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Bayesian Prediction of Satisfaction Indices via Sequential Analysis and Experimental Design in Hybrid and Full Bayesian Frameworks

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ABSTRACT: This paper proposes a methodology for phase II clinical trials, grounded in both hybrid and fully Bayesian designs. The approach leverages predictive probabilities to monitor trial progress, particularly focusing on the probability of rejecting the null hypothesis and satisfaction index inversely related to the $p-value$. The methodology is applied to a negative binomial model, which is adapted to binary outcomes. This model allows for the estimation of the number of trials required to achieve a pre-specified success rate, thereby accounting for variability in observed outcomes. The proposed framework combines operational flexibility with statistical rigor, supporting interim decision-making based on futility or efficacy criteria. Ilustrative simulation demonstrate the clinical relevance of the approach, particularly its potential to optimize resource allocation, reduce patient risk, and expedite the evaluation of promising therapeutic candidates.

Key Words:: Predictive probabilities, sequential analyses, Bayesian approaches, experimantal analyses, negative binomial.

Contents

1 Introduction **1**

2 Methodologie **3**
2.1 Satisfaction indices 3
2.1.1 Satisfaction index in the classic setting 3
2.1.2 satisfaction index in the Bayesian setting 3

3 Prediction of the satisfaction index for the two-design study **4**
3.1 The prevision in the classical frameworks 4
3.2 The perivision in the Bayesian framework 4

4 The Experimental Satisfaction Index according to the negative binomial distribution **5**

5 The Sequential Satisfaction Index according to the negative binomial distribution **6**

6 Application **7**

7 Conclusion **13**

1. Introduction

Prediction is one of the most important advances in Bayesian statistics. It provides a rational and probabilistic basis for predicting future observations with uncertain parameters and data. Unlike frequentist methods, which seek a point estimate. Bayesian statistics uses the posterior predictive distribution to naturally produce probabilistic predictions. From this perspective, Bayesian prediction probabilities are highly useful for interacting with researchers. To answer fundamental questions such as, 'Given the current data, what is the probability that the final outcome will be, to some extent, conclusive or, conversely, inconclusive?', they offer an extremely interesting approach. (In the context of clinical trials which has a crucial role in drug development, serving as a critical step to assess preliminary efficacy and inform approval or rejection decisions before conducting larger, more definitive studies. Traditional trial protocols often rely on frequentist approaches and fixed sample sizes, which may lack the flexibility to adapt to

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accumulating data or evolving therapeutic evidence. To address these limitations, Bayesian methodologies have emerged as powerful alternatives, offering adaptive features and probabilistic decision-support tools well-suited to complex and uncertain clinical environments, Berry (1985), Stangl Berry (1998), Spiegelhalter et al. (1994), and Lee Feng (2005) explore the comparison between Bayesian and frequentist designs.)

Our article presents a comparison between two major methodologies in phase II trials: the experimental (or fixed) approach and the sequential (or adaptive) approach. Using Bayesian and hybrid modeling, along with the negative binomial distribution employed to estimate the number of trials required before a given success threshold is reached we compare their ability to optimize decisions while maintaining statistical validity. The fiducial-Bayesian (hybrid) inference used in our article constructs a distribution over parameters without relying on an explicit subjective prior, unlike traditional Bayesian inference, which uses an explicit prior. It bridges fiducial and Bayesian inference, providing a less subjective alternative when questionable subjective priors are a concern.

The Bayesian approach offers exceptional adaptive flexibility through the seamless integration of prior information and real-time adjustments to stopping rules or sample size, thereby enhancing mid-trial efficiency and decision-making in clinical trials. Fiducial-Bayesian (hybrid) inference enables objective evaluation without resorting to a subjective approach, yielding correct intervals even for small samples and coherent confidence distributions, thereby enhancing transparency for regulatory authorities. Both methods provide complete distributions over parameters, allowing probabilistic justification for protocol modifications and early stopping decisions in clinical trials (see Lecoutre Poitevineau, 2022). The experimental protocol (Chang, 2008; Chow et al., 2012), characterized by a rigorous two-phase design without interim analyses, relies on exhaustive data collection before any interpretation. It ensures impeccable statistical robustness and strict control of type I errors, making it particularly suited for confirmatory trials where result stability is paramount. However, its lack of flexibility may lead to resource wastage or unnecessary patient exposure to ineffective treatments. In contrast, the sequential method (Choi Chang, 2006; Lee Liu, 2008; Merabet, 2013 provide key insights into innovative sequential and adaptive procedures and their application in phase II trials) incorporates interim analyses guided by Bayesian predictive probabilities of futility or efficacy for early stopping. This flexibility enables cost savings, improved decision-making, and minimized ethical risks but requires sophisticated methodological adjustments to avoid bias.

The distinctive appeal of each methodology lies in its suitability for specific scenarios. The experimental approach is particularly adapted for trials requiring reproducibility and rigorous confirmation, such as regulatory pivotal trials (e.g., FDA (U.S. Food and Drug Administration) or EMA (European Medicines Agency) drug approval assessments), where result stability and stringent type I error control are critical. Conversely, the sequential strategy is essential in uncertain and dynamic settings, such as pediatric cancer or rare disease trials (e.g., testing a treatment for a rare genetic mutation with sparse recruitment), where protocol flexibility is vital to reassess endpoints or stop early due to futility or substantial efficacy.

Although seemingly equivalent, these two methods compensate for each other. The sequential method incorporates an adaptive component into the very structure of the experimental approach, while maintaining its statistical foundation (negative binomial model to determine the number of trials until success) and augmenting it with Bayesian interim analysis. It leverages the strengths of both frameworks

- The a posteriori validity is very robust (experimental approach).
- Real-time (sequential) optimization enables, for example, early stopping to avoid unnecessary expenses or to accelerate access to a promising treatment.

This combination of scientific rigor and operational agility thus meets the diverse needs of modern clinical research.

In this article, we present phase II trial designs incorporating both hybrid and fully Bayesian approaches. The use of predictive probabilities to guide interim monitoring forms the core of this methodology. Specifically, we evaluate: the predictive probability of rejecting the null hypothesis and satisfaction indices inversely proportional to $p - values$, these quantities provide interpretable, dynamic decision-making indicators throughout the trial durationframework initially proposed by Lecoutre et al. (1995)

and subsequently extended by Merabet Raoult (1995), Merabet (2004a, 2004b), Labdaoui (2022), and Djeridi (2024). This methodology is applied to a negative binomial model adapted for binary outcomes, estimating the expected number of trials required to reach a predefined success rate. This model formulation accounts for overdispersion while providing a robust mechanism to capture patient response variability. Integration of this model within the Bayesian framework enables flexible trial designs that may be stopped early for either futility or efficacy based on predefined thresholds.

2. Methodologie

2.1. Satisfaction indices

In the statistical decision, we wish to enrich the simple binary decision to reject/not reject with a continuous index in the interval [0 ,1] of "satisfaction" or "utility", defined from the data. This index has already been used by (Brown et al, 1987, Choi and Pepple, 1989). Two identically independent experiments are proposed, distributing $x \in \chi$ the first-phase trial (given or present) and $y \in \gamma$ the second phase results (given or future). The two variables (x, y) associated with an unknown parameter $\theta \in \Theta$.

2.1.1. Satisfaction index in the classic setting. In the frequentist approach, we aim to complement the binary decision of reject/not-reject with a continuous satisfaction index. denoted by ϕ to resolve a conclusion about the study, and test the following hypothesis:

$$H_0 : \theta \geq \theta_0 \quad \text{vs} \quad H_1 : \theta < \theta_0$$

In the experimental framework it assigns a continuous value (between 0 and 1) reflecting the intensity of the evidence against H_0, the lower the $p - value$, the closer ϕ is to 1.

$$\phi(y) = \begin{cases} 1 - p(y) & \text{if } y \in R^\alpha, \\ 0 & \text{if else.} \end{cases} \tag{2.1}$$

- $p(y)$:$p - value$ associated with y.
- R^α: the rejection region of the frequentist test at the α, where

$$R^\alpha = \{y \mid 1 - p(y) > 1 - \alpha\}.$$

- α: the significance level of the test (for example, 5%).

In the sequential framework: from data $z = (x, y)$ resulting from the two phases of a study. Let z=x+y be the combination between phase 1 and 2 to solve the final conclusion of the study, and determine satisfaction under the hypotheses, we note the satisfaction index $\phi(z)$

$$\phi(z) = \begin{cases} 1 - p(z) & \text{if } z \in R^\alpha, \\ 0 & \text{if else.} \end{cases} \tag{2.2}$$

- $p(z)$: the p-global value associated with z.
- R^α: the rejection region of the frequentist test at the α, or

$$R^\alpha = \{z \mid 1 - p(z) > 1 - \alpha\} = \{z \mid p(z) < \alpha\}.$$

2.1.2. satisfaction index in the Bayesian setting. In a purely Bayesian approach, we replace the $p - value$ with the posterior probability of the alternative hypothesis, thus defining a satisfaction index based directly on the degree of scientific belief. We begin by specifying an a priori law π on the space of parameters Θ, then we calculate the posterior law $\pi(\theta|.)$. The probability $\pi(\Theta_1|.)$ that the parameter belongs to the alternative hypothesis Θ_1 constitutes an index of satisfaction in it self, without reference to a frequentist level of precaution. We note by $\tilde{\varphi}$.
In the experimental setting, the satisafaction index

$$\widetilde{\phi}(y) = \begin{cases} \pi(\Theta_1 \mid y) & \text{if } y \in \widetilde{R}^\alpha, \\ 0 & \text{if else.} \end{cases} \tag{2.3}$$

- $\pi(\Theta_1 \mid y)$: The distribution of the a posteriori law given the observation y is as follows.
- $\widetilde{R}^{\alpha}$: The rejection region of the Bayesian test at the α, où

$$\widetilde{R}^{\alpha} = \{y \mid \pi(\Theta_1 \mid y) > 1 - \alpha\}.$$

In the sequential framework, the satisfaction index

$$\widetilde{\phi}(z) = \begin{cases} \pi(\Theta_1 \mid z) & \text{if } z \in \widetilde{R}^{\alpha}, \\ 0 & \text{if else.} \end{cases} \tag{2.4}$$

- $\pi(\Theta_1 \mid z)$: The distribution of the a posteriori law given the observation z.
- $\widetilde{R}^{\alpha}$: The rejection region of the Bayesian test at the α, où

$$\widetilde{R}^{\alpha} = \{z \mid \pi(\Theta_1 \mid z) > 1 - \alpha\}.$$

The use of $\pi(\Theta_1|.)$ as an index removes the need to calibrate a $p - value$ and naturally frames risk tolerance via a priori choice of law. These formulas are easily integrated into sequential and empirical forecasting methods where predictive probability plays the central role.

3. Prediction of the satisfaction index for the two-design study

Even before initiating phase II, we can estimate the expected level of final satisfaction based on the intermediate outcomes. To achieve this, we utilize the predictive law $f(.|x)$, which indicates the probability of observing each outcome$y$ in phase II, given x and our current knowledge of the parameter θ. The satisfaction index can then be integrated over the potential values of y and z to derive the predictive expectation $\eta(x)$. This expectation represents, on average, the satisfaction that can be anticipated if the decision is made to continue the study to its conclusion, thereby offering a priori criteria for deciding whether to continue or to stop early. In other words, $\eta(x)$ provides a forward-looking assessment of final test performance before committing resources to phase II. In a Bayesian framework, we substitute the $p - value$ and likelihood with the Bayesian predictive probability, derived from the updated information regarding θ, to similarly define an expectation $\tilde{\eta}(x)$. These expectation measures both frequentist and Bayesian are integral to flexible strategies, as they allow us to compare expected benefits against a predetermined limit. This comparison aids in deciding whether to conclude the study early if it is not progressing as hoped or to adjust the sample size. This approach transforms the study plan into a truly sequential process, driven by decisions informed by real-time calculations of satisfaction expectations. We pose:

3.1. The prevision in the classical frameworks

$\eta(x)$ is the predicted index generalizes the power of the test in the dialectic of the index of satisfaction in te case of experimental and sequenteil disinge.

$$\eta(x) = \mathbb{E}[\phi(\cdot) \mid x] = \int \phi(\cdot)\, f(\cdot \mid x)\, d(\cdot) \tag{3.1}$$

which integrates the classical satisfaction index ϕ weighted by the predictive likelihood of each variable (y or z).

3.2. The perivision in the Bayesian framework

$\tilde{\eta}(x)$ is the practitioner decide a predicted index above which the experiment is carried on. In a purely Bayesian viewpoint, the predicted index for the vriable y or z

$$\tilde{\eta}(x) = \mathbb{E}[\tilde{\varphi}(\cdot) \mid x] = \int \tilde{\varphi}(\cdot)\, f(\cdot \mid x)\, d(\cdot) \tag{3.2}$$

where $\tilde{\varphi}$ is the Bayesian index, and $f(.|x)$ is calculated from the posterior law. either for variable of y or else of z:

$$f(\cdot \mid x) = \int_{\Theta} f(\cdot \mid x, \theta)\, \pi(\theta \mid x)\, d\theta$$

where $\pi(\theta|x)$ is the a posteriori law obtained after the first phase . We compare $\eta(x)$ (or $\tilde{\eta}(x)$) with a predefined threshold. If the expectation falls below the futility threshold, we stop the study. If the expectation is high, we can reinforce the resource allocation or adjust the sample size to maximize the probability of success.

4. The Experimental Satisfaction Index according to the negative binomial distribution

We propose to apply the index and the prediction of satisfaction on the negative binomial law either $X \sim \mathrm{NB}(h, \theta)$ with a probability distribution is

$$P(X = x) = \binom{x + h - 1}{x} \theta^h (1-\theta)^x \quad \theta \in [0,1],\ x = 0, 1, \ldots, \infty \text{ et } h \in \mathbb{R}_+^*.$$

And $Y \sim \mathrm{NB}(l, \theta)$ the probability distribution is:

$$P(Y = y) = \binom{y + l - 1}{y} \theta^l (1-\theta)^y, \quad \theta \in [0,1],\ y = 0, 1, \ldots, \infty,\ \text{et } l \in \mathbb{R}_+^*$$

In all that follows, we have the following simplified notations:
π: density of prior law of θ.
f: density of the conditional predictive law of y knowing x.
F: distribution function of the law of y for the value θ_0 of the parameter.
G: is the likelihood associated with the variable.
$\tilde{\varphi}$ or ϕ is the satisfaction index associated with the results of the second phase (y or z depending on the type of index) of a two stage clinical trial. It measures the statistical credibility of the rejection of the null hypothesis H_0 based on the observed data. The experimental test is used for the following two hypotheses:

$$\begin{cases} H_0 : & \theta \geq \theta_0 \\ H_1 : & \theta < \theta_0 \end{cases} \tag{4.1}$$

The distribution of the posterior law is proportional as follows:

$$\pi(\theta \mid x) \propto G(x \mid \theta)\pi(\theta).$$

So

$$\pi(\theta \mid x) \sim \beta(h + a, x + b). \tag{4.2}$$

The satisfaction index in the classical approach is given by:

$$\phi(y) = \begin{cases} \sum_{e=0}^{y-1} \binom{e+l-1}{e} \theta^l (1-\theta)^e & \text{if } \ y \geq q \\ 0 & \text{if else.} \end{cases} \tag{4.3}$$

Or

$$q = \inf \left\{ u,\ \sum_{e=u}^{y-1} \binom{e + l - 1}{e} \theta^l (1-\theta)^e \geq 1 - \alpha \right\}$$

The satisfaction index in the Bayesian approach is given by:

$$\tilde{\varphi}(y) = \begin{cases} 1 - F_{l+a, y+b}(\theta_0) & \text{if } y \geq \tilde{q} \\ 0 & \text{if else} \end{cases} \tag{4.4}$$

Or

$$\tilde{q} = \inf\left\{ y \mid \int_{\theta_0}^{1} \beta(l+a, y+b)\, d\theta \leq \alpha \right\}$$

The predictive distribution of y conditional by x

$$f(y \mid x) = \int_{\Theta} f(y \mid \theta)\, \pi(\theta \mid x)\, d\theta$$

$$f(y \mid x) = \binom{y+l-1}{y} \frac{\beta(l+h+a, y+b+x)}{\beta(h+a, x+b)} \tag{4.5}$$

Finally, the prediction of satisfaction in both approaches.
The following equation expresses the prevision in the case of the hybrid approach

$$\eta_{\text{hybride.exp}}(x) = \sum_{y=q}^{\infty} \phi(y) \cdot f(y \mid x)$$

$$= \sum_{y=q}^{\infty} \left(\sum_{e=0}^{y-1} \binom{e+l-1}{e} \theta^l (1-\theta)^e \right) \binom{y+l-1}{y} \frac{\beta(h+l+a, y+x+b)}{\beta(h+a, x+b)} \tag{4.6}$$

The following equation expresses the prevision in the case of the fulle Bayesian approach

$$\tilde{\eta}_{\text{bay.exp}}(x) = \sum_{y=\tilde{q}}^{\infty} \tilde{\varphi}(y) \cdot f(y \mid x)$$

$$= \sum_{y=\tilde{q}}^{\infty} \left[1 - F_{l+a, y+b}(\theta_0)\right] \binom{y+l-1}{y} \frac{\beta(l+h+a, y+b+x)}{\beta(h+a, x+b)} \tag{4.7}$$

5. The Sequential Satisfaction Index according to the negative binomial distribution

Sequential group testing involves planning one or more interim analyses to allow for data comparison according to stopping rules. These sequential group designs include rules for stopping experiments when there is insufficient evidence of efficacy to discontinue the regulatory decision or when the experiments appear unable to provide evidence of efficacy. Typically, a convincing claim of the efficacy of a treatment is required. This claim is based on the Bayesian law of absolute necessity (fully Bayesian) or the hybrid view of value p(frequency Bayesian).
Initially, we consider Z as the new variable, defined as the sum of two variables already mentioned previously $Z = X + Y$.
The sequential test is used for the following two hypotheses:

$$\begin{cases} H_0 : & \theta \geq \theta_0 \\ H_1 : & \theta < \theta_0 \end{cases} \tag{5.1}$$

These concepts apply to the probability distribution of z, while $z \sim \text{NB}(l+h, \theta)$

$$P(Z = z) = \binom{z+l+h-1}{z} \theta^{h+l} (1-\theta)^z, \quad \theta \in [0,1],\ Z = 0, 1, \ldots, \infty,\ h, l \in \mathbb{R}_+^*$$

The satisfaction index in the hybrid approach is given by:

$$\phi(z) = \begin{cases} \sum_{e=0}^{z-1} \binom{e+l+h-1}{e} \theta^{l+h} (1-\theta)^e & \text{if } z \geq q \\ 0 & \text{if else} \end{cases} \tag{5.2}$$

Or

$$q = \inf \left\{ u \in \mathbb{N} \;\middle|\; \sum_{e=u}^{z-1} \binom{e+l+h-1}{e} \theta^{l+h} (1-\theta)^e \geq 1-\alpha \right\}$$

The satisfaction index in the Bayesian approach is given by:

$$\tilde{\varphi}(z) = \begin{cases} 1 - F_{h+l+a,z+b}(\theta_0) & \text{if } z \geq \tilde{q} \\ 0 & \text{if else} \end{cases} \tag{5.3}$$

Or:

$$\tilde{q} = \inf \left\{ z \in \mathbb{N} \;\middle|\; \int_{\theta_0}^{1} \beta(h+l+a, z+b)\, d\theta \leq \alpha \right\}$$

Let be $f(z|\, x)$ the predictive distribution of z conditional by x after the first phase.

$$f(z \mid x) = \int_{\Theta} f(z \mid \theta)\, \pi(\theta \mid x)\, d\theta$$

$$f(z \mid x) = \binom{z+h+l-1}{z} \frac{\beta(l+2h+a, z+b+x)}{\beta(h+a, x+b)}. \tag{5.4}$$

Finally, the prediction of satisfaction in both cases is

$$\eta_{\text{hybride.seq}}(x) = \mathbb{E}[\phi(z) \mid x] = \sum_{z=q}^{\infty} \psi_1(z) \cdot f(z \mid x)$$

$$= \sum_{z=q}^{\infty} \left(\sum_{e=0}^{z-1} \binom{e+l+h-1}{e} \theta^{l+h} (1-\theta)^e \right) \cdot \binom{z+h+l-1}{z} \cdot \frac{\beta(l+2h+a, z+b+x)}{\beta(h+a, x+b)} \tag{5.5}$$

And in the Bayesian framework defined by:

$$\tilde{\eta}_{\text{bay.seq}}(x) = \mathbb{E}[\tilde{\varphi}_2(z) \mid x] = \sum_{z=\tilde{q}}^{\infty} \tilde{\varphi}_2(z) \cdot f(z \mid x)$$

$$= \sum_{z=\tilde{q}}^{\infty} [1 - F_{h+l+a,z+b}(\theta_0)] \binom{z+h+l-1}{z} \frac{\beta(l+2h+a, z+b+x)}{\beta(h+a, x+b)} \tag{5.6}$$

Remark: the $\beta(1,1)$ prior is simply the uniforme distribution on [0,1], is a common choice within Bayesian statistics due to its seemingly non-informative nature as well as computational simplicity. Theoretical aspects of this prior are investigated here, with emphasis placed on its advantages e.g., natural conjugacy when combining with binomial and negative binomial likelihoods along with its drawback, i.e., lack of invariance under reparameterization. We contrast its performance against other competing priors (e.g., Jeffreys' prior and weakly informative priors) and provide guidelines for its optimal use in applied Bayesian inference.

6. Application

In this section we propose a numerical application on the satisfaction index of the negative binomial distribution. The experimental and sequential representation for both approches (hybride and fully Bayesien). We propose two response variables x and y which are iid, such that $X \sim \text{NB}(h=3, \theta)$ and $Y \sim \text{NB}(l=5, \theta)$. $Z = X + Y$ is also a negative binomial distribution of $Z \sim \text{NB}(h+l=8, \theta)$.
We are looking to test $H_1 \colon \theta < 0.8$ whether the drug can be moved to phase 3. From a statistical point of view, the sequential and experimental test is used for the following two hypotheses:

$$\begin{cases} H_0 : & \theta \geq 0.8 \\ H_1 : & \theta < 0.8 \end{cases}$$

Table 1: Representation of prediction in sequential plans.

Scenario	x	$\tilde{\eta}(x)_{\text{Bay-seq}}$	$\eta(x)_{\text{Hybr-seq}}$
1	1	0.390023	0.321064
2	2	0.567075	0.490732
3	3	0.698171	0.626805
4	4	0.790334	0.729072
5	5	0.853746	0.803550
6	6	0.897058	0.856993
7	7	0.926625	0.895104
8	8	0.946843	0.922226
9	9	0.960681	0.941512
10	10	0.970127	0.955200
11	11	0.976508	0.964865
12	12	0.980717	0.971606
13	13	0.983353	0.976198
14	14	0.984826	0.979182
15	15	0.985416	0.980944
16	16	0.985315	0.981754
17	17	0.984659	0.981810
18	18	0.983542	0.981252
19	19	0.982031	0.980182
20	20	0.980175	0.978674
21	21	0.978008	0.976785
22	22	0.975557	0.974555
23	23	0.972840	0.972017
24	24	0.969874	0.969194
25	25	0.966670	0.966106

The table 1 compares, for each number of successes x, the predictive probability $\pi(x)$ of obtaining adequate evidence according to two sequential designs: pure Bayesian ($Bay - seq$) and hybrid ($Hybr - seq$). For x between 1 and 8, $\pi(x)$ it grows rapidly: the $Bay - seq$ method crosses 0.95 from $x = 9(\ \pi(9) = 0,9607)$, while the hybrid version only reaches$x = 10$ ($\pi(10) = 0,9552$), thus demonstrating the greater sensitivity of the pure Bayesian design. Bay-seq values are always higher than Hybr-seq values, which explains an earlier termination (efficiency gain), but a slightly higher risk of type 1 error. After a peak at around $x = 15(Bay - seq \approx 0.985)$, both curves slowly decline due to the redundancy of information and the increasing uncertainty of subsequent predictions.[1]

[1] The choice of 25 is arbitrary

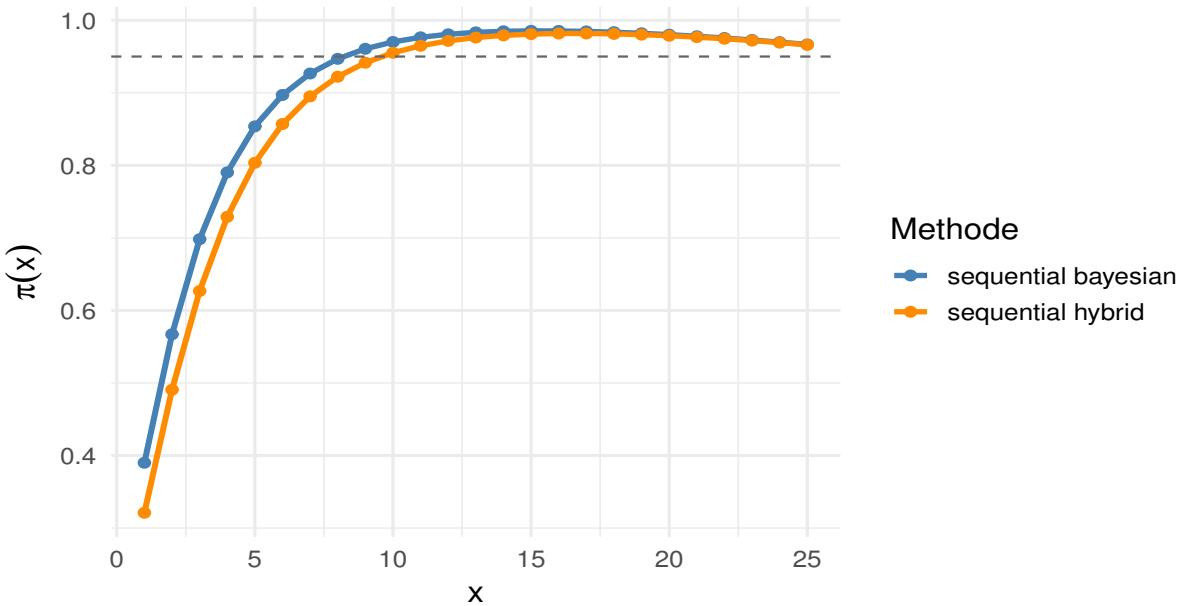

Figure 1: Sequential for Bayesian and hybrid prediction with a uniform Beta$(1, 1)$prior distribution

The graphical 1, plot of the Bay-seq and hybr-seq predictive probability curves $\pi(x)$ indicates that, from the first successes ($x = 1$ to 5), the pure Bayesian method reacts more aggressively (from 0.39 to 0.85) compared to the hybrid method (from 0.32 to 0.80), meaning that it is more sensitive to early data. Eventually, the Bay-seq curve crosses the 0.95 mark at $x = 9$, while the hybrid variant crosses it at $x = 10$, revealing an earlier but possibly riskier pre-termination of the type I error. Between $x = 10$ and $x = 15$, both curves converge to a plateau around 0.98, suggesting that with enough information, the Bayesian and hybrid choices converge. Finally, for values of x greater than $x \approx 15$, we observe a moderate decrease due to the increase in predictive uncertainty on subsequent successes, more dramatically for the Bay-seq approach; this trend reflects the conservative power of the hybrid policy which introduces frequentist control without becoming non-adaptive.

Table 2: Representation of prediction in experimental designs.

Scenario	x	$\eta(x)_{\text{Hybrid-experimental}}$	$\tilde{\eta}(x)_{Bayes-experimental}$
1	1	0.236327	0.312054
2	2	0.375689	0.46665
3	3	0.497821	0.590766
4	4	0.598537	0.686107
5	5	0.679202	0.758115
6	6	0.742942	0.812275
7	7	0.793049	0.853107
8	8	0.832422	0.884062
9	9	0.863423	0.907701
10	10	0.887917	0.925899
11	11	0.907348	0.940024
12	12	0.922825	0.951078
13	13	0.935197	0.959797
14	14	0.945116	0.966728
15	15	0.953085	0.972277
16	16	0.959491	0.97675
17	17	0.964633	0.980378
18	18	0.968746	0.983338
19	19	0.972013	0.985767
20	20	0.974579	0.987768
21	21	0.976557	0.989424
22	22	0.97804	0.9908
23	23	0.979099	0.991946
24	24	0.979793	0.992902
25	25	0.980169	0.993702

Table 2 shows the evolution of the predictive probability $\pi(x)$ for two experimental designs: the Bayesian-experimental design and the hybrid-experimental method. For each number of successes x obtained, the table illustrates the rate at which each approach credits the rejection of the null hypothesis. It thus allows us to observe how quickly the Bayesian model reaches high confidence levels (and more precisely the barrier of 0.95) compared to the more conservative hybrid version.

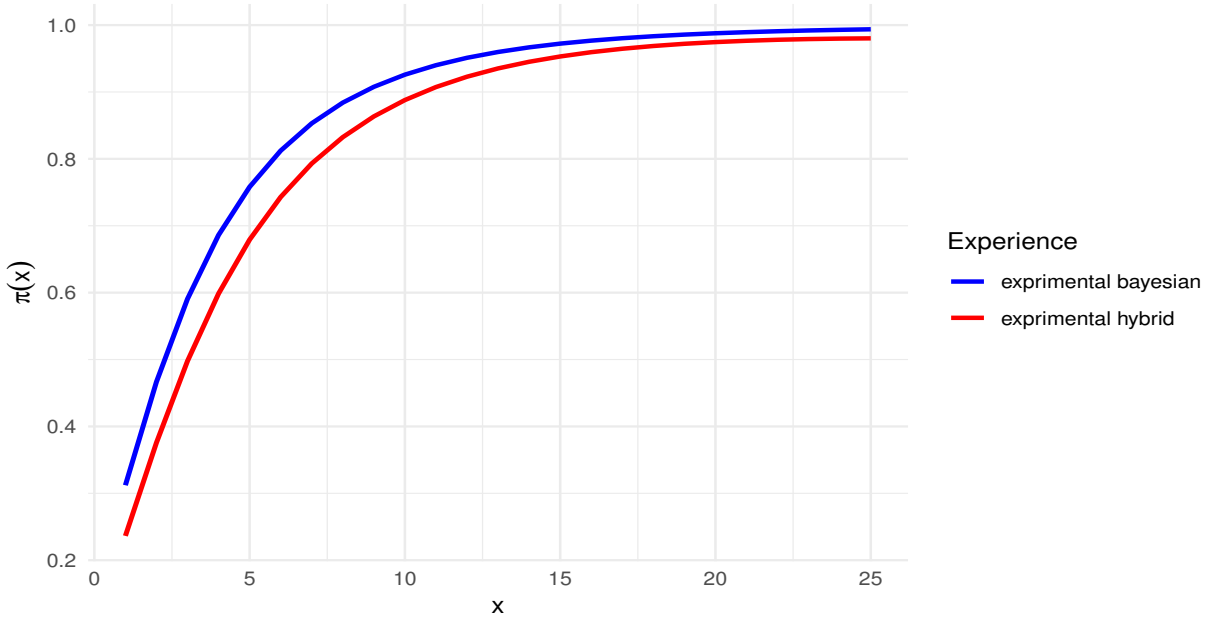

Figure 2: Experimental hybrid and Bayesian prediction with a uniform Beta$(1, 1)$prior distribution

In figure 2, the predictive probabilities $\pi(x)$ of the hybrid-experimental and Bayesian-experimental models increase monotonically, but the Bayesian curve begins to cross the critical threshold of 0.95 as soon as $x = 12$ $(\pi = 0, 9511)$,while the hybrid version does so, $x = 15$ $(\pi = 0, 9531)$,reflecting increased responsiveness of the Bayesian model. This three-shot main curve shows the ability of the Bayesian-experimental model to suggest anticipated acceptance of the trial. Afterward, both lines diverge to a plateau at 0.99, illustrating that after a few observations, the additional information provides a very slight improvement in certainty. In practice, the Bayesian formulation reduces the number of patients needed to achieve 95% confidence in rejecting H_0, and the hybrid solution provides a more conservative calibration.

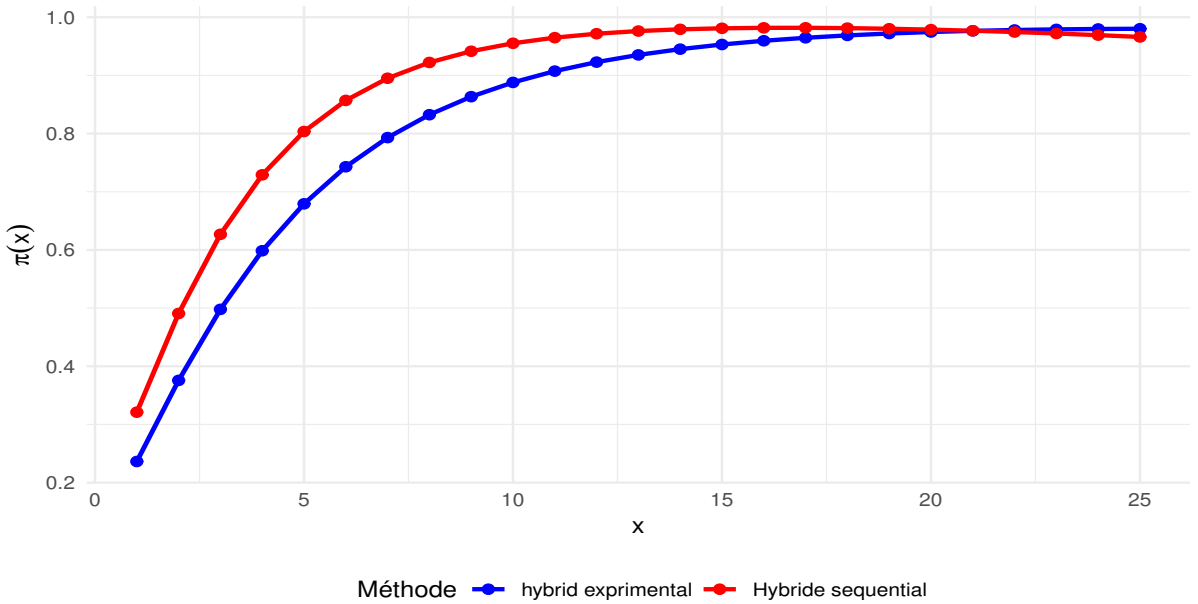

Figure 3: Comparison between experimental and sequential in the hybrid approach with a uniform Beta$(1,1)$prior distribution

Figure 3, shows a comparison of experimental and sequential performance using a mixed method with a uniform a priori distribution Beta$(1,1)$. The results indicate that both methods gradually converge to a stable value of $\pi(x)$ as x increases. The empirical hybrid approach (in blue) increases slowly for $x < 10$ until it reaches about 9, then quickly levels off at around 0.96 after $x = 10$. In contrast, the sequential hybrid approach (in orange) rises more steadily and quickly reaches a predictive probability of 0.97 at $x = 10$. After x goes beyond 15, both curves rise together. After the x value exceeds 15, the two curves increase in parallel. Using the uninformative a priori distribution Beta$(1,1)$ allows us to clearly observe the effect of data on inference. This analysis reveals that the sequential approach is preferable for small values of x, while both approaches become equivalent for sufficiently large samples. These results underline the importance of methodological choice in the early stages of Bayesian inference.

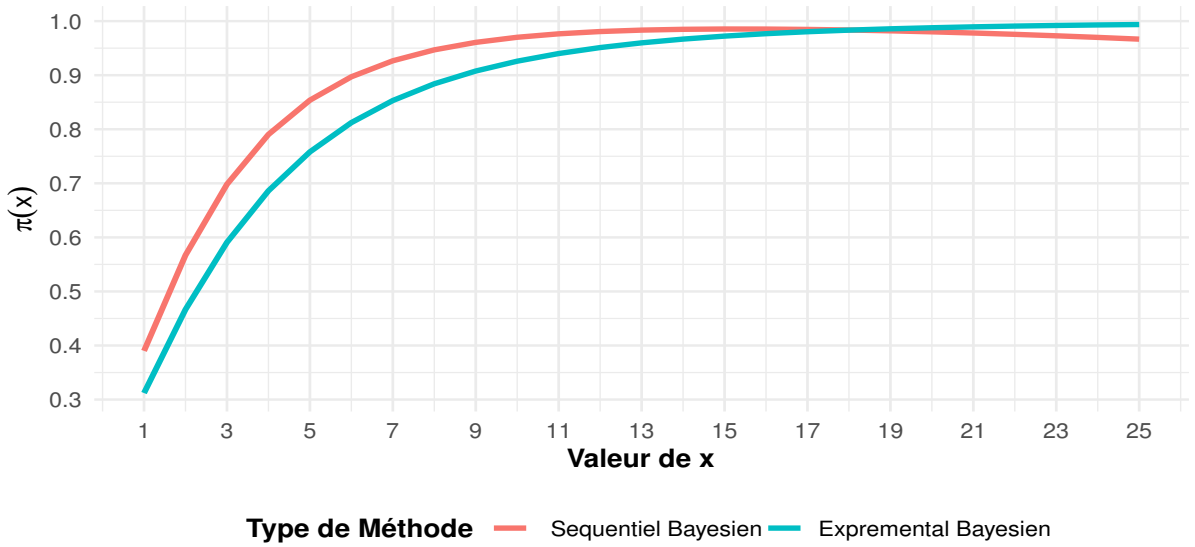

Figure 4: Comparison between experimental and sequential in the Bayesien approach with a uniforma uniform Beta$(1,1)$prior distribution

Figure 4, a comparison of the sequential and experimental curves using a uniform a priori Beta$(1,1)$ shows big differences in the probability estimate $\pi(x)$. The sequential method, iteratively updating the a posteriori distribution after each observation, shows faster convergence towards the true value of $\pi(x)$, with credibility intervals that narrow monotonically. On the other hand, the experimental approach, based on aggregated data, shows greater variability, reflecting the uncertainty associated with batch sampling.

The differences between the two curves diminish as x increases, suggesting a stabilisation of the Bayesian estimators. Nevertheless, the sequential method offers superior efficiency for small values of x by immediately exploiting the new information. This result highlights the significance of selecting an update protocol in Bayesian inference, particularly when collecting data sequentially. In concrete terms, the sequential method is to be preferred for real-time analyses, while the experimental approach remains useful for retrospective studies.

7. Conclusion

This research proposes a useful approach to phase II clinical trials by integrating sequential or experimental Bayesian modeling and the negative binomial distribution to simplify satisfaction index prediction and interim decision-making. Comparing sequential procedures, it shows that the pure Bayesian approach offers greater sensitivity to early data, allowing early stopping for efficacy after certain successes , while the more conservative hybrid adaptation offers better control of type I errors at the cost of stopping a little later. Numerical simulations demonstrate that both methods converge to high certainty successes, but diverge in uncertainty management for high values of x. This duality offers statistical rigor (via preserved frequentist properties) and operational flexibility, thus reducing patient exposure to unnecessary therapies, optimizing resource allocation, and accelerating the evaluation of promising therapies. The accompanying R codes facilitate their practical implementation, increasing their viability in diverse situations, from regulatory pivotal trials to research on rare populations. As a hybrid model with robust validation and adaptive flexibility, this method addresses both the ethical and logistical challenges of modern clinical research, offering insights into more responsive and ethical trial designs.

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