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Frequentist Test in Bayesian Two-Stage Designs Applied in Experimental Trials

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ABSTRACT: Prediction provides discipline and pragmatic importance to empirical research. The design with the predictive probability approach provides an excellent alternative for conducting multi-stage phase II trials; it is efficient and flexible and possesses desirable statistical properties. . In this paper we consider the Bayesian predictive procedures within the experimental design, for this, we define indices of satisfaction related to a test as a decreasing function of the p-value and satisfaction is higher than the null hypothesis is rejected wider. This design possesses good frequentist properties and allows early termination of the trial. We treated our applications by simulation and real data in experimental planning and sequential designs with binary outcomes.

Key Words: Bayesian approach, Prediction, Binomial model, Interim monitoring.

Contents

1. Introduction

A major strength of the Bayesian paradigm is the ease with which one can make predictions about future observations. The predictive idea is central in experimental investigations. Furthermore Bayesian predictive probabilities are efficient tools for designing and monitoring experiments. Bayesian predictive procedures give the applied researcher a very appealing method to evaluate the chances that an experiment will end up showing a conclusive result, or on the contrary a non-conclusive result. These procedures are far more intuitive and much closer to the thinking of scientists than frequentist procedures [1]. Experimental (or interventional) studies, as the name implies, these are studies in which the participants undergo some kind of intervention in order to evaluate its impact. An intervention could include a medical or surgical intervention, a new drug, or an intervention to change lifestyle. Because they are the most methodologically rigorous design, experiments are the default choice for providing evidence for best practice in patient management, so this discussion will begin with them. The experimental researcher has control over the intervention, its timing, and dose or intensity. In its simplest form, an experimental study to test the effect of a treatment requires that the researcher formally states the hypothesis to be tested where he must selects people eligible for the treatment, in which the sample is divided into two groups and each group (the experimental, or intervention group) is given the intervention while the other

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(the control group) is not, and the outcomes of interest are recorded over time, and the results compared between the two groups [2]. Prediction models will become more relevant in the medical field with the increase in knowledge on potential predictors of outcome, e.g. from genetics. Also, the number of applications will increase, e.g. with targeted early detection of disease, and individualized approaches to diagnostic testing and treatment. The current era of evidence-based medicine asks for an individualized approach to medical decision-making. Evidence-based medicine has a central place for meta-analysis to summarize results from randomized controlled trials; similarly prediction models may summarize the effects of predictors to provide individualized predictions of a diagnostic or prognostic outcome [3]. In this paper we consider the Bayesian predictive procedures within the experimental design, for this, we define a hypothesis is defined indices of satisfaction and anticipation of satisfaction related to a test as a decreasing function of the p-value, satisfaction is higher than the null hypothesis is rejected wider, that is to say, the p-value is small. We consider the case of a two-step procedure, which is often done in the case of experimental trials where these satisfaction indices are interesting protocols and when the inference concerns an effect evaluated from the future sample. We treated our applications in experimental planning and sequential designs with binary outcomes. The computations and the simulation results concern an inferential problem are given by software: Matlab and R.

2. Statistical Methodology

2.1. Experimental designs

2.1.1. ***Bayesian predictive design.*** We use the Bayesian framework as a tool to design clinical trials with desirable frequentist properties. Taking the Bayesian approach, we derive an efficient and flexible design. Statistical methodology has already been used. Remember that, the Bayesian model was introduced in the context of [4] and after improved in [5], [6], and [7].
We specify the experimental context by choosing $(P_\theta)_{\theta\in\Theta}$ a family of probability observations on a space Ω and where Θ is the space of unknown parameters and is to test the null hypothesis Θ_0 against the alternative hypothesis Θ_1. In classical asymmetric design test problems, such a situation is generally in the experimenter, a desire to put in evidence a significant result, that is to say, to conclude the rejection of the null hypothesis.

- Step 1: If $P_\theta < \theta_L$, stop the trial and reject the alternative hypothesis;
- Step 2: If $P_\theta < \theta_U$, stop the trial and reject the null hypothesis;
- Step 3: Otherwise continue to the next stage until reaching the number maximum of patients.

Typically, we choose θ_L as a small positive number and θ_U as a large positive number, both between 0 and 1 (inclusive). $P_\theta < \theta_L$ indicates that it is unlikely the response rate will be larger than θ_0 at the end of the trial given the current information. When this happens, we may as well stop the trial and reject the alternative hypothesis at that point. On the other hand, when $P_\theta < \theta_L$, the current data suggest that, if the same trend continues, we will have a high probability of concluding that the treatment is efficacious at the end of the study we can see [8]. This result, then, provides evidence to stop the trial early due to efficacy. By choosing $\theta_L > 0$ and $\theta_U < 1$, the trial can terminate early due to either futility or efficacy. For phase IIA trials, we often prefer to choose $\theta_L > 0$ and $\theta_U = 1$ to allow early stopping due to futility, but not due to efficacy.

2.1.2. ***Satisfaction index.*** If adopted a procedure deterministic test, relative to a level α, leading to partition Ω in a region of not- rejection $\Omega_0^{(\alpha)}$ and a rejection region $\Omega_1^{(\alpha)}$, an index particularly simple satisfaction is the indicator function of $\Omega_0^{(\alpha)}$. It is satisfied if the result is significant at α, if dissatisfied. But very often users want rather face an outcome that seems likely to lead to their rejection of Θ_0, know what its degree of significance; that is to say, know how far the results appear significant. Using the fact that any reasonable test technique leads to a family of not -rejection regions $\Omega_0^{(\alpha)}$ in the sense of decreasing inclusion when α increases, that is to say, when our precautions s' mitigate , then use a new index of satisfaction , a little less rough than the previous one , denoted $\Phi^{(\alpha)}$, and defined as a function of p- value , the simplest as zero on the region of not- rejection $\Omega_0^{(\alpha)}$ and equal to $(1-p)$, or more generally

$(1-p)^l$ with $l > 0$ otherwise. In other words it offers a satisfaction index which is zero if it is not detected significant and otherwise a decreasing function of the p- value, and therefore, the more p is small and the experimenter believes that the result is significant [9] remind that the p- value is considered as a measure of credibility to attach to the null hypothesis that practitioners often use to meet several critical and disadvantages of approach Neymann of Pearson. The value of this index satisfaction and an extended family of indices in the concept of predicting satisfaction of a sample future as a first sample.

2.1.3. ***Prediction of satisfaction.*** Experimental contexts that we have mentioned in the introduction often lend themselves to analysis in several phases, and we limit ourselves to two phases and the situation , which corresponds to the requirements in the experimental trials, where the first phase is that indicative and is intended only to consider whether to resume testing for a second phase , conducted independently of the first and of which only the test result based on the conclusion of which is the ultimate purpose of the study . We note here Ω, Ω' and Ω'' sets complete results, the results of the first phase and the results of the second phase ($\Omega = \Omega' + \Omega''$). It is in this context that has proposed to introduce a Bayesian model with a prior distribution on Θ and the family of probabilities $(P_\theta)_{\theta\in\Theta}$ on Ω. He sees in this model the probability of Ω'' , influenced by the outcome of the first phase ω', which we denote by $P^{\omega'}_{\Omega''}$, recall that, according to the usual Bayesian terminology , the term predictive probability , the probability P_Ω on the space of complete results , which is used here is the probability on Ω'' which is deduced by conditioning by ω' . We find as a prediction on the view of the first phase of a significant result in the second phase, the value $P^{\omega'}_{\Omega''}$ ($\Omega_1^{''(\alpha)}$), where $\Omega_1^{''(\alpha)}$ is the rejection region of the classical test made on the basis of the results of the second phase. It is in this sense that here is practice both classical statistics and Bayesian statistics. We propose here, more typically associate with any satisfaction index on the second phase index forecasting is the mathematical expectation with respect to $P^{\omega'}_{\Omega''}$, satisfaction provided by consider the second phase of the experiment and the predicted using the first. Consider a single-arm phase II clinical trial in which all patients are assigned to experimental treatment E. The dose level of E is determined by a previous phase I trial and, thus, is considered to be fixed. Patients are recruited, treated, and evaluated group sequentially, but the size of a group may vary because the group size after the first interim look is determined based on the most up-to-date observations during the trial. The total number of interim looks may also vary from trial to trial, depending on the observations and defined loss function, but we assume an upper bound on the number of patients that could be accrued to the phase II trial. The decision space for the whole phase II clinical trial is defined as $D = \{d_1, d_2, d_3\}$. At each interim evaluation, three possible decisions could be made:

- d_1 : Stop the phase II trial and recommend no further study of E.
- d_2 : Stop the phase II trial and recommend E to a subsequent phase III trial.
- d_3 : Continue to enroll patients to the phase II trial.

It is shown elementarily that the value ω' an index of prediction can also be obtained as the expectation with respect to the posterior distribution based on ω', the average value of the index of satisfaction related to the law sampling the second phase. The problem that arises is that of the calculation of this hope in situations of tests, for a choice of prior distribution. Several models are considered to illustrate the Bayesian predictive procedure proposed.

2.1.4. ***Statistical inference for the design.*** We define the indices of satisfaction and anticipation of satisfaction related to a decreasing hypothesis test as a function of the p-value, satisfaction is higher than the null hypothesis is rejected more broadly, that is to say that p-value is small. We consider the case of a two-step procedure, which is often done in the case of clinical trials where these satisfaction indices are interesting protocols and when the inference concerns an effect evaluated from the future sample only. Being fixed α, a level α test defined by the critical first satisfaction index region $\Omega_1^{''(\alpha)}$:

$$\phi(\omega'') = 1_{\Omega''^{(\alpha)}}(\omega'') \tag{2.1}$$

The default of the above rudimentary index is that it expresses a satisfaction in "all or nothing". It is interesting to take into account to what level will the result always 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 are an increasing function of the classical indicator of significance that is in theory of tests, the p-value. One thus uses a new index of satisfaction defined by:

$$\begin{aligned} \phi(\omega'') = 0 \quad & if \quad p(\omega'') \geq 1-\alpha \\ = L(p(\omega'')) \quad & else. \end{aligned} \tag{2.2}$$

Where L is a decreasing function. We can generalize this procedure to a family of limited indices defined by:

$$L(p) = L(1-p)^l \quad where\, l \geq 0 \tag{2.3}$$

It is preferable to choose limited indexes because of their easier interpretation. In the case where $l = 1$, $1-\phi(\omega'')$ is the p-value and in the case where $l = 0$, one finds the indicator function of the critical region. For the sequel, we choose $l = 1$, $L(p) = (1–p)$ therefore

$$\begin{cases} \phi(\omega'') & = 0 \quad if \quad p(\omega'') \geq 1-\alpha \\ & = 1-p \quad else. \end{cases}$$

Based on the fact that most clinical trials meeting "legal" requirements (imposed by the control authorities for the authorization of placing drugs on the drug market) use as primary criterion of evaluation the significance level of a frequentist test, which is no else than the p-value. May we recall for this purpose that the p-value is always 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 Neymann Pearson approach Recall that $p = \inf\{\beta, \omega'' \in \Omega_1^{''(\beta)}\}$ is what practitioners note the associated ω'' and is called the p-value, it is considered a measure of credibility to be attached to the null hypothesis and practitioners often use to meet several critical and disadvantages of the approach Neymann -Pearson, you can see why. Therefore, the more that p is, the more the practitioner Considers that the results significant. An indicator of prediction is given by:

$$\begin{aligned} \pi(\omega') &= \int_{\Omega_1^{''(\alpha)}} \phi(\omega'') P_{\Omega''}^{\omega'}(d\omega'') \\ &= \int_{\{\omega''; p(\omega'') \geq 1-\alpha)\}} L(p(\omega'')) P_{\Omega''}^{\omega'}(d\omega'') \\ &= \int_{\Theta} \left(\int_{\Omega_1^{''(\alpha)}} \phi(\omega'') P_{\Omega''}^{\theta}(d\omega'') \right) P_{\Theta}^{\omega'}(d\theta') \end{aligned} \tag{2.4}$$

It is noticed that $\int_{\Omega_1^{''(\alpha)}} \phi(\omega'') P_{\Omega''}^{\theta}(d\omega'')$ generalizes the power of the test in the logic of the index of satisfaction proposed. Therefore, this index of prediction can be used to determine whether the trial should be stopped early due to efficacy/futility or continued because the current data are not yet conclusive; it is the experimenter to take the final decision.

2.1.5. ***Application.*** It is proposed to calculate the prediction of satisfaction *in this Bayesian design with two kinds of prior distributions* in the binomial model, where the law of the unknown parameter θ is a conjugate prior or non-informative. Several phase II clinical trial designs are proposed in the statistical literature anmost of them are conducted in two stages. Let X_i be the dichotomous response variable, which assumes value 1 if the clinicians classify the patient i as responder to the treatment t and 0 otherwise. In a typical two-stage design, T patients are accrued and treated at the first stage and T' additional patients in the second stage. We denote θ the probability that an individual suffering from a disease is cured with the treatment t. It is also considered that the medication (treatment related t) may be marketed only if $\theta \geq \theta_0$. From a statistical point of view, we can formulate the problem using the following test: $H_0 : \theta \leq \theta_0$. We work in the framework of the sampling model where we assume that are realizations of independent random variables X_i and even Bernoulli parameter θ , again for the sake

of completeness we take $\omega' = \sum_{i=1}^{T} X_i$. If we choose as prior distribution for θ a beta law $B(a,b)$ is then known that the posterior distribution of θ/ω' is still a beta law $B(\overline{\alpha},\overline{\delta})$ with $\overline{\alpha} = a+\omega'$ and $\overline{\delta} = b+T-\omega'$. The satisfaction index for observation $\omega'' = \sum_{i=1}^{T'} X_i$ is:

$$\phi(\omega'') = 0 \quad \text{if} \quad \omega'' < q_0 \tag{2.5}$$

$$= \sum_{t=0}^{\omega''-1} C_N^t \theta_0^t (1-\theta_0)^{N-t} \quad \text{if} \quad \omega'' \geq q_0 \tag{2.6}$$

Where

$$q_0 = \inf\{u; \sum_{t=u}^{T'} C_{T'}^t \theta_0^t (1-\theta_0)^{T'-t} \leq \alpha\} \tag{2.7}$$

Then the Bayesian prediction distribution of ω''/ω'

$$f(\omega''/\omega') = \int_0^1 f(\omega''/\theta) f(\theta/\omega')\, d\theta \tag{2.8}$$

$$= \int_0^1 C_{T'}^{\omega''} \theta^{\omega''} (1-\theta)^{(T'-\omega'')} [\beta(\overline{\alpha},\overline{\delta})\overline{\beta}]^{-1} \theta^{\overline{\alpha}-1} (1-\theta)^{\overline{\delta}-1} \tag{2.9}$$

$$= C_{T'}^{\omega''} \frac{[\beta(\overline{\alpha}+\omega'', \overline{\delta}+T'-\omega'')]}{[\beta(\overline{\alpha},\overline{\delta})]}$$

From here on, observed the response of the first step ω', the prediction $\pi(\omega')$ is :

$$\pi(\omega') = \sum_{\omega''=q_0}^{T'} \sum_{t=0}^{\omega''-1} C_{T'}^t \theta_0^t (1-\theta_0)^{T'-t} \frac{C_{T'}^{\omega''} \beta(a+\omega'+\omega'', b+T+T'-\omega'-\omega'')}{\beta(a+\omega', b+T-\omega')} \tag{2.10}$$

Moreover, due to ethical considerations, the phase II clinical studies are planned as a multi-stage design to ensure that the trials do not last too long if the treatment shows a clear inadequateness.

2.1.6. ***Simulation sittings***. The aim of exploratory clinical trials, such as phase II trials and proof-of-concept studies, is to determine whether a new intervention is promising for further testing in confirmatory clinical trials, such as phase III randomized controlled trials. The clinical trial, a prospective study to evaluate the effect of interventions in humans under prespecified conditions, is a standard and integral part of modern medicine. Many adaptive and sequential approaches have been proposed for use in clinical trials to allow adaptations or modifications to aspects of a trial after its initiation without undermining the validity and integrity of the trial. In all rigor, the Jeffreys rule gives different priors for the different designs, since it is based on the Fisher information, showd that Jeffreys prior offers new perspectives for the development of Bayesian procedures with good frequentist properties in hypothesis testing procedures.

Suppose two imaging modalities (e.g., CT vs.MRI) for diagnosing lung cancer are to be compared on the basis of test accuracy (sensitivity, specificity, and the area under the ROC curve).

Suppose $T = T' = 20$ are the sample sizes of the two groups and the prior probability of the null hypotheses is$\theta_0 = 0.6$, The predictive probability at each point $\pi(\omega')$ is calculated via simulation in table (1), where $\pi_1(\omega')$ represented the uniform prior beta $(1,1)$ $\pi_2(\omega')$ represented the non-informative prior beta $(0.5, 0.5)$ and the other case $\pi_3(\omega')$ is the real data with a vague prior beta $(0.6, 04)$, we can see [10]

We note in table (1) with:

- The prior Beta $(1,1)$ where ω' is included in $[0,17]$, the result of $\theta_0 = 0.6$ varies from 0.00000004 to 0.6694. Therefore we conclude H_0 for $\omega' < 17$. On the other hand, when ω' is included in $[18,20]$ the result $\pi_1(\omega')$ varies from 0.8057 to 0.9763.

Table 1: Representation of prediction in experimental designs

scenarios	ω'	$\pi_1(\omega')$	$\pi_2(\omega')$	$\pi_3(\omega')$
1	0	0.000000004	0.000000001	0.000000002
2	1	0.00000006	0.00000003	0.00000004
3	2	0.0000005	0.0000003	0.0000003
4	3	0.000003	0.000002	0.000100
5	4	0.000108	0.000008	0.000368
6	5	0.000376	0.0003	0.000376
7	6	0.001126	0.0010	0.001150
8	7	0.002990	0.0028	0.003157
9	8	0.007164	0.0071	0.007760
10	9	0.015690	0.0160	0.017329
11	10	0.031708	0.0331	0.035516
12	11	0.059535	0.0633	0.067316
13	12	0.104377	0.1124	0.118618
14	13	0.171459	0.1861	0.195014
15	14	0.264466	0.2880	0.299757
16	15	0.383432	0.4170	0.431174
17	16	0.522629	0.5650	0.580360
18	17	0.669467	0.7161	0.730649
19	18	0.805738	0.8490	0.860491
20	19	0.912228	0.9437	0.950618
21	20	0.976381	0.9914	0.993835

- The prior Beta $(1, 1)$ where ω' is included in $[0, 17]$, the result of $\theta_0 = 0.6$ varies from 0.0000007 to 0.7161. Therefore we conclude H_0 for $\omega' < 17$. On the other hand, when ω' is included in $[18, 20]$ the result $\pi_2(\omega')$ varies from 0.8490 to 0.9914.

- The real data with prior Beta $(0.6, 0.4)$ where ω' is included in $[0, 17]$, the result of $\theta_0 = 0.6$ varies from 0.00000002 to 0.7306. Therefore we conclude H_0 for $\omega' < 17$. On the other hand, when ω' is included in $[18, 20]$ the result $\pi_3(\omega')$ varies from 0.8604 to 0.9938.

2.2. Sequential designs

The concept of sequential statistical methods was originally motivated by the need to obtain clinical benefits under certain economic or ethical constraints. For a trial with a positive result, early stopping means that a new product can be exploited sooner. If a negative result is indicated, early stopping ensures that resources are not wasted. [11]
We propose in the sequential designs, a satisfaction made by both the first and the second phase of

the experiment (ω', ω'') in the case of a classical test study, and is predicted using the first phase unlike previous work where only the result of the second phase ω'' is to establish the formal conclusion of the study (2.1), with the precedent Binomial model. We use a usual test on the results z of the first and second phase defined by: $z = \omega' + \omega''$

Group sequential methods are used routinely to monitor clinical trials and to provide early stopping when there is evidence of a treatment effect, a lack of an effect or concerns about patient safety. In many studies, the response of clinical interest is measured some time after the start of treatment and there are subjects at each interim analysis who have been treated but are yet to respond. The satisfaction index

for observation z is

$$\phi(z) = 0 \quad \text{if} \quad z < q_0 \tag{2.11}$$

$$= \sum_{t=0}^{z-1} C_{T+T'}^{t}(1-\theta_0)^{T+T'-t} \quad \text{if} \quad z \geq q_0, \tag{2.12}$$

Where

$$q_0 = \inf\{u;\ \sum_{t=u}^{T+T'} C_{T+T'}^{t}(1-\theta_0)^{T+T'-t} \leq \alpha\}. \tag{2.13}$$

Then the Bayesian prediction distribution of z/ω'

$$f(z/\omega') = \int_0^1 f(z/\theta) f(\theta/\omega')\, d\theta \tag{2.14}$$

$$= \int_0^1 C_{T+T'}^{z}\theta^z(1-\theta)^{(T+T'-z)} \frac{\theta^{a+\omega'-1}(1-\theta)^{T+b-\omega'-1}}{B(a+\omega', T+b-\omega')}\, d\theta \tag{2.15}$$

$$= C_{T+T'}^{z} \frac{B(a+\omega'+z, 2T+T'+b-z-\omega')}{B(a+\omega', T+b-\omega')} \tag{2.16}$$

From here on, observed the response of the first step ω', the prediction $\Pi(\omega')$ is

$$\Pi(\omega') = \sum_{z=q0}^{T+T'} \sum_{t=0}^{z-1} C_{T+T'}^{t}\theta^t(1-\theta)^{(T+T'-t)} C_{T'}^{\omega''} \frac{B(a+\omega'+\omega'', T+T'+b-\omega'-\omega'')}{B(a+\omega', b+T-\omega')} \tag{2.17}$$

2.2.1. ***Simulation sittings.*** Group sequential design is probably one of the most commonly used clinical trial designs in clinical research and development, the primary reasons for conducting interim analyses of accrued data. Suppose are the sample sizes of the two groups and the prior probability of the null hypotheses is $\theta_0 = 0.6$, the predictive probability at each point $\Pi(\omega')$ is calculated via simulation in table (2) , where $\Pi_1(\omega')$ represented the uniform prior beta$(1,1)$,$\Pi_2(\omega')$ represented the non informative prior beta(0.5,0.5) and the other case $\Pi_3(\omega')$ is the real data with a vague prior beta $(0.6, 0.4)$.

Table 2: Representation of prediction in sequential designs

scenarios	ω'	$\Pi_1(\omega')$	$\Pi_2(\omega')$	$\Pi_3(\omega')$
1	0	0.0000001	0.00000007	0.00000005
2	1	0.000002	0.0000009	0.000001
3	2	0.00014	0.000008	0.00010
4	3	0.00065	0.00047	0.00055
5	4	0.0023	0.0019	0.0022
6	5	0.0070	0.0060	0.0067
7	6	0.0174	0.0159	0.0173
8	7	0.0382	0.0362	0.0390
9	8	0.0746	0.0728	0.0776
10	9	0.1314	0.1311	0.1383
11	10	0.2115	0.2144	0.2241
12	11	0.3141	0.3216	0.3335
13	12	0.4337	0.4466	0.4597
14	13	0.5611	0.5788	0.5919
15	14	0.6846	0.7051	0.7170
16	15	0.7932	0.8136	0.8231
17	16	0.8789	0.8964	0.9032
18	17	0.9387	0.9515	0.9555
19	18	0.9746	0.9821	0.9841
20	19	0.9922	0.9956	0.9963
21	20	0.9986	0.9995	0.9997

We note in table (2) with:

- The prior $B(1,1)$ where ω' is included in $[0,15]$, the result of $\theta_0 = 0.6$ varies from 0.0000001 to 0.7932. Therefore we conclude H_0 for $\omega' < 15$. On the other hand, when ω' is included in $[16,20]$ the result $\Pi_1(\omega')$ varies from 0.8789 to 0.9986.

- The prior $B(0.5,0.5)$ where ω' is included in $[0,15]$, the result of $\theta_0 = 0.6$ varies from 0.00000007 to 0.8136. Therefore we conclude H_0 for $\omega' < 15$. On the other hand, when ω' is included in $[16,20]$ the result $\Pi_2(\omega')$ varies from varies from 0.8964 to 0.9995.

- The real data with prior $B(0.6,0.4)$ where ω' is included in $[0,15]$, the result of $\theta_0 = 0.6$ varies from 0.00000005 to 0.8231. Therefore we conclude H_0 for $\omega' < 15$. On the other hand, when ω' is included in $[16,20]$ the result $\Pi_3(\omega')$ varies from varies from 0.9032 to 0.9997.

3. Comparison of prevision indices

If we denote by $\pi_1(\omega')$, $\pi_2(\omega')$ and $\pi_3(\omega')$, the prevision index in the case of experimental design, and $\Pi_1(\omega')$, $\Pi_2(\omega')$ and $\Pi_3(\omega')$, the prevision index in the case of sequential design, figures (1), (2), and (3) show compared curves $\pi_1(\omega')$ and $\Pi_1(\omega')$, $\pi_2(\omega')$ and $\Pi_2(\omega')$ and $\pi_3(\omega')$ and $\Pi_3(\omega')$ of the prevision indices in a study of frequentist test respectively in experimental design and in sequential analysis.

One can see that when we choose the sequential design the prediction is better.

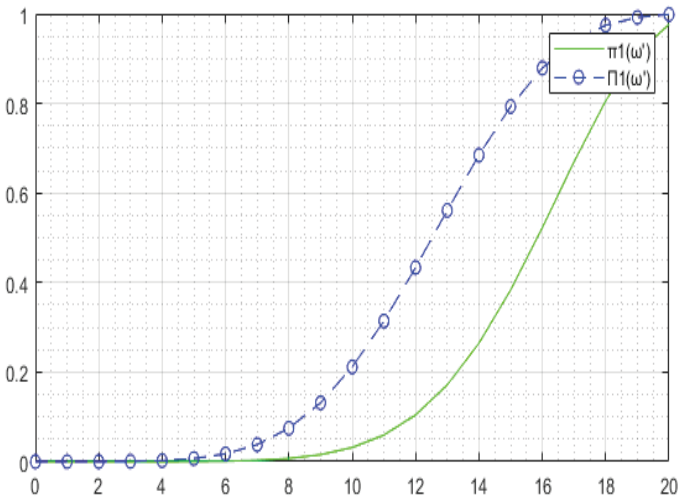

Figure 1: Prediction in experimental and sequential with uniform prior Beta$(1, 1)$

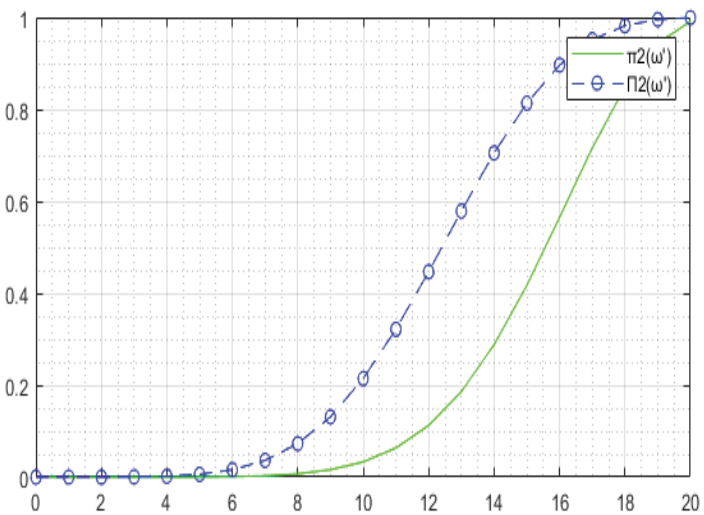

Figure 2: Prediction in experimental and sequential design s with non-informative prior Beta $(0.5, 0.5)$

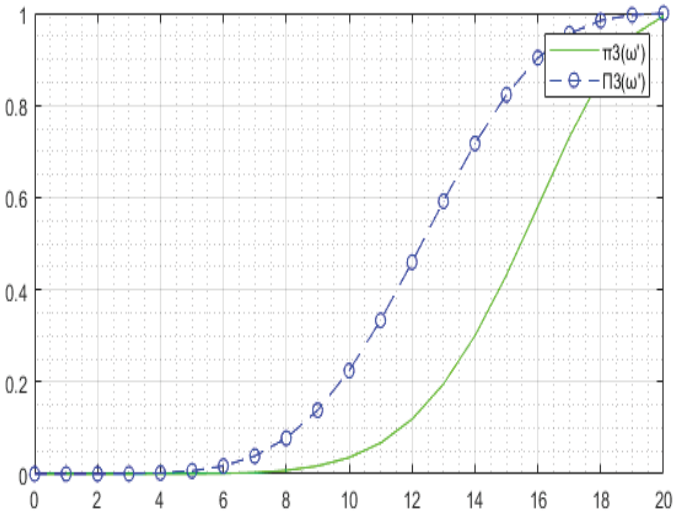

Figure 3: Prediction in experimental and sequential designs with a vague prior Beta $(0.6, 0.4)$

4. Conclusion

The aim of our work was to propose a Bayesian experimental designs and sequential adaptation design in experimental trials, considered the procedure based on satisfaction of the prediction index concept design, we believe that we can say that the Bayesian predictive approach proposed can be used to predict on the basis of statements frequentist results, we nevertheless believe that the frequentist approach sheds a different light on data and should not be excluded from further our goal is to develop an effective and flexible design that has desirable statistical properties . We have improved the methodology in the design of clinical trials by providing a prediction indices in a Bayesian framework, as is always the case in the experimental trial protocol and we illustrate our results using the binomial model.

References

1. Guosheng Yin, Nan Chen, J. Jack Lee , *Phase II trial design with Bayesian adaptive randomization and predictive probability* ,Appl. Statist. (2012) 61, Part 2, pp. 219–235.
2. Lisa V. Hampson, Christopher Jennison, *Group sequential tests for delayed responses*, J. R. Statist. Soc. B (2013) 75, Part 1, pp. 3–54.. J. Differential Equations 7, 554-589, (1970).
3. E.W .Steyerberg, *Clinical Prediction Models A Practical Approach to Development*, Validation, and Updating, XXVIII, (2009) ,500p, Hardcover.
4. Lecoutre, G. Derzko, J. M. Grouin. *Bayesian predictive approach for inference about proportions*, Statistics in Medicine, (1995)14, pp. 1057-1063.
5. H. Merabet, *Index and prevision of satisfaction in exponential models for clinical trials*, Statistica, anno LXIV, n.3, (2004), 441-453.
6. S. M Berry, B.P. Carlin, J.J Lee, P. Muller, *Bayesian Adaptive Methods for Clinical Trials*, Chapman & Hall/CRC biostatistics series. , (2011).
7. G. Koop, D.J. Poirier, and J. L. Tobias, *Bayesian Econometric Methods*,(2007).
8. C .M. C. Shein Chung, *Adaptive design methods in clinical trials*, Chapman & Hall/CRC, (2011).
9. Luke Akong'o Orawo.J. Andrés Christen, *Bayesian sequential analysis for multiple-arm clinical trials*, Stat Comput (2009) 19: 99–109 DOI 10.1007/s11222-008-9074-y.
10. N. A Azadi, P. Fearnhead, G Ridall and J. H. Blok, *Bayesian Sequential Experimental Design forn Binary Response Data with Application to Electromyographic Experiments*, Bayesian Analysis (2014), 9 , Number 2, pp. 287-306.
11. N. Stallard, Tim Friede, *A group-sequential design for clinical trials with treatment selection*, Statist. Med. (2008); 27:6209–622.

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