $(x + a, t_1 + b)$ distribution . If $x < s_1$, we continue to the second stage where y counts are observed during person-time t_2 .

Thus $y \sim Poisson(t_2\theta)$ with probability function

$$f(y|t_2, \theta) = \frac{(t_2\theta)^y}{y!} \exp[-t_2\theta], \quad y = 0, 1, 2, \dots \quad (8)$$

Consider the one sided test $H_0 : \theta \geq \theta_0$ vs $H_1 : \theta < \theta_0$ where θ_0 is the desired efficiency threshold. Then, we determine t and s , given that the first stage has been completed and x have been observed with $x \leq s_1$.

The usual test on the results z of the first and second phase defined by:

$$R^\alpha = \{z; z < q_\alpha\}$$

with $q_\alpha = \sup\{c; Pr(z < c|\theta_0) \leq \alpha\}$

In the Bayesian approach

$$\tilde{R}^\alpha \{z; z < \tilde{q}_\alpha\}$$

with $\tilde{q}_\alpha = \sup\{z; \Pi(\theta < \theta_0|z) \geq 1 - \alpha\}$

We have those formulas for sequential designs:

$$\varphi_0(z) = 1_{R^\alpha(z)},$$

$$\tilde{\varphi}_0(z) = 1_{\tilde{R}^\alpha(z)},$$

$$\varphi(z) = (1 - \Phi_{\theta_0}^P(z)) \mathbf{1}_{z < q_\alpha},$$

$$\tilde{\varphi}(z) = \tilde{\Phi}_{a+z; b+t}(\theta_0) \mathbf{1}_{z < \tilde{q}_\alpha},$$

where $\Phi_{\theta_0}^P(z)$ the left-continuous cumulative distribution function of a Poisson distribution, and $\tilde{\Phi}_{(a_1, b_1)}$ is the cumulative distribution function of a *Gamma*(a_1, b_1) distribution.

The predictive distribution of y given x is a Gamma-Poisson distribution given by:

$$f(y|x) = \frac{t_2^{(y)}(b+t_1)^{(a+x)}\Gamma[a+x+y]}{(b+t_1+t_2)^{(a+x+y)}\Gamma[a+x]y!} \tag{9}$$

Then, our predictive satisfaction indexes for the frequentist approach are:

$$\eta_0(x) = E(\varphi_{0(\alpha)}(z)|x) = \sum_{y=0}^{q_\alpha-x-1} \frac{t_2^{(y)}(b+t_1)^{(a+x)}\Gamma[a+x+y]}{(b+t_1+t_2)^{(a+x+y)}\Gamma[a+x]y!} \tag{10}$$

$$\eta(x) = E(\varphi_{(\alpha)}(z)|x) = \sum_{y=0}^{q_\alpha-x-1} (1 - \Phi_{\theta_0}^P(x+y)) \frac{t_2^{(y)}(b+t_1)^{(a+x)}\Gamma[a+x+y]}{(b+t_1+t_2)^{(a+x+y)}\Gamma[a+x]y!} \tag{11}$$

For the bayesian approach, we have

$$\tilde{\eta}_0(x) = E(\tilde{\varphi}_{0(\alpha)}(z)|x) = \sum_{y=0}^{\tilde{q}_\alpha-x-1} \frac{t_2^{(y)}(b+t_1)^{(a+x)}\Gamma[a+x+y]}{(b+t_1+t_2)^{(a+x+y)}\Gamma[a+x]y!} \tag{12}$$

$$\tilde{\eta}(x) = E(\tilde{\varphi}_{(\alpha)}(z)|x) = \sum_{y=0}^{\tilde{q}_\alpha-x-1} \tilde{\Phi}_{a+x+y; b+t_1+t_2}(\theta_0) \frac{t_2^{(y)}(b+t_1)^{(a+x)}\Gamma[a+x+y]}{(b+t_1+t_2)^{(a+x+y)}\Gamma[a+x]y!} \tag{13}$$

3.2 A Bayesian two-stage strategy for Gamma outcomes

We consider here the case of Gamma-Gamma conjugate families. The Gamma distribution is a flexible family of distributions for continuous non-negative random variables. Gamma distributions are used in many fields such as finance, medical science, wait time modeling, reliability, service time modeling.

At the first stage, n_1 and n_2 subjects are included whose individual responses are x_i and y_i . Let $x = \sum_{i=1}^{n_1} x_i$, $y = \sum_{i=1}^{n_2} y_i$, $N_1 = n_1p$ and $N_2 = n_2p$, with p known. The distribution for x is

a gamma distribution with parameters (n_1p, θ) and with probability function

$$f(x, n_1p, \theta) = \frac{\theta^{n_1p}}{\Gamma(n_1p)} x^{n_1p-1} \exp[-\theta x] \tag{14}$$

where $x = 0, 1, 2, \dots$ *We assume the prior distribution $\theta \sim \text{gamma}(a, b)$. The posterior distribution on θ after the first stage is a gamma $(a + n_1p, b + x)$ distribution. Although there is a vast literature available on the estimation of the gamma parameters using the

frequentist approach, not many work has been done on the Bayesian inference of the gamma parameter.

The second-stage sampling is also a gamma distribution $y \sim \text{gamma}(n_2p, \theta)$ /

Define $z = x + y$ which is a sufficient statistics, Gamma distributed with parameters (np, θ) , and $n = n_1 + n_2$ is the total number of subject to be treated or events until failure depending on the field of application.

$$f(z, np, \theta) = \frac{\theta^{np}}{\Gamma(np)} z^{(np)-1} \exp[-(\theta z)] \quad (15)$$

where $z = 0, 1, 2, \dots$

We consider the one sided test $H_0 : \theta \leq \theta_0$ vs $H_1 : \theta > \theta_0$, where θ_0 is the desired efficacy threshold.

The usual test on the results z of the first and second phase defined by:

$$R^\alpha = \{z; z < q_\alpha\}$$

with $q_\alpha = \sup\{c; Pr(z > c | \theta_0) \geq 1 - \alpha\}$

In the Bayesian approach

$$\tilde{R}^\alpha = \{z; z < \tilde{q}_\alpha\}$$

with $\tilde{q}_\alpha = \sup\{z; \Pi(\Theta_1 | z) \geq 1 - \alpha\}$

We have those formulas for sequential designs:

$$\varphi_0(z) = 1_{R^\alpha(z)}$$

$$\tilde{\varphi}_0(z) = 1_{\tilde{R}^\alpha(z)}$$

$$\varphi(z) = 1 - \Phi_{\theta_0}^G(z)_{1_{z < q_\alpha}}$$

$$\tilde{\varphi}(z) = 1 - \tilde{\Phi}_{a+n_1p; b+z}(\theta_0)_{1_{z < \tilde{q}_\alpha}}$$

Where $\Phi_{\theta_0}^G(z)$ the cumulative distribution function of a Gamma distribution, and $\tilde{\Phi}_{(a_2, b_2)}$ is the cumulative distribution function of a *Gamma*(a_2, b_2) distribution.

The predictive distribution of y given x is an Inverse Beta distribution:

$$f(y|x) = \frac{y^{(n_2p-1)}(b+x)^{(a+n_1p)}}{\beta(n_2p, a+n_1p)(b+x+y)^{(a+n_1p+n_2p)}} \sim InBe(y, a+n_1p, b+x) \quad (16)$$

Then, our predictive satisfaction indexes in frequentist approach are:

$$\eta_0(x) = E(\varphi_{0(\alpha)}(z)|x) = \int_0^{q_\alpha-x} \frac{y^{(n_2p-1)}(b+x)^{(a+n_1p)}}{\beta(n_2p, a+n_1p)(b+x+y)^{(a+n_1p+n_2p)}} dy \quad (17)$$

$$\eta(x) = E(\varphi^{(\alpha)}(z)|x)$$

$$\eta(x) = \int_0^{q_\alpha-x} 1 - \Phi_{\theta_0}^G(z) \frac{y^{(n_2p-1)}(b+x)^{(a+n_1p)}}{\beta(n_2p, a+n_1p)(b+x+y)^{(a+n_1p+n_2p)}} dy \quad (18)$$

For the bayesian approach, we have

$$\tilde{\eta}_0(x) = E(\tilde{\varphi}_{0^{(\alpha)}}(z)|x) = \int_0^{\tilde{q}_{\alpha-x}} \frac{y^{(n_2p-1)}(b+x)^{(a+n_1p)}}{\beta(n_2p, a+n_1p)(b+x+y)^{(a+n_1p+n_2p)}} dy \quad (19)$$

$$\tilde{\eta}(x) = E(\tilde{\varphi}^{(\alpha)}(z)|x)$$

$$\tilde{\eta}(x) = \int_0^{\tilde{q}_{\alpha-x}} 1 - \tilde{\Phi}_{(a+n_1p; b+z)}(\theta_0) \frac{y^{(n_2p-1)}(b+x)^{(a+n_1p)}}{\beta(n_2p, a+n_1p)(b+x+y)^{(a+n_1p+n_2p)}} dy \quad (20)$$

4 Simulation Results

We show in this section the results of our simulation, which present a comparison study of the predicted satisfaction index associated to frequentist and Bayesian tests for several values of the hyper-parameter. We also display the effective sample size (ESS) associated to the prior [see appendix].

4.1 Results for Poisson outcomes

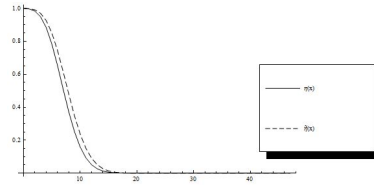


Figure 1: Predicted indexes $\eta(x)$ and $\tilde{\eta}(x)$ in sequential design for frequentist and bayesian test $H_0 : \theta < \theta_0 = 0.5$ with $\alpha = 0.05, a = 1, b = 2, t_1 = 15, t_2 = 5, q_\alpha = 15, \tilde{q}_\alpha = 17, (ESS = 2)$

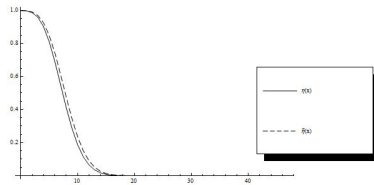


Figure 2: Predicted indexes $\eta(x)$ and $\tilde{\eta}(x)$ in sequential design for frequentist and bayesian test $H_0 : \theta < \theta_0 = 0.5$ with $\alpha = 0.05, a = 1, b = 2, t_1 = 15, t_2 = 20, q_\alpha = 25, \tilde{q}_\alpha = 26, (ESS = 2)$

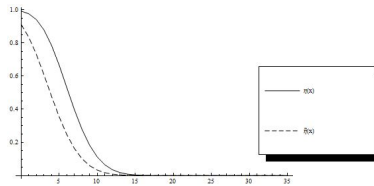


Figure 3: Predicted indexes $\eta(x)$ and $\tilde{\eta}(x)$ in sequential design for frequentist and bayesian test $H_0 : \theta < \theta_0 = 0.5$ with $\alpha = 0.05, a = 6, b = 4, t_1 = 15, t_2 = 5, q_\alpha = 15, \tilde{q}_\alpha = 13, (ESS = 4)$

In Fig.1 with a time-person value t_2 small and a prior centered on the threshold θ_0 , we

can observe that the predicted satisfaction index graphs corresponding to the frequentist and Bayesian tests may be different.

In Fig.2, we observe that when the value t_2 of time-person is large both the frequentist and Bayesian predicted indexes are very close.

Fig.3 shows, as expected, that when the prior favors the efficacy of the treatment, the predicted satisfaction index based on the Bayesian test is higher than that based on the frequentist test.

4.2 Results for Gamma outcomes

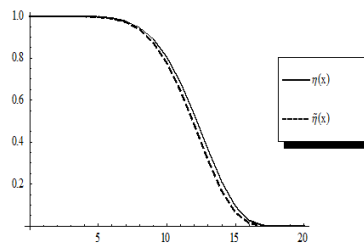


Figure 4: Predicted indexes $\eta(x)$ and $\tilde{\eta}(x)$ in sequential design for frequentist and bayesian test $H_0 : \theta < \theta_0 = 0.5$ with $\alpha = 0.05, a = 1, b = 2, n_1 = 10, n_2 = 5, p = 1, q_\alpha = 18.4927, \tilde{q}_\alpha = 18.0719, (ESS = 1)$

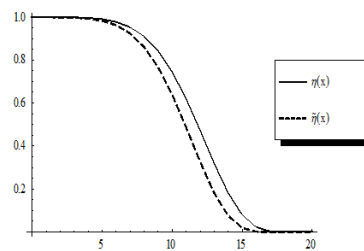


Figure 5: Predicted indexes $\eta(x)$ and $\tilde{\eta}(x)$ in sequential design for frequentist and bayesian test $H_0 : \theta < \theta_0 = 0.5$ with $\alpha = 0.05, a = 3, b = 6, n_1 = 10, n_2 = 5, p = 1, q_\alpha = 18.4927, \tilde{q}_\alpha = 17.2686, (ESS = 3)$

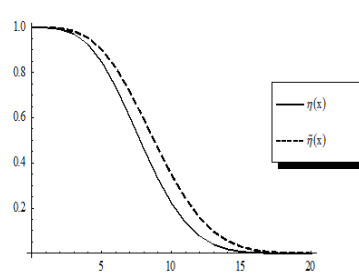


Figure 6: Predicted indexes $\eta(x)$ and $\tilde{\eta}(x)$ in sequential design for frequentist and bayesian test $H_0 : \theta < \theta_0 = 0.5$ with $\alpha = 0.05, a = 3, b = 2, n_1 = 5, n_2 = 15, q_\alpha = 26.5093, \tilde{q}_\alpha = 29.4390, (ESS = 3)$

Fig.4 corresponds to a weak informative prior with $ESS = 1$ centered on the threshold value θ_0 whereas Fig.5 corresponds to a more informative prior centered on the same value.

Fig.6 corresponds to a prior that favor the efficacy of the treatment.

5 Real data analysis

The Poisson-Gamma model has an application for both the clinical trials and the reliability. For example, test the performance of a new heart valve, modeling failure time data ?time to death? used in survival analysis and ?time to interrupt? used in reliability.

We test the relevance of the previously seen of poisson model on real count data. We consider a data presented in (Hamada et al., 2008), which consists of modeling the monthly number of failures of the Los Alamos National Laboratory Blue Mountain supercomputer components (shared memory processors or SMPs) by a Poisson distribution with an unknown average number of failures, θ . The supercomputer consists of 47 identical SMPs and the following table presents their monthly number of failures for the first month of operation.

Table 1: Monthly number of failures for 47 supercomputer components

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 5 | 1 | 4 | 2 | 3 | 1 | 3 | 6 | 4 | 4 | 4 |
| 2 | 3 | 2 | 2 | 4 | 5 | 5 | 2 | 5 | 3 | 2 | 2 |
| 3 | 1 | 1 | 2 | 5 | 1 | 4 | 1 | 1 | 1 | 2 | 1 |
| 3 | 2 | 5 | 3 | 5 | 2 | 5 | 1 | 1 | 5 | 2 | |

For modeling these data, the monthly number of failures is assumed to follow a Poisson distribution. To represent this, the prior information for the parameter assumed to be a conjugate gamma prior distribution with a mean of 5, that is $\theta \sim \text{Gamma}(5, 1)$

We choose $\theta_0=1.2$ and after the calcul we obtain $q_\alpha=69$, $\tilde{q}_\alpha=66$.

Predicted indexes in sequential design for frequentist and bayesian test are given in the following figure and table:

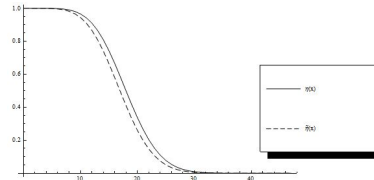


Figure 7: Predicted indexes $\eta(x)$ and $\tilde{\eta}(x)$ in sequential design for frequentist and bayesian test $H_0 : \theta < \theta_0 = 1.2$ with $\alpha = 0.05, a = 5, b = 1, t_1 = 17, t_2 = 30, q_\alpha = 69, \tilde{q}_\alpha = 66, (ESS = 1)$

This real data analysis leads to the conclusion that the results obtained from the Predicted indexes in sequential design for Bayesian test and frequentist test are close to each other but purely Bayesian approach is better than frequentist approach.

Moreover, we observe by looking at the table in full Bayesian approach, a good satisfaction at the event 28 that provides accurate inferences for a parameter of interest and makes the practitioner very satisfied.

Table 2: Predicted indexes $\eta(x)$ and $\tilde{\eta}(x)$ in sequential design for frequentist and bayesian test $H_0 : \theta < \theta_0 = 1.2$ with $\alpha = 0.05, a = 5, b = 1, t_1 = 17, t_2 = 30, q_\alpha = 69, \tilde{q}_\alpha = 66, (ESS = 1)$

| x | $\eta(x)$ | $\tilde{\eta}(x)$ |
|-----|-----------|-------------------|
| 0 | 1 | 1 |
| 1 | 0.999992 | 0.999979 |
| 2 | 0.999969 | 0.999920 |
| 3 | 0.999894 | 0.999739 |
| 4 | 0.999675 | 0.999250 |
| 5 | 0.999114 | 0.998076 |
| 6 | 0.997817 | 0.995541 |
| 7 | 0.99510 | 0.990563 |
| 8 | 0.989891 | 0.981602 |
| 9 | 0.980688 | 0.966713 |
| 10 | 0.965612 | 0.943742 |
| 11 | 0.94260 | 0.910663 |
| 12 | 0.909716 | 0.866007 |
| 13 | 0.865554 | 0.865554 |
| 14 | 0.809618 | 0.741181 |
| 15 | 0.742586 | 0.663776 |
| 16 | 0.666373 | 0.580180 |
| 17 | 0.583949 | 0.494194 |
| 18 | 0.498964 | 0.409772 |
| 19 | 0.415244 | 0.330489 |
| 20 | 0.336296 | 0.259134 |
| 21 | 0.264905 | 0.197484 |
| 22 | 0.202896 | 0.146266 |
| 23 | 0.151084 | 0.105292 |
| 24 | 0.109380 | 0.073684 |
| 25 | 0.077001 | 0.050141 |
| 26 | 0.052723 | 0.033190 |
| 27 | 0.035121 | 0.021379 |
| 28 | 0.022771 | 0.013407 |
| 29 | 0.014374 | 0.008189 |
| 30 | 0.008838 | 0.004874 |
| 31 | 0.005296 | 0.002828 |
| 32 | 0.003094 | 0.00160 |
| 33 | 0.001763 | 0.000883 |
| 34 | 0.000980 | 0.000476 |
| 35 | 0.000532 | 0.000250 |

6 Conclusion

The Bayesian predictive approach is a useful tool in group sequential design to evaluate the strength of the treatment efficacy, which is based on both available and future observations. It can be used for Bayesian or frequentist assessment of the efficiency of a treatment and allows to stop early an experiment either for lack of or at contrary sufficient predicted. One main advantage of the Bayesian predictive method is that it automatically takes into account the level of information available and the predicted information bring by future observations. Another advantage is that it can be used either in hybrid Bayesian-frequentist procedures or full Bayesian procedure. We have shown in this paper how to use this procedure in Gamma-Poisson and Gamma-Gamma models.

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Appendices

Appendix A. determining the effective sample size

We determine here the effective sample size of a prior distribution for our Gamma-Poisson and Gamma-Gamma model as proposed by (Morita et al.,2008). The idea is to match a given prior $p(\theta)$ with the posterior $q_m(\theta|x)$ arising from an earlier prior $q_0(\theta)$ that is chosen to be vague in a suitable sense and that is updated by a sample x of size m . The value of m that minimize the distance between $p(\theta)$ and $q_m(\theta|X)$ will be the effective sampling (*ESS*) associated to the prior $p(\theta)$.

The distance between $q_m(\theta|X_m)$, and $p(\theta)$ is defined in terms of the curvature (second derivatives) of $\log(p(\theta))$ and $\log(q_m(\theta|X_m))$.

Given the likelihood $f_m(X_m|\theta)$ and prior $p(\theta|\tilde{\theta})$, we denote the posterior by $q_m(\theta|\tilde{\theta}, x_m) \propto p(\theta|\tilde{\theta})f_m(x_m|\theta)$, let $\bar{\theta} = E_p(\theta)$ denote the prior mean under $p(\theta|\tilde{\theta})$.

We denote $D_p(\theta) = \frac{-\partial^2(\log(p(\theta|\tilde{\theta})))}{\partial\theta^2}$ and $D_q(\theta) = -\int \frac{\partial^2(\log(q_m(\theta|\tilde{\theta}, X_m)))}{\partial\theta^2} f_{X_m}(x_m) dx_m$ is the marginal distribution of X_m for the prior $q_0(\theta)$.

Define $\delta(m, \bar{\theta}, p, q) = |D_p(\bar{\theta}) - D_q(m, \bar{\theta})|$ as be the distance between $p(\theta|\tilde{\theta})$ and $q_m(\theta|\tilde{\theta}, x_m)$ for sample size m . The ESS is obtained by computing the implied sample sizes in standard models (Table 1) for which commonly reported prior-equivalent sample sizes.

In the case of Gamma-Poisson model

$$\delta(m, \bar{\theta}, p, q) = \left| \frac{\bar{\alpha} - 1}{\bar{\theta}^2} - \frac{\frac{\bar{\alpha}}{c} + \sum_{X=0}^m x_m f_m(X_m) - 1}{\bar{\theta}^2} \right| = \left| \frac{1}{\bar{\theta}^2} (\bar{\alpha} - m\bar{\theta}) \right| \quad (21)$$

In the case of Gamma-Gamma model

$$\delta(m, \bar{\theta}, p, q) = \left| \frac{\bar{\alpha} - 1}{\bar{\theta}^2} - \frac{\frac{\bar{\alpha}}{c} + mp - 1}{\bar{\theta}^2} \right| = \left| \frac{1}{\bar{\theta}^2} (\bar{\alpha} - mp) \right| \quad (22)$$

Table 3: Prior, likelihood, and corresponding posterior q_m with respect to the information prior, and traditionally reported prior effective sample size, *ESS*, for some models, where the hyper-parameter c , is very large constants chosen to inflate the variances of the elements of θ under the q_0 .

| $p(\theta \tilde{\theta})$ | $f(X_m \theta)$ | $q_m(\theta \tilde{\theta}, X_m)$ | <i>ESS</i> |
|----------------------------|------------------|---|-----------------------|
| $Ga(\tilde{a}, \tilde{b})$ | $Pois(\theta)$ | $Ga(\frac{\tilde{a}}{c} + X, \frac{\tilde{b}}{c} + m)$ | \tilde{b} |
| $Ga(\tilde{a}, \tilde{b})$ | $Ga(mp, \theta)$ | $Ga(\frac{\tilde{a}}{c} + mp, \frac{\tilde{b}}{c} + X)$ | $\frac{\tilde{a}}{p}$ |

The methods proposed for computing the effective sample size are useful in Bayesian analysis, particularly in settings with elicited priors or where the data consist of a relatively small number of observations.

By computing ESSs, one may avoid the use of an overly informative prior in the sense that the inference is dominated by the prior rather than the data. When eliciting a prior from an area expert, ESS values may be provided as a readily interpretable form of feedback. The area expert may use this as a basis to modify his/her judgments, if desired, and this process may be iterated. The ESS can be used to confirm that the chosen prior carries little information, as desired.

When interpreting or formally reviewing a Bayesian data analysis, the ESS of the analyst's prior provides a tool for evaluating the reasonableness of the analysis. In particular, if it is claimed that a vague or uninformative prior was used, the ESS provides an objective index to evaluate this claim. If appropriate, one may alert the analyst if a prior appears to be overly informative. Similarly, if an informative prior based on historical data is used in the analysis, reporting the ESS enables the reviewer to verify that the prior data are given appropriate weight.

When interpreting or formally reviewing a Bayesian design, such as that given in a clinical trial protocol, the ESS of the prior provides a tool for determining the extent to which the prior may influence the design's decisions.

In designing outcome-adaptive experiments, when formulating a prior as part of a Bayesian model to be used in a sequentially outcome-adaptive experiment, the ESS may be used to calibrate the prior to ensure that the data, rather than the prior, will dominate early decisions during the trial.

Other uses of ESS values include interpreting or reviewing others' Bayesian analyses or designs, using the ESS values themselves to perform sensitivity analyses in the prior's informativeness, and calibrating the parameters of outcome-adaptive Bayesian designs (Morita et al.,2008).

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