

Multinomial Group Testing with Small-Sized Pools and Application to California HIV Data: Bayesian and Bootstrap Approaches

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Summary. This paper consider multinomial group testing which is concerned with classification each of N given units into one of k disjoint categories. In this paper, we propose exact Bayesian, approximate Bayesian, bootstrap methods for estimating individual category proportions using the multinomial group testing model proposed by Bar-Lev et al (2005). By the comparison of Mean Square Error (MSE), it is shown that the exact Bayesian method has a better efficiency and consistency than maximum likelihood method. We suggest an approximate Bayesian approach using Markov Chain Monte Carlo (MCMC) for posterior computation. We derive exact credible intervals based on the exact Bayesian estimators and present confidence intervals using the bootstrap and MCMC. These intervals are shown to often have better coverage properties and similar mean lengths to maximum likelihood method already available. Furthermore, the proposed models are illustrated using data from a HIV blood test study throughout California, 2000.

Keywords: Group testing; Multinomial distribution; Interval estimator; Bayesian analysis; Markov Chain Monte Carlo; WinBUGS; Dirichlet distribution; Bootstrap Interval

1 Introduction

The concept of group-testing originated with Dorfman (1943) in the context of identifying all syphilitic men by Wasserman-type blood testing. Instead of testing units (bloods) individually, observations are made on groups of units amalgamated together with group size $s > 1$. In most applications, the group response is binary, classified as either non-infected or infected. A group being non-infected is taken to mean no infected unit in the group, while a group testing defective is taken to mean that at least one of the units is infected. Group testing may be used simply to obtain an estimate of the proportion of infected units in a given population (the estimation problem) or to exhaustively identify all infected members in the population (the classification problem).

The first recorded application of Group testing is screening draftees for syphilis during World War II (See the monograph by Du and Hwang (2000)). Modern applications of Group testing are made to many important areas such as quality control for industrial production systems (Sobel and Groll, 1959; Li, 1962, Hwang, 1984, Bar-Lev et al., 1990), transmission of viruses by vectors (Walter et al., 1980; Swallow, 1985), fisheries (Worlund and Taylor, 1983), communication networks (Wolf, 1985), plant disease assessment (Rodoni et al., 1994; Hepworth, 1996; Hughes and Gottwald, 1998; Hepworth, 2004), genetics (Chick, 1996; Uhl et al., 2001), DNA library screening (Marcula, 1999a,

b), drug discovery (Xie et al., 2001; Zhu et al., 2001), distributed data system (Hwang and Zang, 2002), and DNA Microarray design (Schliep et al. 2003). In molecular biology, group testing has been applied to the problem of screening DNA clone libraries sequence tagged sites to aid in the construction of physical maps (Baillot, et al., 1991; Bruno, et al., 1995; Dogget, et al., 1995). In public-health studies, not only does group testing reduce the cost of testing, but it also preserves individual anonymity (Gastwirth and Hammick, 1989; Tu, et al. 1994, 1995). Applications to HIV screening are given, among others, by Emmanuel et al. (1988), Cahoon-Young et al. (1989), Behets et al. (1990), Hammick and Gastwirth (1994), Litvak et al. (1994), Tu et al. (1995), Wein and Zenios (1996), Gupta and Malina (1999), and Xie (2001).

Hung and Swallow (2000) considered group testing problems wherein the probability of response is a function of one or more covariates. In general for a single covariate T with $k \geq 2$ levels, let p_1, p_2, \dots, p_k correspond to the probabilities that individuals at each of k levels possess the characteristic. To extend the idea to situations involving other types of restriction such as umbrella orderings or antitonic constraints, Tebbs and Swallow (2003) presented an isotonic group testing when the probability of response is increasing across the levels of an observed covariate. The group testing suggested by Tebbs and Swallow (2003) has an isotonotic constraint $p_1 \leq p_2 \leq \dots \leq p_k$. In general, it is hard to apply the isotonic group testing to the medical researches which do not keep the ordering constraint because of several complicated biological factors. So authors had a motivation to find the literature review of the multinomial group testing, which is more realistic method compared to a binary group testing. Kumar (1970a) proposed multinomial combinatorial group testing procedure which considers the classification of each of a finite number N of given units into one of the k disjoint categories. Also, Kumar (1970b, 1972) considered the problem of trinomial combinatorial group testing which is concerned with classification each of N given units into one of three disjoint categories such as good, mediocre, and defective. Hwang and Xu (1987) considered Group testing to identify one defective and one mediocre item which consider that a set N of n items consists of $n - 2$ good items and two questionable items M and D such that M is mediocre and D is defective. Hwang and Yao (1989) considered cutoff point and monotonicity properties for multinomial combinatorial group testing. Under the assumption that a probability distribution on the number of defective items exists, multinomial probability group testing models have been considered by Hughes-Oliver and Rosenberger (2000) and, in the context of drug discovery, by Xie

et al. (2001) and Zhu et al. (2001) and , in the context of genetic, by Pfeiffer (2002). Recently, Bar-Lev et al. (2005) proposed multinomial probability group testing which assume that every of the pooled items has none or some of k attributes, one of them causing contamination. The objective of the Bar-Lev et al. (2005) model is to choose an optimal group size for pooled screening so as to collect prespecified numbers of items of the various types with minimum testing expenditures. Estimation of proportions in the Bar-Lev et al. (2005) model is derived by MLE approach.

In the group testing literature, estimating the interested proportion, p , via maximum likelihood has been the traditional approach and has been studied extensively (Thompson, 1962; Swallow, 1985, 1987; Chen and Swallow, 1990, 1995; Hughes-Oliver and Swallow, 1994; Hung and Swallow, 1999). However, since group testing is often most effective when the prevalence p is suspected to be small, some authors have considered implementing this prior knowledge with a Bayesian approach. Chaubey and Li (1995) use a two-parameter Beta prior distribution for p and derive the Bayes estimator using a squared error loss function. Chick (1996) also uses a two-parameter eta prior for p and considers the use of unequal group sizes. Chick (1996) clearly mentioned the advantage of Bayesian method compared to the classical approach. The advantage is as follows; "Certain proportions are more likely than others for many experiment. The classical statistical approach does not permit the belief that some proportions are more likely than others. A bayesian probability approach is therefore recommended when such information is available. The bayesian approach also allows for more flexibility than MLE approach for describing such information." However, neither Chaubey and Li (1995) nor Chick (1996) addresses Bayesian estimation of the papameter in the context of multinomial group testing design.

In this article, we consider the Bayesian approach to multinomial distributed responses and explore some potential advantages of the Bayesian multinomial group testing model. In addition, we propose a approximate Bayes estimates using Monte Carlo Markov Chain (MCMC) employed by WinBUGS and consider interval estimates using the bootstrap.

The purpose of this article is to propose several methods for estimating of parameters of multinomial group testing model. To illustrate our findings we have applied the proposed method to California HIV counseling and testing study data which has three categories such as HIV positive, HIV inconclusive (currently not HIV positive but potentially HIV positive), and HIV negative.

The rest of the article is arranged as follows. Section 2 gives a short review of multinomial distribution and Dirichlet distribution and presents a maximum likelihood estimator in the Bar-Lev (2005) multinomial group testing. In Section 3, we derive an exact Bayesian multinomial group testing model and its exact confidence interval, and compare MLE and Bayes estimator, on frequentist grounds, in terms of mean-squared error (i.e., risk). In Section 4, we consider interval estimates using the bootstrap and propose approximate Bayes estimates using Monte Carlo Markov Chain (MCMC), and the proposed methods are illustrated using a real HIV dataset throughout California, 2000. In Section 5, we conclude with a brief summary discussion.

2 Multinomial Group testing

When data are more complex and have more than two categories, we need a new technique to give alternative solutions for some of these specific problems. In multinomial group testing model, there are more than two possibilities which is more applicable in real application. We present in detail the general setting of the Bayesian multinomial group testing models. The multinomial distribution is a generalization of the binomial for the situation in which each trial results in one and only one of several categories, as opposed to just two, as in the case of the binomial experiment. We discuss briefly below multinomial distribution and Dirichlet distribution. Let $Y = (Y_1, \dots, Y_k)$, where Y_i is the number of k independent trials that result in category i , $i = 1, \dots, k$. The standard multinomial model can be written as

$$Y = \{Y_1, Y_2, \dots, Y_{k-1}\} \sim \text{Multinomial}(n, \pi_1, \pi_2, \dots, \pi_{k-1}) = \frac{n!}{\prod_{i=1}^k y_i!} \prod_{i=1}^k \pi_i^{y_i},$$

where π_i , called model probability, is the probability that a given trial results in category i , $i = 1, \dots, k$ and $\sum_{i=1}^k y_i = n$. The observed number of cases that gives response i to the dependent variable is denoted y_i and k denotes the number of possible response. The parameter space is $\Pi = \{\pi : \pi_i \geq 0, i = 1, \dots, k; \sum_{i=1}^k \pi_i = 1\}$.

A prior distribution $f(\pi)$ is said to be conjugated to a likelihood $L(x|\pi)$, if the posterior distribution $g(\pi|x)$ has the same parameter form as the prior distribution. Conjugate prior has following properties; first, it allows arbitrary numbers of updates to be made to the distribution as more data becomes available, second, it has computational flexibility. The probability density of Dirich-

let distribution (Aitchison, 1986) for variables $\Pi = (\pi_1, \dots, \pi_k)$ with parameter $\tilde{\alpha} = (\alpha_1, \dots, \alpha_k)$ is defined by

$$f(\Pi; \tilde{\alpha}) = \frac{\Gamma(\sum_{i=1}^k \alpha_i)}{\prod_{i=1}^k \Gamma(\alpha_i)} \prod_{i=1}^k \pi_i^{\alpha_i - 1} I_{\Pi}(\pi), \quad (1)$$

where $\pi_1, \dots, \pi_k \geq 0$; $\sum_{i=1}^k \pi_i = 1$ and $\alpha_1, \dots, \alpha_k > 0$. In the Dirichlet distribution, each π_i follows a $Beta(\alpha_i, \alpha - \alpha_i)$, where $\alpha = \sum_{i=1}^k \alpha_i$ distribution. In order to fully specify the Bayesian model, Dirichlet priors are assigned to the $\pi_i, i = 1, 2, \dots, n$, i.e., $\Pi \sim \text{Dirichlet}(\alpha_1, \alpha_2, \dots, \alpha_n)$, where $\alpha_i, i = 1, 2, \dots, n$ are the hyperparameter of the prior distribution. It is straight forward to show that the joint posterior distribution is also Dirichlet distribution of the form

$$\pi_i \sim^{iid} \text{Dirichlet}_k(\alpha_1 + y_1, \dots, \alpha_k + y_k), \quad (2)$$

where $\text{Dirichlet}_k(\alpha_1, \dots, \alpha_k)$ denotes on a $k - 1$ dimensional simplex with parameter $(\alpha_1, \dots, \alpha_k)$. Therefore, the posterior distribution of the π_i given an observation of multinomially distributed Y_1, \dots, Y_k is also Dirichlet distribution since

$$P(\pi|Y) \propto \prod_{i=1}^k \pi_i^{\alpha_i + y_i}$$

The Dirichlet distribution is the conjugate prior of the parameters of the multinomial distribution. Dirichlet distribution is a multivariate generalization of the Beta distribution. Recently, Bar-Lev (2005) proposed multinomial group testing model which deals with more than two category responses. Bar-Lev (2005) focus on choosing an optimal group size for pooled screening so as to collect prespecified numbers of items of the various types with minimum testing expenditures and derived exact results for the underlying distributions of the stopping times. In their work, they considered the k attributes v_1, \dots, v_k and fix the group size s . For a given group, let (Z_{j1}, \dots, Z_{jk}) be the random vector of '1's and '0's defined by

$$Z_{jv} = 1 \quad \text{if the } j\text{th item in the group possesses attribute } v,$$

and $Z_{jv} = 0$ if it does not. Let

$$\mathbf{Z} = (Z_{jv})_{j=1, \dots, s, v=1, \dots, k}$$

be the $(s \times k)$ -matrix of the Z_{jv} . For $1 \leq h \leq k$ and distinct indices $1 \leq x_1, \dots, x_h \leq k$, they denote by $\mathbf{B}_{x_1, \dots, x_h}$ the event that the attributes v_{x_1}, \dots, v_{x_h} are present in at least one item of the

given group while the other attributes are missing in all s items. Let \mathbf{B} be event that none of the attributes is present in the group. Bar-Lev (2005) expressed the probabilities of these events in terms of the distribution of \mathbf{Z} . Therefore,

$$\begin{aligned} P(\mathbf{B}_{x_1, \dots, x_h}) &= P\left(\sum_{j=1}^s Z_{jx_v} \geq 1 \text{ for } v = 1, \dots, h, \sum_{j=1}^s Z_{jx} = 0 \text{ for } x \notin \{x_1, \dots, x_h\}\right) \\ &= \sum P(\mathbf{Z} = \mathbf{a}) \end{aligned}$$

where the sum is over all matrices $\mathbf{a} = (a_{jx})_{j=1, \dots, s, x=1, \dots, k}$ satisfying

$$\begin{aligned} a_{jx} &\in \{0, 1\} \\ \sum a_{jx_v} &\geq 1 \text{ for } v = 1, \dots, k \\ a_{jx} &= 0, x \notin \{x_1, \dots, x_h\}. \end{aligned}$$

Similarly,

$$P(\mathbf{B}) = P(Z_{jv} = 0 \text{ for all } j, v).$$

The presence of attribute v_k contaminates a group combining all types containing v_k into one; therefore they distinguish between the $l = 2^{k-1} + 1$ types

$$\mathbf{B}_{x_1, \dots, x_h}, \quad 1 \leq h \leq k-1, \quad 1 \leq x_1 < \dots < x_h \leq k-1 \quad (3)$$

$$\mathbf{B} \text{ and } \bigcup_{h=0}^{k-1} \bigcup_{1 \leq x_1 < \dots < x_h \leq k-1} \mathbf{B}_{x_1, \dots, x_h, k}. \quad (4)$$

The types in (3) are the clean ones containing at least one of the attributes v_1, \dots, v_{k-1} ; \mathbf{B} is purely clean and the second type in (4) is the contaminated one. Number the types from 1 to l and call the types $\mathbf{B}^{(1)}, \dots, \mathbf{B}^{(l)}$, where $\mathbf{B}^{(1)} = \mathbf{B}$ and $\mathbf{B}^{(l)}$ is the contaminated type.

Every item can have any combination of attributes independently of the other items. Usually, the population prevalence rate of contaminated items is much smaller than those of the clean types taken together. The occurrence of the k attributes v_1, \dots, v_k in an item can be assumed to be independent. In this paper, we denote by p_i the probability that an item possesses attribute i .

By the independence of the rows of \mathbf{Z} it follows that

$$P(\mathbf{B}) = P(Z_{jv} = 0, v = 1, \dots, k)^s.$$

In particular, if the attributes are independent,

$$P(\mathbf{B}) = \prod_{v=1}^k (1 - p_v)^s.$$

The probabilities in (3) are difficult to compute in general. However, in the case of independent attributes it is easily seen that

$$P(\mathbf{B}_{v_1, \dots, v_k}) = \prod_{v \notin \{x_1, \dots, x_h\}} (1 - p_v)^s \prod_{i=1}^k (1 - p_{x_i}^s).$$

Finally,

$$P(\mathbf{B}^{(l)}) = P\left(\sum_{j=1}^s Z_{jk} \geq 1\right) (1 - p_k)^s.$$

Under the multinomial group testing of Bar-Lev et al (2005), π_1 is the case when there is no element for attribute present, π_2 is the case when there is an element for attribute 1 but not for attribute 2 present, π_3 is the case when there is an element for attribute 2 present. Assume that the attributes are independently distributed in the population. Then in a group test of size s the probabilities of the three different categories are

$$\begin{aligned} \pi_1 &= (1 - p_1)^s (1 - p_2)^s \\ \pi_2 &= (1 - p_2)^s [1 - (1 - p_1)^s] \\ \pi_3 &= 1 - (1 - p_2)^s. \end{aligned}$$

By using invariant property of MLE, the ML estimates of p_1, p_2, p_0 are given by

$$\begin{aligned} \hat{p}_1 &= 1 - \left(1 - \frac{\hat{\pi}_2}{1 - \hat{\pi}_3}\right)^{1/s} = 1 - \left(\frac{n_1}{n_1 + n_2}\right)^{1/s} \\ \hat{p}_2 &= 1 - (1 - \hat{\pi}_3)^{1/s} = 1 - \left(\frac{n_1 + n_2}{n_1 + n_2 + n_3}\right)^{1/s} \\ \hat{p}_0 &= 1 - \hat{p}_1 - \hat{p}_2 = \left(\frac{n_1 + n_2}{n_1 + n_2 + n_3}\right)^{1/s} + \left(\frac{n_1}{n_1 + n_2}\right)^{1/s} - 1, \end{aligned}$$

where $\hat{\pi}_1 = n_1/n$, $\hat{\pi}_2 = n_2/n$, and $\hat{\pi}_3 = n_3/n$. For example, assuming no testing errors, N_3 , has a binomial distribution with parameter n and $1 - (1 - p_2)^s$. For interval estimation, the confidence intervals to the group testing model is given by

$$\hat{p}_2 \pm z_{\alpha/2} \sqrt{\frac{\widehat{Var}(\hat{p}_2)}{n}},$$

where

$$\widehat{Var}(\widehat{p}_2) = \frac{\{1 - (1 - \widehat{p}_2)^s\}(1 - \widehat{p}_2)^{2-s}}{s^2},$$

and $z_{\alpha/2}$ denotes the upper $\alpha/2$ percentile of the standard normal distribution.

3 Exact Bayesian multinomial group testing

The objective of Bayesian modeling is to obtain a conditional distribution of the unknown parameters of the model given the model structure, prior information about unknown parameters and observed data. In group testing problem, we are interested in improving procedures for estimating the proportion p . Bayesian approach provide a formal way of making statistical inference on parameters of interest based on observed data and prior information. In the Bayesian approach, the uncertainty about the parameter values given the observed data and prior information are expressed in terms of probabilities.

Bayesian methods have not been extensively used in group testing problem. Moreover, so far there is no published paper which deal with detailed full Bayesian multinomial group testing model. The ultimate goal of this study is to improve procedure for estimating the parameters in group testing model.

Now we introduce the Bayesian multinomial group testing estimation problem which is more applicable in practice. We show that Bayesian approach provides a more reliable proportion estimator than that of classical approach in group testing problem. Finally, we show that the estimator by the proposed approach is consistently preferred over the classical estimator in real application in group testing problem.

3.1 Computing the Exact Joint Posterior Distribution

We denote by p_i the probability that an subject/item possesses attribute/category i and $\sum_{i=1}^k p_i = 1$. We assume that the attributes are fixed and *iid* Bernoulli(p_i) random variables, $0 < p_i < 1$ and a common group size s . Note that since $\sum_{i=1}^k p_i = 1$, there are actually only two unknown parameters. We assume that the response vector $(Y_{i1}, Y_{i2}, \dots, Y_{ik})$ for subject (i.e., item or individual) i with

$i = 1, 2, \dots, n$ and for attribute/category j with $j = 1, 2, \dots, k$ consisting of zero and one, in addition to that we consider vectors having at least one non zero entry. To formally introduce group testing problem, we need to fix the group size s . Therefore $N = (N_1, \dots, N_k)$ has a multinomial distribution with parameters n and $\Pi = (\pi_1, \dots, \pi_k)$. So it follows that based on the observed values $\tilde{n} = (n_1, \dots, n_k)$, the likelihood function of N given that $\Pi = (\pi_1, \dots, \pi_k)$ is

$$f_{N|\Pi}(\tilde{n}|\tilde{\pi}) = \frac{n!}{\prod_{i=1}^k n_i} \prod_{i=1}^k \pi_i^{n_i},$$

In this study, we will formally introduce the Bayesian method in a general framework but we will focus on a *trinomial group testing model* which is concerned with classification each of N given units into one of three disjoint categories. Note that in many cases, it is not easy to calculate the desired joint posterior distribution using analytical method. In our work, we analytically derived the joint and marginal posterior distribution for multinomial group testing model.

The number of defective groups, $\tilde{N} = (N_1, N_2, N_3)$, has a multinomial distribution with parameters $\tilde{n} = (n_1, n_2, n_3)$ and $\tilde{\pi} = (\pi_1, \pi_2, \pi_3)$. Thus, the likelihood for trinomial distribution of group testing problem can be expressed as

$$f_{\tilde{N}|\tilde{\Pi}}(\tilde{n}|\tilde{\pi}) = \frac{n!}{n_1!n_2!(n - n_1 - n_2)!} \pi_1^{n_1} \pi_2^{n_2} (1 - \pi_1 - \pi_2)^{n - n_1 - n_2}$$

where $\pi_1 + \pi_2 + \pi_3 = 1$ and $n = n_1 + n_2 + n_3$. In order to complete the model specification from a Bayesian framework, we specify a joint prior distribution for all parameter of the model. In this work, we adopted Dirichlet distribution as a prior information. There are several advantages of incorporating the Dirichlet distribution in multinomial set up. First, Dirichlet distribution is a conjugate family of multinomial distribution. Second, Dirichlet prior $\tilde{\alpha} = (\alpha_1, \dots, \alpha_k)$ is a appropriate for small p , since for large value of α , the majority of the probability distribution of the random variable is closed to zero. Third, estimates derived using Dirichlet prior are consistent, and can be computed efficiently.

The Dirichlet prior, the probability distribution function for \tilde{p} , is given by

$$f_{\tilde{\Pi}}(\tilde{p}|\tilde{\alpha}) = \frac{\Gamma(\alpha)}{\Gamma(\alpha_1)\Gamma(\alpha_2)\Gamma(\alpha - \alpha_1 - \alpha_2)} \pi_1^{\alpha_1-1} \pi_2^{\alpha_2-1} (\pi - \pi_1 - \pi_2)^{\alpha - \alpha_1 - \alpha_2 - 1},$$

for values of $\alpha = \sum_{i=1}^3 \alpha_i$.

The joint distribution of N and $\tilde{\pi}$, conditioned on $\tilde{\alpha}$, is given by

$$\begin{aligned} f_{\tilde{N}, \tilde{P}}(\tilde{n}, \tilde{\pi} | \tilde{\alpha}) &= f_{\tilde{N} | \tilde{\pi}}(\tilde{n} | \tilde{\pi}) \times f_{\tilde{\pi}}(\tilde{\pi} | \tilde{\alpha}) \\ &= \frac{n!}{n_1! n_2! (n - n_1 - n_2)!} \times \frac{\Gamma(\alpha)}{\Gamma(\alpha_1) \Gamma(\alpha_2) \Gamma(\alpha - \alpha_1 - \alpha_2)} \\ &\quad \times \pi_1^{n_1 + \alpha_1 - 1} \pi_2^{n_2 + \alpha_2 - 1} (\pi - \pi_1 - \pi_2)^{n - n_1 - n_2 + \alpha - \alpha_1 - \alpha_2 - 1}, \end{aligned}$$

Using transformation $\pi_1 = (1 - p_1)^s (1 - p_2)^s$, $\pi_2 = (1 - p_2)^s [1 - (1 - p_1)^s]$, and $1 - \pi_1 - \pi_2 = [1 - (1 - p_2)^s]$ so that $\Pi = (\pi_1, \pi_2, \pi_3)$, the joint distribution of \tilde{N} and \tilde{P} , conditioned on $\tilde{\alpha}$, is given by

$$\begin{aligned} f_{\tilde{N}, \tilde{P}}(\tilde{n}, \tilde{p} | \tilde{\alpha}) &= \frac{n!}{n_1! n_2! (n - n_1 - n_2)!} \times \frac{\Gamma(\alpha)}{\Gamma(\alpha_1) \Gamma(\alpha_2) \Gamma(\alpha - \alpha_1 - \alpha_2)} (1 - p_1)^{s(n_1 + \alpha_1 - 1)} \\ &\quad \times [1 - (1 - p_1)^s]^{(n_2 + \alpha_2 - 1)} (1 - p_2)^{s(n_1 + n_2 + \alpha_1 + \alpha_2 - 2)} [1 - (1 - p_2)^s]^{(n - n_1 - n_2 + \alpha - \alpha_1 - \alpha_2 - 1)}. |J|, \end{aligned}$$

for $0 < p_1, p_2 < 1$ and the Jacobian is $|J| = |s^2(1 - p_1)^{s-1}(1 - p_2)^{2s-1}|$. The marginal distribution of \tilde{N} is given by

$$\begin{aligned} f_N(\tilde{n} | \tilde{\alpha}) &= \int_0^1 f_{N, \mathbf{P}}(\tilde{n}, \tilde{p} | \tilde{\alpha}) d\tilde{p} \\ &= \frac{n!}{n_1! n_2! (n - n_1 - n_2)!} \times \frac{\Gamma(\alpha)}{\Gamma(\alpha_1) \Gamma(\alpha_2) \Gamma(\alpha - \alpha_1 - \alpha_2)} \times s^2 \\ &\quad \times \int_0^1 (1 - p_1)^{s(n_1 + \alpha_1 - \frac{1}{s})} [1 - (1 - p_1)^s]^{(n_2 + \alpha_2 - 1)} dp_1 \\ &\quad \times \int_0^1 (1 - p_2)^{s(n_1 + n_2 + \alpha_1 + \alpha_2 - \frac{1}{s})} [1 - (1 - p_2)^s]^{(n - n_1 - n_2 + \alpha - \alpha_1 - \alpha_2 - 1)} dp_2 \\ &= \frac{n!}{n_1! n_2! (n - n_1 - n_2)!} \times \frac{\Gamma(\alpha)}{\Gamma(\alpha_1) \Gamma(\alpha_2) \Gamma(\alpha - \alpha_1 - \alpha_2)} \times \\ &\quad \times \frac{\Gamma(n_1 + \alpha_1) \Gamma(n_2 + \alpha_2) \Gamma(n - n_1 - n_2 + \alpha - \alpha_1 - \alpha_2)}{\Gamma(n + \alpha)}, \end{aligned} \tag{5}$$

which is the product of gamma function.

The joint posterior distribution is given by

$$\begin{aligned} f_{\mathbf{P} | \mathbf{N}}(\tilde{p} | \tilde{n}, \tilde{\alpha}) &= \frac{f_{N, \mathbf{P}}(\tilde{n}, \tilde{p} | \tilde{\alpha})}{f_N(\tilde{n} | \tilde{\alpha})} \\ &= \frac{s^2 \Gamma(n + \alpha)}{\Gamma(n_1 + \alpha_1) \Gamma(n_2 + \alpha_2) \Gamma(n - n_1 - n_2 + \alpha - \alpha_1 - \alpha_2)} \\ &\quad \times (1 - p_1)^{s(n_1 + \alpha_1 - \frac{1}{s})} [1 - (1 - p_1)^s]^{(n_2 + \alpha_2 - 1)} \\ &\quad \times (1 - p_2)^{s(n_1 + n_2 + \alpha_1 + \alpha_2 - \frac{1}{s})} [1 - (1 - p_2)^s]^{(n - n_1 - n_2 + \alpha - \alpha_1 - \alpha_2 - 1)}. \end{aligned} \tag{6}$$

The joint posterior distribution is a product of the joint prior distribution and the likelihood function. We obtain analytically the marginal posterior distribution by integration over some parameters. This joint posterior distribution is all that is needed to make inference about the unknown parameters.

The full conditional distributions are derived from the joint posterior distribution. The final full conditional distribution for proportion p_1 is given by

$$\begin{aligned}
f_{P_1|N}(p_1|\tilde{n}, \tilde{\alpha}) &= \int_0^1 \frac{f_{N,\mathbf{P}}(\tilde{n}, \tilde{p}|\tilde{\alpha})}{f_N(\tilde{n}|\tilde{\alpha})} dp_2 \\
&= \frac{s^2\Gamma(n+\alpha)}{\Gamma(n_1+\alpha_1)\Gamma(n_2+\alpha_2)\Gamma(n-n_1-n_2+\alpha-\alpha_1-\alpha_2)} \\
&\quad \times (1-p_1)^{s(n_1+\alpha_1-\frac{1}{s})} [1-(1-p_1)^s]^{(n_2+\alpha_2-1)} \\
&\quad \times \int_0^1 (1-p_2)^{s(n_1+n_2+\alpha_1+\alpha_2-\frac{1}{s})} [1-(1-p_2)^s]^{(n-n_1-n_2+\alpha-\alpha_1-\alpha_2-1)} dp_2 \\
&= \frac{s\Gamma(n_1+n_2+\alpha_1+\alpha_2)}{\Gamma(n_1+\alpha_1)\Gamma(n_2+\alpha_2)} \\
&\quad \times (1-p_1)^{s(n_1+\alpha_1-\frac{1}{s})} [1-(1-p_1)^s]^{(n_2+\alpha_2-1)}. \tag{7}
\end{aligned}$$

and, similarly, p_2 is given by

$$\begin{aligned}
f_{P_2|N}(p_2|\tilde{n}, \tilde{\alpha}) &= \int_0^1 \frac{f_{N,\mathbf{P}}(\tilde{n}, \tilde{p}|\tilde{\alpha})}{f_N(\tilde{n}|\tilde{\alpha})} dp_1 \\
&= \frac{s^2\Gamma(n+\alpha)}{\Gamma(n_1+\alpha_1)\Gamma(n_2+\alpha_2)\Gamma(n-n_1-n_2+\alpha-\alpha_1-\alpha_2)} \\
&\quad \times \int_0^1 (1-p_1)^{s(n_1+\alpha_1-\frac{1}{s})} [1-(1-p_1)^s]^{(n_2+\alpha_2-1)} dp_1 \\
&\quad \times (1-p_2)^{s(n_1+n_2+\alpha_1+\alpha_2-\frac{1}{s})} [1-(1-p_2)^s]^{(n-n_1-n_2+\alpha-\alpha_1-\alpha_2-1)} \\
&= \frac{s\Gamma(n+\alpha)}{\Gamma(n_1+n_2+\alpha_1+\alpha_2)\Gamma(n-n_1-n_2+\alpha-\alpha_1-\alpha_2)} \\
&\quad \times (1-p_2)^{s(n_1+n_2+\alpha_1+\alpha_2-\frac{1}{s})} [1-(1-p_2)^s]^{(n-n_1-n_2+\alpha-\alpha_1-\alpha_2-1)} \tag{8}
\end{aligned}$$

With $f_{P_i|N}(p_i|\tilde{n}, \tilde{\alpha})$ and a given loss function, say, $L(p_i, a)$, (where a denotes the action taken), the Bayes estimate of p_i with respect to $L(p_i, a)$ is the value of a that minimizes

$$E[L(P_i, a)|\tilde{n}, \tilde{\alpha}] = \int_0^1 L(p_i, a) f_{P_i|N}(p_i|\tilde{n}, \tilde{\alpha}) dp_i,$$

for $i = 1, 2$. For the remainder of this section, and for all comparisons in Section 5, only squared-error loss is considered; i.e., $L(p_i, a) = (p_i - a)^2$, so that the Bayes estimate of p_i is the mean of

posterior $f_{P_i|N}(p_i|\tilde{n}, \tilde{\alpha})$. A closed-form expression for \hat{p}_{B_1} , the mean of the posterior, is given by

$$\begin{aligned}\hat{p}_{B_1} &= \int_0^1 p_1 f_{P_1|N}(p_1|\tilde{n}, \tilde{\alpha}) dp_1 \\ &= s \times \frac{\Gamma(n_1 + n_2 + \alpha_1 + \alpha_2)}{\Gamma(n_1 + \alpha_1)\Gamma(n_2 + \alpha_2)} \int_0^1 p_1 (1-p_1)^{s(n_1 + \alpha_1 - \frac{1}{s})} [1 - (1-p_1)^s]^{(n_2 + \alpha_2 - 1)} dp_1 \\ &= 1 - \frac{\text{Beta}(n_1 + \alpha_1 + \frac{1}{s}, n_2 + \alpha_2)}{\text{Beta}(n_1 + \alpha_1, n_2 + \alpha_2)}\end{aligned}$$

where

$$\text{Beta}(\alpha, \beta) = \int_0^1 x^{\alpha-1} (1-x)^{\beta-1} dx = \frac{\Gamma(\alpha)\Gamma(\beta)}{\Gamma(\alpha+\beta)}.$$

Similarly, a closed-form expression for \hat{p}_{B_2} , the mean of the posterior, is given by

$$\begin{aligned}\hat{p}_{B_2} &= \int_0^1 p_2 f_{P_2|N}(p_2|\tilde{n}, \tilde{\alpha}) dp_2 \\ &= \frac{s\Gamma(n+\alpha)}{\Gamma(n_1+n_2+\alpha_1+\alpha_2)\Gamma(n-n_1-n_2+\alpha-\alpha_1-\alpha_2)} \\ &\quad \times \int_0^1 p_2 (1-p_2)^{s(n_1+n_2+\alpha_1+\alpha_2-\frac{1}{s})} [1 - (1-p_2)^s]^{(n-n_1-n_2+\alpha-\alpha_1-\alpha_2-1)} dp_2 \\ &= 1 - \frac{\text{Beta}(n_1+n_2+\alpha_1+\alpha_2+\frac{1}{s}, n-n_1-n_2+\alpha-\alpha_1-\alpha_2)}{\text{Beta}(n_1+n_2+\alpha_1+\alpha_2, n-n_1-n_2+\alpha-\alpha_1-\alpha_2)}\end{aligned}$$

3.2 Credible Intervals

In the group testing literature, methods for confidence intervals construction have not been studied extensively. Thompson (1962) provide an approximate confidence intervals for the population proportion of viruliferous insects, based on the exact variance and Student-t approach. Bhattacharyya, Karandinos and DeFoliart (1979) develop a method for a confidence interval using the asymptotic normality assumption. The predominant strategy is to use approximate Wald-type confidence intervals, based on the normal distribution, using the asymptotic variance of \hat{p}_{M_i} , for $i = 1, 2$. Straightforward calculations show this interval is given by

$$\hat{p}_{M_i} \pm z_{\alpha/2} \sqrt{\{1 - (1 - \hat{p}_{M_i})^s\} (1 - \hat{p}_{M_i})^{2-s} / ns^2},$$

where $z_{\alpha/2}$ denotes the upper $\alpha/2$ percentile of the standard normal distribution.

By constructing the exact posterior distribution, we can calculate a $100(1-\alpha)\%$ credible intervals for p_i as follows

$$\int_{L_{p_i}}^{U_{p_i}} f_{P_i|N}(p_i|\tilde{n}, \tilde{\alpha}) dp_i = 1 - \alpha,$$

where $0 < L_{p_i} < U_{p_i} < 1$ for $i = 1, 2$. We denote credible interval by (L_{p_i}, U_{p_i}) , in practice, L_{p_i} and U_{p_i} may be determined using an equal-tail credible interval (95% equal-tail credible interval, i.e., 2.5 % and 97.5% posterior percentiles) or highest posterior density (HPD) interval method. In this study, we can find a nice closed-form expression for the equal-tail credible interval. The lower bound (LB) of p_1 may find by solving following equation

$$\begin{aligned} \frac{\alpha}{2} &= \int_0^{L_{p_1}} f_{P_1|N}(p_1|\tilde{n}, \tilde{\alpha}) dp_1 \\ &= \int_0^{L_{p_1}} \frac{s\Gamma(n_1 + n_2 + \alpha_1 + \alpha_2)}{\Gamma(n_1 + \alpha_1)\Gamma(n_2 + \alpha_2)} \times (1 - p_1)^{s(n_1 + \alpha_1 - \frac{1}{s})} [1 - (1 - p_1)^s]^{(n_2 + \alpha_2 - 1)} dp_1 \end{aligned}$$

Then using the u_1 substitution of $u_1 = 1 - (1 - p_1)^s$ produces

$$\int_0^{1-(1-L_{p_1})^s} \frac{\Gamma(n_1 + n_2 + \alpha_1 + \alpha_2)}{\Gamma(n_2 + \alpha_2)\Gamma(n_1 + \alpha_1)} u_1^{(n_2 + \alpha_2 - 1)} (1 - u_1)^{(n_1 + \alpha_1 - 1)} du_1 = \frac{\alpha}{2}$$

Thus, $1 - (1 - L_{p_1})^s$ is $\text{Beta}(\frac{\alpha}{2}; n_2 + \alpha_2, n_1 + \alpha_1)$, where $\text{Beta}(\gamma; a, b)$ denotes the γ quantile of the usual two-parameter Beta distribution. It follows that $L_{p_1} = 1 - \{1 - [\text{Beta}(\frac{\alpha}{2}; n_2 + \alpha_2, n_1 + \alpha_1)]^{1/s}\}$. Similarly, $U_{p_1} = 1 - \{1 - [\text{Beta}(1 - \frac{\alpha}{2}; n_2 + \alpha_2, n_1 + \alpha_1)]^{1/s}\}$. Similarly, the lower bound for \hat{p}_{B_2} is found by solving following equation

$$\begin{aligned} \frac{\alpha}{2} &= \int_0^{L_{p_2}} f_{P_2|N}(p_2|\tilde{n}, \tilde{\alpha}) dp_2 \\ &= \int_0^{L_{p_2}} \frac{s\Gamma(n + \alpha)}{\Gamma(n_1 + n_2 + \alpha_1 + \alpha_2)\Gamma(n - n_1 - n_2 + \alpha - \alpha_1 - \alpha_2)} \\ &\quad \times (1 - p_2)^{s(n_1 + n_2 + \alpha_1 + \alpha_2 - \frac{1}{s})} [1 - (1 - p_2)^s]^{(n - n_1 - n_2 + \alpha - \alpha_1 - \alpha_2 - 1)} dp_2 \end{aligned}$$

Then using the u_2 substitution of $u_2 = 1 - (1 - p_2)^s$ produces

$$\int_0^{1-(1-L_{p_2})^s} \frac{\Gamma(n + \alpha)}{\Gamma(n - n_1 - n_2 + \alpha - \alpha_1 - \alpha_2)\Gamma(n_1 + n_2 + \alpha_1 + \alpha_2)} \times u_2^{(n - n_1 - n_2 + \alpha - \alpha_1 - \alpha_2 - 1)} (1 - u_2)^{(n_1 + n_2 + \alpha_1 + \alpha_2 - 1)} du_2 = \frac{\alpha}{2}$$

Thus, $1 - (1 - L_{p_2})^s$ is $\text{Beta}(\frac{\alpha}{2}; n - n_1 - n_2 + \alpha - \alpha_1 - \alpha_2, n_1 + n_2 + \alpha_1 + \alpha_2)$. It follows that $L_{p_2} = 1 - [\text{Beta}(\frac{\alpha}{2}; n - n_1 - n_2 + \alpha - \alpha_1 - \alpha_2, n_1 + n_2 + \alpha_1 + \alpha_2)]^{1/s}$. Similarly, $U_{p_2} = 1 - [\text{Beta}(1 - \frac{\alpha}{2}; n - n_1 - n_2 + \alpha - \alpha_1 - \alpha_2, n_1 + n_2 + \alpha_1 + \alpha_2)]^{1/s}$.

Note that confidence intervals based on the MLE and credible sets based on $f_{P_i|N}(p_i|\tilde{n}, \tilde{\alpha})$ have different interpretations. In Section 4, we will compare 95% approximate Wald-type confidence intervals of the maximum likelihood estimators, \hat{p}_{M_i} , and credible intervals of exact Bayes estimators, \hat{p}_{B_i} , approximate Bayes estimators, \hat{p}_{G_i} and Bootstrap estimators \hat{p}_{R_i} , respectively.

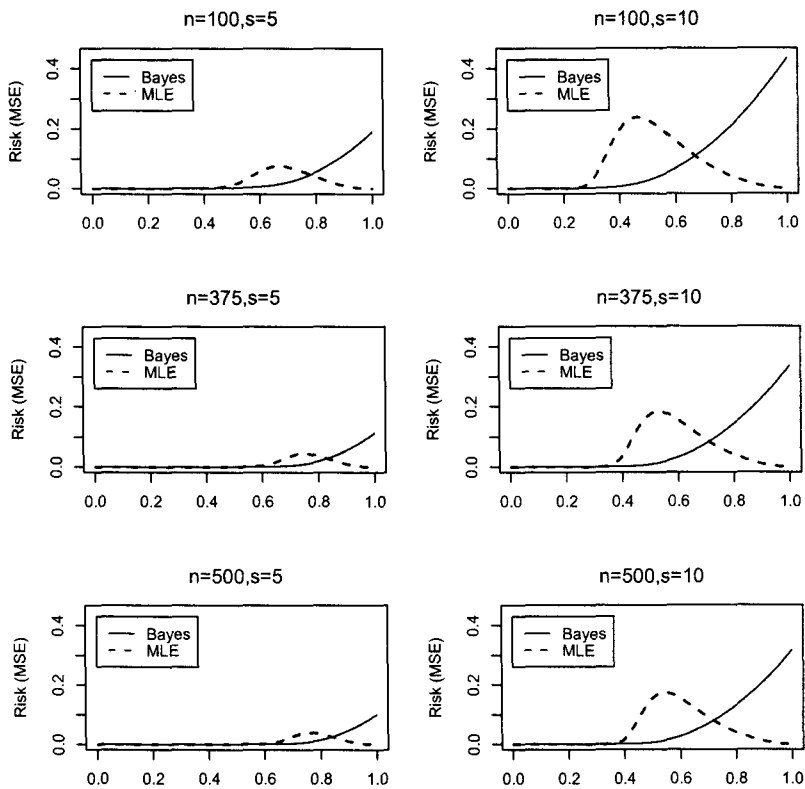


Figure 1: Top panel - MSE of \hat{p}_{M_2} , \hat{p}_{B_2} when group sizes $s = 5$ and $s = 10$, p_2 ranges from 0 to 1, and $n = 100$; middle panel - MSE of \hat{p}_{M_2} , \hat{p}_{B_2} when group sizes $s = 5$ and $s = 10$, p_2 ranges from 0 to 1, and $n = 375$; bottom panel - MSE of \hat{p}_{M_2} , \hat{p}_{B_2} when $s = 5$ and $s = 10$, p_2 ranges from 0 to 1, and $n = 500$

3.3 Comparison of Point Estimates

In this subsection, we are investigating two different estimators, exact Bayes estimators $\hat{\pi}_{B_i}$ and maximum likelihood estimators, $\hat{\pi}_{M_i}$, in order to assess the impact due to prior information. The exact Bayes estimators are compared here with the MLE using mean square error (MSE). We do this on frequentist terms and thus do not consider the loss function in the comparison. For a fixed p_i , the mean square errors of $\hat{\pi}_{M_i}$ and $\hat{\pi}_{B_i}$ are given by

$$\text{MSE}(\hat{p}_{M_i}) = \sum_{l=0}^n (\hat{p}_{M_i} - p_i)^2 \times \binom{n}{l} [1 - (1 - p_i)^s]^l (1 - p_i)^{s(n-l)}.$$

and

$$\begin{aligned} \text{MSE}(\widehat{p}_{B_i}) &= E_{N|P_i} [(\widehat{p}_{B_i} - p_i)^2] \\ &= \sum_{t=0}^n (\widehat{p}_{B_i} - p_i)^2 \times \binom{n}{t} [1 - (1 - p_i)^s]^t (1 - p_i)^{s(n-t)}. \end{aligned}$$

The purpose of the numerical computation is to confirm that the Bayesian multinomial group testing model is more efficient than ML approach in terms of MSE. The numerical results are graphically displayed to facilitate interpretation.

In practice, it is unlikely that the experimenter will ever use the optimal group size, since its value depends on the unknown p_i . Thus, we examine the performance of our estimators when sub-optimal values of s are used. In our work, we choose the most interested probability, p_2 , which is a positive trait proportion in the HIV or other disease tests from Bar-Lev (2005) model setting. Figure 1 displays plots of the $\widehat{\pi}_{B_2}$ and $\widehat{\pi}_{M_2}$ for values of $0 \leq p_2 \leq 1$ and for fixed s . We consider six cases: (i) $n = 100$ and $s = 5$, (ii) $n = 100$ and $s = 10$, (iii) $n = 375$ and $s = 5$, (iv) $n = 375$ and $s = 10$, (v) $n = 500$ and $s = 5$, and (vi) $n = 500$ and $s = 10$. For the non-informative priors, when (i) $n = 100$ and $s = 5$ and (ii) $n = 100$ and $s = 10$, the Bayes estimators outperform the maximum likelihood estimators for $0 < p_2 \leq 0.7$. When $n = 375$ and $n = 500$, the reduction in MSE realized by using a Bayes procedure also diminishes; however, all estimators based on non-informative priors still continue to have smaller MSE when $0 < \pi < 0.7$. In light of LeCam's (1958) results concerning the convergence of posterior distributions to a normal distribution, one would expect that for larger values of n , the reduction in MSE realized by the Bayes procedure would be even smaller than those when $n = 500$.

Four cases in Figure 1 display that there are large reductions in MSE by using Bayesian multinomial group testing and $\widehat{\pi}_{B_2}$ is more consistent than $\widehat{\pi}_{M_2}$.

4 Interval Estimation

4.1 Interval estimation using Bootstrap

The confidence intervals discussed in Section 3.2 utilize the large-sample distribution of the MLE p_i , $i = 0, 1, 2$. While this may provide a good approximation to the true sampling distribution

of p_i when a sample of size n is large, it may be a poor approximation when n is small (and especially when p_i and/or s is small). In the group testing procedure, much attention has been given to the small-sample problem. The problem of finding the best estimator for small samples is particularly intriguing. For small sample of size, the bootstrap resampling method may enhance the estimation efficiency and coverage sufficiency of confidence intervals. The bootstrap method introduced by Efron (1979) is a very general resampling procedure for estimating the distributions of statistics based on independent observations. The bootstrap method is shown to be successful in many situation, which is being accepted as an alternative to the asymptotic approach. The bootstrap method is a computer-intensive techniques for investigating the properties of estimators and for deriving estimates.

In light of this, we consider using the bootstrap to estimate the sampling distribution of p_i . A large number of resamples, say R , are taken from the original sample, and the statistic of interest p_i which we derived in Section 2 is calculated for each resample. The bootstrap distribution is then formed from the R values of p_i . Bootstrap confidence interval for a particular sample can be readily observed from the nonparametric distribution of the means of its 1,000 bootstrap replicates in our simulation work. For a two-sided 95 % bootstrap confidence interval, we select the values that cut off the lower and upper 2.5 percentiles. In this work, we implement the percentile method to estimate a confidence interval using Bootstrap sampling.

Efron and Tibshirani (1993) and Davison and Hinkley (1997) each summarize a variety of bootstrap confidence interval procedures. For full descriptions of these and other procedures, the reader is referred to the aforementioned references.

4.2 Application and MCMC

Current HIV screening tests are designed to detect antibodies to HIV. California publicly funded HIV conseling and testing data were collected for 2000 using the HIV Counseling Information System. Overall annual testing volume reported to the Office of AIDS (OA). There were 181,910 OA-funded tests and 25,095 tests funded by other non-OA sources. They reported HIV testing by race, gender, age, geographic area and risk behavior category based on risk behavior information provided at risk assessment and disclosure counseling sessions. Monthly testing volume ranged

between 12,000 - 17,000 OA-funded tests per month. In this application, we only consider 181,910 OA-funded tests per month for multinomial group testing model.

The group testing model is often used when there is a rare trait among a large population of size n . The proposed model is used to analyze the HIV data, making it the first application of this multinomial group testing model to data. Although we have obtained the closed-form joint posterior distribution in Section 3, we may use MCMC technique, introduced by Geman and Geman (1984), Tanner and Wong (1987) and Gelfand and Smith (1990), to sample from the joint posterior distribution of parameters. Computationally, it is rather easy to implement the model in WinBUGS (Bayesian inference Using Gibbs Sampling), a free software can be downloaded from <http://www.mrc-bsu.cam.ac.uk/bugs>. The software uses Gibbs sampling with necessary Metropolis-Hasting algorithm to obtain samples from the posterior distribution. As the model used was quite complex and high dimensional, MCMC method were used to approximate the posterior distributions. One important feature of Bayesian approach using MCMC is that while the method achieves important computational economics by using WinBUGS, it does not have any impact on the estimates of parameters.

The focus of this article is essentially on deriving of closed-form Bayes estimates of parameters but we are also concerned with estimating approximate Bayes estimates using MCMC implemented by WinBUGS. We want to show that two Bayesian approaches yield consistent estimates of the parameters of interest. Bayesian approaches we present give a more flexible and reliable estimates taking into prior information than classical estimates. In the framework of binomial group testing data, some works have been done by Chaubey and Li (1995) and Chick (1996).

In particular, approximate Bayes approach over exact Bayes approach is very beneficial since there is computationally flexibility using in-built software WinBUGS. Therefore, it is recommendable to use the Bayesian multinomial group testing model since, in doing so, we obtain a reliable estimates for rate trait proportion.

Using the WinBUGS, we obtain samples from the posterior distributions of the parameters. After some preliminary studies, we run three parallel chains with dispersed starting values for each parameter. From the consistent results of multiple chains and convergence tests, we conclude that the chains have mixed well. In this paper, we have investigated the performance of the various ap-

Table 1: *Office of AIDS (OA)-funded HIV counseling and testing services by month throughout California for testing year 2000*

Month	# of Positive	# of Negative	# of Inconclusive	# of Total
	181 (0.0125)	14321 (0.9858)	25 (0.0017)	14527
February	180 (0.0117)	15188 (0.9874)	14 (0.0009)	15382
March	214 (0.0126)	16738 (0.9863)	19 (0.0011)	16971
April	194 (0.0124)	15372 (0.9862)	21 (0.0013)	15587
May	186 (0.0116)	15802 (0.9876)	13 (0.0008)	16001
June	240 (0.0146)	16141 (0.9826)	45 (0.0027)	16426
July	213 (0.0137)	15290 (0.9844)	29 (0.0019)	15532
August	200 (0.0125)	15733 (0.9852)	36 (0.0023)	15969
September	183 (0.0130)	13822 (0.9854)	22 (0.0016)	14027
October	181 (0.0115)	15477 (0.9866)	30 (0.0019)	15688
November	161 (0.0116)	13719 (0.9866)	25 (0.0018)	13905
December	134 (0.0113)	11748 (0.9876)	13 (0.0011)	11895
Total	2267 (0.0124)	179351 (0.9859)	292 (0.0016)	181910

proaches, ML approach, exact Bayes approach, approximate Bayes approach and bootstrap method in terms of point and interval estimation (See Table 2). In Table 2, we use the abbreviations M, B, G and R for ML estimate, exact Bayes estimate, approximate Bayes estimate and Bootstrap estimate, respectively. The confidence intervals of Approximate bayes estimates in Table 2 are based on three chains of 27,000 iterations each after a burn-in period of 3,000 iterations using the WinBUGS.

With non-informative prior, the difference observed in the length of the confidence intervals for classical approach, bootstrap method and credible intervals for Bayesian approach are not much different. But we find some interesting result in the month of June. The numbers of HIV positive and HIV inconclusive persons during the month of June are higher than the numbers of HIV positive and HIV inconclusive during other months. Most of cases in Table 2, we also notice that the length of the confidence intervals using the bootstrap method is smaller than the ones of the confidence intervals using the other methods. From the results of Table 2, when the number of infected people are large, the bootstrap method in multinomial group testing procedure may be recommended.

The results in Table 2 also confirm that the exact Bayes approach and the approximate Bayes approach using MCMC have the similar parameter estimates and credible intervals. Another common approach to Bayesian inference is to present an HPD (Highest Posterior Density Interval) region for the parameters. Using MCMC method, we show the approximate Bayesian the equal-tail

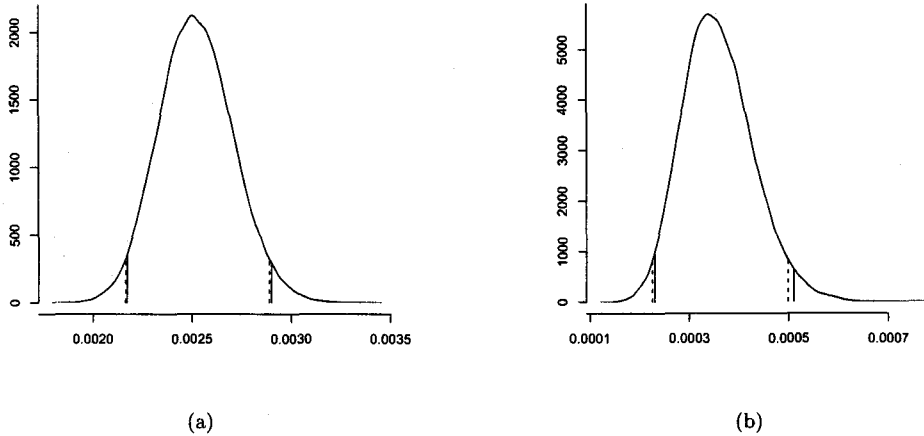


Figure 2: (a) Equal-tail 95% posterior credible interval (solid line) and the HPD interval (dashed line) of the proportion of the number of positive for January, (b) Equal-tail 95% posterior credible interval (solid line) and the HPD interval (dashed line) of of the proportion of the number of inconclusive for January.

95% posterior credible intervals and the HPD by computing the 2.5 and 97.5 percentiles of the posterior distribution of the parameters (Figure 2). In summary, although ML estimates for rare traits have good asymptotic properties, we have some evidence that Bayesian approach and Bootstrap approach provide more appropriate and reliable parameter estimates than the MLE for rate trait proportions.

5 Discussion

Group testing is extensively used for treating dichotomous data when the probability of being defective is very small. In this article, we consider a multinomial group testing model having more than two categories. We propose and compare four different alternatives to perform statistical inference for the multinomial group testing model parameter, especially rate traits; maximum likelihood estimator, exact Bayes estimator, approximate Bayes estimator and Bootstrap estimator.

The multinomial models were allowed to adopt more specifications or categories in group testing experiment design. In group testing problem, ML estimates may lie outside the boundary of the parameter space or are typically more extreme (or can be zero) than the Bayes estimates for rare

traits (Tebbs et al. (2003)). Here, in the context of multinomial group testing problem, we apply Bayesian analysis to conveniently estimate parameters as well as precision. Figure 1 displays that the exact Bayes estimates are reliable than ML estimates and have comparable efficiency in terms of MSE. We also recommend the Bayesian approach to multinomial group testing for two following reasons. First, we obtain a more reliable estimates for rare trait proportion in group testing problem using Bayesian analysis than classical approach. Second, Bayes estimates with non-informative prior information provide a comparable efficiency to classical estimates for small sample sizes. We have also introduced the bootstrap as a possible strategy in multinomial group testing. Bootstrap method may be able to capture small lengths of the confidence intervals for small samples or large samples.

In binomial group testing, Chick (1996) proposes forming credible intervals using a Beta prior distribution with hyperparameters chosen by the researcher. Recently, Tebbs et al. (2003) propose a similar credible interval, but using a one-parameter Beta prior and an empirical Bayes approach. Both intervals could be used provided the use of the chosen prior is justified. In the context of the multinomial group testing, we have introduced four different confidence intervals using maximum likelihood estimator, exact Bayes estimator, approximate Bayes estimator and Bootstrap estimator. In addition, we have incorporated one of the popular statistical methods, MCMC using the WinBUGS into the multinomial group testing model to find the approximate bayes estimates. The approximate Bayes approach over exact Bayes approach is very beneficial since there is computationally flexibility using in-built software WinBUGS.

It should be pointed out that the proposed methods for the multinomial group testing may strengthen the group testing experimental design to minimize the expected number of tests and reduce the costs. Our work advances the study of interval estimation procedures in various group-testing applications such as environmental issues, medical screening experiments, and drug discovery which require more than two categories.

References

- Aitchison, J. (1985). A general class of distributions on the simplex. *J. Roy. Statist. Soc. Ser. B*, **47**, 1, 136-146.
- Barillot, E., Lacroix, B., and Cohen, D. (1991) Theoretical analysis of library screening using an

- n-dimensional pooling strategy. *Nucleic Acids Research*, **19**, 22, 62416247.
- Bar-Lev, S., Boneh, A., Perry, D. (1990). Incomplete identification models for group-testable items. *Naval Res. Logist.*, **37**, 647659.
- Bar-Lev, S., Stadge, W., Van der, D.S. (2005). Optimal group testing with processing times and incomplete identification. *J. Statist. Plann. Inference*, In Press.
- Behets, F., Bortozzi, S., Kasali, M., Kashamuka, M., Atikala, L., Brown, C., Ryder, R., and Quinn, C. (1990). Successful use of pooled sera to determine HIV-1 seroprevalence in Zaire with development of cost efficiency models. *AIDS*, **4**, 737-741.
- Bhattacharyya, G., Karandinos, M., and DeFoliart, G. (1979). Point Estimates and Confidence Intervals for Infection Rates Using Pooled Organisms in Epidemiological Studies. *Amer. J. of Epidemiology*, **109**, 124-131.
- Bruno, W., Balding, D., Knill, E., Bruce, D., Whittaker, C., Doggett, N., Stallings, R., and Torney, D. (1995). *Design of efficient pooling experiments*. **26**, 2130.
- Cahoon-Young, B., Chandler, A., Livermore, T., Gaudino, J., and Benjamin, R. (1989). Sensitivity and specificity of pooled versus individual sera in a HIV-antibody prevalence study. *J. of Clinical Microbiology*, **27**, 1893-1895.
- Chaubey, Y. and Li, W. (1995). Comparison between maximum likelihood and Bayes methods for estimation of binomial probability with sample compositing. *J. of Official Statist.*, **11**, 379-390.
- Chen, C. L. and Swallow, W. H (1990). Using group testing to estimate a proportion, and to test the binomial model *Biometrics*, **46**, 1035-1046.
- Chen, C. L. and Swallow, W. H (1995). Sensitivity analysis of variable-size group testing and its related continuous models. *Biom. J.*, **2**, 173-181.
- Chick, S. (1996). Bayesian models for limiting dilution assay and group test data. *Biometrics* **52**, 1055-1062.

- Davison, A., and Hinkley, D. (1997). *Bootstrap Methods and Their Application*, Cambridge: Cambridge University Press.
- Doggett, N., Goodwin, L., Tesmer, J., Meincke, L., Bruce, D., Clark, L., Altherr, M., Ford, A., Chi, H., Marrone, B., et al. (1995). An integrated physical map of human chromosome 16. *Nature*, **377**, 335365.
- Dorfman, R. (1943). The detection of defective members of large populations. *Ann. Math. Statist.*, **14**, 436440.
- Du, D.Z., and Hwang, F. (2000). *Combinatorial Group Testing and Its Applications*. 2nd edition. World Scientific, Singapore.
- Efron, B. (1979). Bootstrap methods: another look at the jackknife. *Ann. Statist.*, **7**, 1, 1-26.
- Efron, B., and Tibshirani, R. (1993). *An introduction to the bootstrap*. Chapman and Hall, New York.
- Emmanuel, J., Bassett, M., Smith, H., and Jacob, J. (1988). Pooling of sera for HIV testing: An economical method for use in developing countries. *J. of Clinical Pathology*, **41**, 582-585.
- Gastwirth, J., and Hammick, P. (1989). Estimation of the prevalence of a rare disease, preserving the anonymity of the subjects by group testing: Application to estimating the prevalence of AIDS antibodies in blood donors. *J. Statist. Plann. Inference*, **22**, 15-27.
- Gelfand, A.E. and Smith, A.F.M. (1990). Sampling based approaches to calculating marginal densities. *J. Amer. Statist. Assoc.* **85**, 398-409.
- Geman, S. and Geman, D. (1984). Stochastic relaxation, Gibbs distribution and the bayesian restoration of images. *IEEE Trans. Pattern Anal. Machine Intell.*, **6**, 721-741.
- Gupta, D., and Malina, R. (1999). Group testing in presence of classification errors. *Statistics in Medicine*, **18**, 10491068.
- Hammick, P., and Gastwirth, J. (1994). Group testing for sensitive characteristics: extensions to higher prevalence. *Internat. Statist. Rev.*, **62**, 319331.

- Hepworth, G. (1996). Exact confidence intervals for proportions estimated by group testing. *Biometrics*, **52**, 1134-1146.
- Hepworth, G. (2004). Mid- P confidence intervals based on the likelihood ratio for proportions estimated by group testing. *Aust. N. Z. J. Stat.*, **46**, 391-405.
- Hughes, G., and Gottwald, T. (1998). Survey methods for assessment of citrus tristeza virus incidence. *Phytopathology*, **88**, 715-723.
- Hughes-Oliver, J., and Rosenberger, W. (2000). Efficient estimation of the prevalence of multiple rare traits. *Biometrika*, **87**, 2, 315-327.
- Hughes-Oliver, J., and Swallow, W. (1994). A two-stage adaptive procedure for estimating small proportions. *J. Amer. Statist. Assoc.*, **89**, 982-993.
- Hung, M., and Swallow, W. (1999). Robustness of group testing in the estimation of proportions. *Biometrics*, **55**, 231-237.
- Hung, M., and Swallow, W. (2000). Use of binomial group testing in tests of hypotheses for classification or quantitative covariables. *Biometrics*, **56**, 1, 204-212.
- Hwang, F. (1984). Robust group testing. *J. of Quality Technology*, **16**, 189-195.
- Hwang, F., and Yao, Y. (1989). Cutoff point and monotonicity properties for multinomial group testing. *SIAM J. Discrete Math.*, **2**, 4, 500-507.
- Hwang, F., and Xu, Y. (1987). Group testing to identify one defective and one mediocre item. *J. Statist. Plann. Inference*, **17**, 3, 367-373.
- Hwang, F., and Zang, W. (2002) Group testing and fault detection for replicated files. *Discrete Appl. Math.*, **116**, 3, 231-242.
- Kumar, S. (1970a). Multinomial group-testing. *SIAM J. Appl. Math.*, **19**, 340-350.
- Kumar, S. (1970b). Group-testing to classify all units in a trinomial sample. *Studia Sci. Math. Hungar.*, **5**, 229-247

- Kumar, S. (1972). Trinomial group-testing with an unknown proportion of units in the three categories. *Ann. Inst. Statist. Math.*, **24**, 171-181.
- LeCam, L. (1958). Les propriétés asymptotiques des solutions de Bayes. *Publications de l'Institut de Statistique de l'Université de Paris*, **7**, 17-35.
- Li, C. (1962). A sequential method for screening experimental variables. *J. Amer. Statist. Assoc.*, **57**, 455-477.
- Litvak, E., Tu, X.M., Pagano, M. (1994). Screening for the presence of a disease by pooling sera samples. *J. Amer. Statist. Assoc.*, **89**, 424-434.
- Macula, A. (1999a). Probabilistic nonadaptive group testing in the presence of errors and DNA library screening. *Ann. Combin.*, **3**, 61-69.
- Macula, A. (1999b). Probabilistic nonadaptive and two-stage group testing with relatively small pools and DNA library screening. *J. Combin. Optim.*, **2**, 385-397.
- Pfeiffer, R., Rutter, J., Gail, M., and Struewing, J., and Gastwirth, J. (2002). Efficiency of DNA Pooling to Estimate Joint Allele Frequencies and Measure Linkage Disequilibrium. *Genetic Epidemiology*, **22**, 94-102.
- Rodoni, B., Hepworth, G., Richardson, C., and Moran, J. (1994). The use of a sequential batch testing procedure and ELISA to determine the incidence of five viruses in Victorian cut-flower Sim carnations. *Austral. J. Agric. Res.*, **45**, 223-230.
- Schliep, A., Torney, D., and Rahmann, S. (2003). Group Testing With DNA Chips: Generating Designs and Decoding Experiments. *IEEE: Proceedings of the Computational Systems Bioinformatics*, 1-8.
- Sobel, M., and Groll, P. (1959). Group testing to eliminate efficiently all defectives in a binomial sample. *Bell System Tech. J.* **28**, 1179-1252.
- Swallow, W. (1985). Group testing for estimating infection rates and probabilities of disease transmission. *Phytopathology*, **75**, 882-889.

- Swallow, W. (1987). Relative mean squared error and cost considerations in choosing group size for group testing to estimate infection rates and probabilities of disease transmission. *Phytopathology*, **77**, 1376-1381.
- Tanner, M. A. and Wong, W. H. (1987). The calculation of posterior distributions by data augmentation (with discussion). *J. Amer. Statist. Assoc.*, **82**, 528-550.
- Tebbs, J., Bilder, C., and Moser, B. (2003). An empirical Bayes group-testing approach to estimating small proportions. *Comm. Statist. Theory Methods*, **32**, 983-995.
- Tebbs, J., Swallow, W., (2003). Estimating ordered binomial proportions with the use of group testing. *Biometrika* **82**, 471-477.
- Thompson, K. (1962). Estimation of the proportion of vectors in a natural population of insects. *Biometrics*, **18**, 568-578.
- Tu, X., Litvak, E., and Pagano, M. (1994). Screening tests: Can we get more by doing less. *Statistics in Medicine*, **13**, 1905-1919.
- Tu, X., Litvak, E., and Pagano, M. (1995). On the informativeness and accuracy of pooled testing in estimating prevalence of a rare disease: Application to HIV screening. *Biometrika*, **82**, 287-297.
- Uhl, G., Liu, Q., Walther, D., Hess, J., Naiman, D. (2001). Polysubstance abuse-vulnerability genes: genome scans for association using 1,004 subjects and 1,494 single-nucleotide polymorphisms. *Amer. J. Human Genet.*, **69**, 1290-1300.
- Walter, S., Hildreth, S. and Beaty, B. (1980). Estimation of infection rates in populations of organisms using pools of variable size. *Amer. J. Epidemiol.*, **112**, 124-128.
- Wein, L., and Zenios, S. (1996). Pooled testing for HIV screening: capturing the dilution effect. *Oper. Res.*, **44**, 543-569.
- Wolf, J. (1985). Born again group testing: multiaccess communications. *IEEE Trans. Inform. Theory IT*, **31**, 185-191.

- Worlund, D., and Taylor, G. (1983). Estimation of disease incidence in fish populations. *Canad. J. Fish. Aquat. Sci.*, **40**, 2194-2197.
- Xie, M. (2001). Regression analysis of group testing samples. *Statistics in Medicine*, **20**, 1957-1969.
- Xie, M., Tatsuoka, K., Sacks, J., and Young, S. (2001). Group testing with blockers and synergism. *J. Amer. Statist. Assoc.*, **96**, 921-930.
- Zhu, L., Hughes-Oliver, J., and Young, S. (2001). Statistical decoding of potent pools based on chemical structure. *Biometrics*, **57**, 992-930.
- California HIV Counseling and Testing HIV Counseling and Testing Annual Report, Department of Health Services Office of AIDS, HIV Education and Prevention Services Branch HIV Prevention Research and Evaluation Section <http://www.dhs.ca.gov/AIDS/>

Table 2: 95% approximate Wald-type confidence intervals of the maximum likelihood estimators ($\hat{\pi}_M$) and credible intervals of exact Bayes estimators ($\hat{\pi}_B$), approximate Bayes estimators ($\hat{\pi}_G$) using MCMC with non-informative Dirichlet prior distributions (i.e., Dirichlet (1,1,1)) and bootstrap confidence interval by percentile method ($\hat{\pi}_R$), respectively

	# of Positive	# of Inconclusive
January	181	25
$\hat{\pi}_M$	(0.00214, 0.00284)	(0.00021, 0.00048)
$\hat{\pi}_B$	(0.00217, 0.00290)	(0.00024, 0.00051)
$\hat{\pi}_G$	(0.00217, 0.00290)	(0.00023, 0.00051)
$\hat{\pi}_R$	(0.00216, 0.00298)	(0.00024, 0.00052)
February	180	14
$\hat{\pi}_M$	(0.00201, 0.00270)	(0.00010, 0.00028)
$\hat{\pi}_B$	(0.00203, 0.00272)	(0.00011, 0.00031)
$\hat{\pi}_G$	(0.00204, 0.00272)	(0.00011, 0.00031)
$\hat{\pi}_R$	(0.00206, 0.00260)	(0.00010, 0.00027)
March	214	19
$\hat{\pi}_M$	(0.00220, 0.00288)	(0.00012, 0.00032)
$\hat{\pi}_B$	(0.00222, 0.00290)	(0.00015, 0.00035)
$\hat{\pi}_G$	(0.00222, 0.00290)	(0.00014, 0.00035)
$\hat{\pi}_R$	(0.00222, 0.00286)	(0.00013, 0.00033)
April	194	21
$\hat{\pi}_M$	(0.00215, 0.00286)	(0.00015, 0.00038)
$\hat{\pi}_B$	(0.00217, 0.00288)	(0.00018, 0.00042)
$\hat{\pi}_G$	(0.00218, 0.00288)	(0.00020, 0.00041)
$\hat{\pi}_R$	(0.00222, 0.00289)	(0.00016, 0.00039)
May	186	13
$\hat{\pi}_M$	(0.00200, 0.00267)	(0.00007, 0.00025)
$\hat{\pi}_B$	(0.00202, 0.00270)	(0.00010, 0.00028)
$\hat{\pi}_G$	(0.00203, 0.00270)	(0.00010, 0.00028)
$\hat{\pi}_R$	(0.00203, 0.00268)	(0.00010, 0.00021)
June	240	45
$\hat{\pi}_M$	(0.00258, 0.00332)	(0.00039, 0.00071)
$\hat{\pi}_B$	(0.00260, 0.00333)	(0.00042, 0.00074)
$\hat{\pi}_G$	(0.00260, 0.00335)	(0.00041, 0.00074)
$\hat{\pi}_R$	(0.00263, 0.00334)	(0.00045, 0.00066)

July	213	29
$\hat{\pi}_M$	(0.00239, 0.00313)	(0.00024, 0.00051)
$\hat{\pi}_B$	(0.00241, 0.00315)	(0.00026, 0.00054)
$\hat{\pi}_G$	(0.00242, 0.00316)	(0.00024, 0.00054)
$\hat{\pi}_R$	(0.00257, 0.00308)	(0.00029, 0.00049)
August	200	36
$\hat{\pi}_M$	(0.00217, 0.00287)	(0.00030, 0.00060)
$\hat{\pi}_B$	(0.00219, 0.00289)	(0.00033, 0.00063)
$\hat{\pi}_G$	(0.00220, 0.00289)	(0.00033, 0.00063)
$\hat{\pi}_R$	(0.00226, 0.00269)	(0.00033, 0.00067)
September	183	22
$\hat{\pi}_M$	(0.00225, 0.00301)	(0.00018, 0.00045)
$\hat{\pi}_B$	(0.00227, 0.00303)	(0.00021, 0.00048)
$\hat{\pi}_G$	(0.00228, 0.00304)	(0.00023, 0.00048)
$\hat{\pi}_R$	(0.00219, 0.00278)	(0.00021, 0.00045)
October	181	30
$\hat{\pi}_M$	(0.00199, 0.00266)	(0.00025, 0.00052)
$\hat{\pi}_B$	(0.00200, 0.00268)	(0.00027, 0.00055)
$\hat{\pi}_G$	(0.00201, 0.00269)	(0.00027, 0.00055)
$\hat{\pi}_R$	(0.00196, 0.00278)	(0.00027, 0.00050)
November	161	25
$\hat{\pi}_M$	(0.00197, 0.00269)	(0.00022, 0.00050)
$\hat{\pi}_B$	(0.00199, 0.00271)	(0.00025, 0.00054)
$\hat{\pi}_G$	(0.00199, 0.00272)	(0.00026, 0.00053)
$\hat{\pi}_R$	(0.00211, 0.00262)	(0.00026, 0.00047)
December	134	13
$\hat{\pi}_M$	(0.00188, 0.00265)	(0.00010, 0.00034)
$\hat{\pi}_B$	(0.00191, 0.00268)	(0.00013, 0.00038)
$\hat{\pi}_G$	(0.00192, 0.00269)	(0.00013, 0.00038)
$\hat{\pi}_R$	(0.00187, 0.00267)	(0.00007, 0.00031)