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On Bayesian Estimation in Group Screening Designs without Errors in Decisions

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Abstract: Group screening or testing has long been recognized as a safe and sensible alternative to one-at-a-time testing in applications wherein the prevalence rate p is small. In this paper, we developed an Empirical Bayes (EB) procedure to estimate p using a beta-type prior distribution and a squared error loss function. We showed that the Empirical Bayes (EB) estimator is preferred over the usual Maximum Likelihood Estimator (MLE) for small group sizes and small p. The methods were illustrated using group testing data from a prospective hepatitis C virus study that was conducted in China.

Keywords: Composite sampling, empirical Bayes estimation, pooling designs, screening experiments

1. INTRODUCTION

The group testing experimental design has received considerable attention in recent years. Unlike one-at-a-time testing, observations are made on groups of individuals pooled together with group size $k>1$. In most applications, the group response is binary, and is classified to be either positive or negative. We defined a positive group to be one that contains at least one positive individual, and a negative group to be one that contains no positive individuals. Gastwirth and Johnson (1994) argue that group testing serves as a cost-effective quality control procedure in the contexts of Human Immunodeficiency Virus (HIV). However, Neill and Conradie (1992, 1994) proposed the use of group testing in screening experiments to estimate hepatitis C prevalence. In addition, Gastwirth and Hammick (1989) and Hammick and Gastwirth (1994) confidentiality discussed issues which are associated with the use of group testing in public health settings. Pritchard and Tebbs (2011) have considered the use of inverse binomial distribution in group testing. In addition, they have considered both point and interval estimation procedures for small p. This gave better estimates compared to the usual binomial distribution.

The gains from group testing (compared to one-at-a-time testing) is the greatest when dealing with rare traits (i.e. when the proportion of interest, p, is small). Group testing experiments do not require as many tests as one-at-a-time testing experiments to obtain an equally good estimator of p. Statistical considerations involved with choosing k have been investigated by Swallow (1985) and Hughes-Oliver and Swallow (1994). Kline et al. (1989) and Munzon et al. (1992) have reported that tests currently used in HIV screening have near perfect sensitivity and specificity when $k \geq 0$. In addition, Neill and Conradie (1992, 1994) have shown that tests used in hepatitis C screening are reliable for group sizes, $k \leq 8$.

The traditional approach to estimating p entails the use of the method of maximum likelihood. Swallow (1985) provided an indepth analysis of the point estimate properties of the maximum likelihood estimator (MLE). Lew and Ley (1989), Gastwirth et al. (1991), Johnson and Gastwirth (1991), Chaubey and Li (1995), and Chick (1996) have each proposed classical Bayesian approaches in the group testing estimation problem. Pritchard and Tebbs (2011) studied a problem of estimating disease prevalence using negative binomial distribution from the Bayesian approach. They derived closed form expressions for posterior distributions and the resulting point and credible interval estimators. Hwang and Mi (2015) showed the existence and uniqueness of maximum likelihood Empirical Bayes (MLEB) and proposed an alternative Bayes estimator whose performance was found

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to be better than MLEB. Such approaches require researchers to specify the values of the model hyper parameters a prior. However, poor choices of such parameters could cause the posterior distribution to be concentrated far away from the truth, especially if there are not enough observed data to dominate the prior. In such situations, the parametric empirical Bayesian approach that we propose may be desirable. there are not enough observed data to dominate the prior. In such situations, the parametric empirical Bayesian approach that we propose may be desirable.

Subsequent sections in this paper were organized as follows. In section 2, we derive a parametric Empirical Bayes (EB) estimator using a beta-type prior and squared-error loss function. In section 3, we compare the MLE and EB point estimators in terms of bias and efficiency, and illustrate it using data from HCV study conducted in China. In section 4, we conclude with a brief summary discussion.

2. ESTIMATION

2.1. The Maximum Likelihood Estimate

In group screening, the responses are assumed to be independent and identically distributed Bernoulli (p) random variables which can be combined into groups of size k > 1. The experimental design calls for units to be randomly assigned to one of g groups with no testing errors. Hence, the number of defective groups observed say, r, has a binomial distribution with parameters g and $1-(1-p)^k$. Under the group screening model, the MLE of p has been shown by Muhua et al. (2010) to be $\hat{p}_{mle} = 1-\left(1-\frac{r}{g}\right)^{\frac{1}{k}}$. Although $\hat{p}_{mle}$ is strongly consistent for large g and $k>1$, it is positively biased for $g<\infty$.

2.2 Empirical Bayes Estimate

Since the probability of a factor being defective is small, we used a family of prior distribution appropriate for rare traits. The beta (α, β) distribution is regarded as a family since for large values of β, the probability distribution of the random variable p is close to zero.

If r is the number of defective groups out of g groups formed, then:

$$f(r\mid p)=\begin{cases}\binom{g}{r}\left[1-(1-p)^k\right]^r(1-p)^{k(g-r)} & r=0,1,\ldots,g\\ 0 & otherwise\end{cases} \qquad [1]$$

Thus, the joint distribution of r and p is given by:

$$f(r,p)=\binom{g}{r}\{B(\alpha,\beta)\}^{-1}p^{\alpha-1}(1-p)^{kg-kr+\beta-1}\left[1-(1-p)^k\right]^r \qquad [2]$$

where;

$$B(\alpha,\beta)=\frac{\Gamma(\alpha)\Gamma(\beta)}{\Gamma(\alpha+\beta)} \qquad [3]$$

The marginal probability density function of r is given by:

$$\begin{aligned} f(r) &= \int_0^1\binom{g}{r}\{B(\alpha,\beta)\}^{-1}\rho^{\alpha-1}(1-\rho)^{kg-kr+\beta-1}[1-(1-\rho)^k]^r\,dp \\ &= \left(\frac{\beta}{\alpha+\beta}\right)^{k(g-r)}\binom{g}{r}\sum_{j=0}^{r}\binom{r}{j}(-1)^j\left(\frac{\beta}{\alpha+\beta}\right)^{kj} \end{aligned} \qquad [4]$$

using the approximation

$$\frac{\Gamma(N+a)}{\Gamma(N+b)}\simeq N^{a-b} \quad \text{for large } N \qquad [5]$$

given by Abramonitz and Stegun (1960).

For the estimates $\hat{\alpha}$ and $\hat{\beta}$ for the hyper parameters α and β, the posterior distribution of p is given by:

$$f(p \mid r) = f(r,p) \Big/ f(r) = \frac{p^{\hat{\alpha}-1}(1-p)^{kg-kr+\hat{\beta}-1}[1-(1-p)^k]^r}{\sum_{j=0}^{r}\binom{r}{j}(-1)^j B(\hat{\alpha}, kj+kg-kr+\beta)} \quad [6]$$

Therefore, this leads to the Bayes estimator of p based on squared error loss which is given as:

$$\hat{p} = \sum_{j=0}^{r}\binom{r}{j}(-1)^j \frac{\hat{\alpha}\hat{\beta}^{k(j+g-r)}}{(\hat{\alpha}+\hat{\beta})^{k(j+g-r)+1}} \quad [7]$$

2.3 Special case: A priori on p with $\alpha = 1$

Here, the probability distribution of p is given by:

$$f(p) = \beta(1-p)^{\beta-1} \quad [8]$$

The joint probability distribution function of r and p conditional on β is

$$f(r,p \mid \beta) = \beta\binom{g}{r}[1-(1-p)^k]^r (1-p)^{k(g-r)+\beta-1} \quad [9]$$

for $r = 0,1,...,g$ and $0 < p < 1$. The marginal distribution function of r is therefore:

$$f(r \mid \beta) = \beta\binom{g}{r}\int_0^1 [1-(1-p)^k]^r (1-p)^{k(g-r)+\beta-1} dp \quad [10]$$

Using the change of variables technique, the equation becomes:

$$f(r \mid \beta) = \frac{\beta\Gamma(g+1)\Gamma\left(g-r+\frac{\beta}{k}\right)}{k\Gamma(g-r+1)\Gamma\left(g+\frac{\beta}{k}\right)} \cong \frac{\beta(g+1)^r}{k\left(g+\frac{\beta}{k}\right)^{r+1}} \quad [11]$$

for $r = 0,1,...,g$. Differentiating with respect to β and equating to zero gives:

$$\hat{\beta} = \frac{gk}{r} \quad [12]$$

The posterior distribution is therefore given by:

$$f(p \mid r) = \frac{k\Gamma\left(g+\frac{g}{k}+1\right)}{\Gamma\left(g-r+\frac{g}{k}\right)\Gamma(r+1)}(1-p)^{k(g-r)+\frac{gk}{r}-1}[1-(1-p)^k]^r \quad [13]$$

for $0 < p < 1$.

Using squared error loss function $L(p,a) = (p-a)^2$, the Bayes estimate of p is the mean of the posterior $f(p \mid r)$ given as:

$$\hat{p}_{eb} = 1 - \left(\frac{g-r}{g+1}\right)^{\frac{1}{k}} \quad [14]$$

2.4. Prior on p^*

Here, we consider an alternative approach to determining the Bayes estimate based on the relationship between p and p^*. This is the probability that a group-factor is declared defective. Therefore, we call the resulting estimate the *Indirect Bayes Estimate*, $\hat{p}_{Ibys}$

The probability of r conditioned on p^* is given by:

$$f(r \mid p) = \begin{cases} \binom{g}{r} p^{*r}(1-p^*)^{g-r} & r = 0,1,...,g \\ 0 & otherwise \end{cases} \qquad [15]$$

The prior probability of p^* is given by:

$$f(p^*) = \{B(\alpha,\beta)\}^{-1} p^{*\alpha-1}\left(1-p^*\right)^{\beta-1}$$

Thus, the joint distribution of r and p^* is given by:

$$f\left(r, p^*\right) = \{B(\alpha,\beta)\}^{-1}\binom{g}{r} p^{*r+\alpha-1}\left(1-p^*\right)^{g-r+\beta-1r} \qquad [16]$$

where;

$$B(\alpha,\beta) = \frac{T(\alpha)T(\beta)}{T(\alpha+\beta)}$$

The marginal probability density function of r is therefore:

$$f(r) = \int_0^1 \{B(\alpha,\beta)\}^{-1}\binom{g}{r} p^{*r+\alpha-1}\left(1-p^*\right)^{g-r+\beta-1} dp^*$$

$$\simeq \binom{g}{r}\left(\frac{\alpha}{\beta}\right)^r \left(\frac{\beta}{\alpha+\beta}\right)^g \qquad [17]$$

The posterior distribution of p^* can be shown to be:

$$f(p^* / r) = \frac{p^{*\alpha+r-1}(1-p^*)^{g-r+\beta-1}}{B(r+\alpha, g-r+\beta)} \qquad [18]$$

The posterior mean based on squared error loss is given by:

$$\hat{p}^* = \frac{r+\alpha}{g+\alpha+\beta} \qquad [19]$$

Therefore, this yields the posterior of p through the transformation $p^* = 1-(1-p)^k$; and we compute the Bayes estimator under the squared error loss as:

$$\hat{p}_{Ibys} = 1-\left(1-\frac{r+\alpha}{g+\alpha+\beta}\right)^{\frac{1}{k}} \qquad [20]$$

3. COMPARISON OF ESTIMATORS

3.1 Point Estimate characteristics

In this section, we compare the Maximum Likelihood Estimate and the Bayesian Estimate through the measures of bias and mean squared error. In a Bayesian framework, the choice of the loss function determines the specific form of the estimator. However, since we are comparing the two estimators on frequentist terms, after the specific form of the estimator is identified, the loss function is no longer used. For p fixed, the bias and mean squared error of $\hat{p}_{bys}$ respectively are given by:

$$\text{Bias}(\hat{p}_{bys}) = \text{E}\left[\hat{p}_{bys} - p\right]$$

$$= \sum_{r=0}^{g}\left(\hat{p}_{bys} - p\right)\binom{g}{r}\left[1-(1-p)^{k}\right]^{r}(1-p)^{k(g-r)}$$

$$\text{MSE}\left(\hat{p}_{bys}\right) = \text{E}\left[\left(\hat{p}_{bys} - p\right)^{2}\right]$$

and

$$= \sum_{i=0}^{g}\left[\left(\hat{p}_{bys} - p\right)^{2}\right]\binom{g}{r}\left[1-(1-p)^{k}\right]^{r}(1-p)^{k(g-r)} \qquad [21]$$

In particular, for indirect Bayes estimator $\hat{p}_{Ibys}$, the Bias is given by:

$$\text{Bias}(\hat{p}_{Ibys}) = \text{E}\left[\hat{p}_{Ibys} - p\right]$$

And the mean squared error is given by:

$$\text{MSE}\left(\hat{p}_{Ibys}\right) = \text{E}\left[\left(\hat{p}_{Ibys} - p\right)^{2}\right]$$

where: $$\hat{p}_{Ibys} = 1-\left(1-\frac{r+\alpha}{g+\alpha+\beta}\right)^{\frac{1}{k}}$$

For comparing the Bayes estimator corresponding to a Beta (α,β) prior on p, the prior on p^{*} is chosen to be Beta (α^{*},β^{*}), where α^{*} and β^{*} are given as:

$$\alpha^{*} = \frac{(1-A)(B-A)}{A^{2}-B}$$

and

$$\beta^{*} = \frac{A(B-A)}{A^{2}-B} \qquad [22]$$

where A and B are the first two moments given as:

$$A = \frac{\Gamma(\alpha+\beta)\Gamma(\beta+k)}{\Gamma\beta\Gamma(\alpha+\beta+k)}$$

and

$$B = \frac{\Gamma(\alpha+\beta)\Gamma(\beta+k)}{\Gamma\beta\Gamma(\alpha+\beta+2k)}$$

For the special case where $\alpha=1$, $\alpha^{*}=1$ and $\beta^{*}=\frac{\beta}{k}$

Example 1

Liu et al. (1997) reported results on 1875 blood donors screened for anti HCV at the Blood Transfusion Service in China. The 1875 serum samples were tested individually (k = 1) to examine the effectiveness of pooling. With a group size of k =5 and g = 375, they got r = 37. Using equation (12),

$$\hat{\beta}=\frac{1875}{37}=50.66$$

The posterior mean is given by:

$$\hat{p}=1-\left(1-\frac{375-37}{376}\right)^{\frac{1}{5}}$$

$$= 1 - 0.97891$$

$$= 0.021083$$

Thus, it compares favorably with $\hat{\beta}=48.1$ and **is** given by Tebbs and Bilder (2003). For the indirect Bayes estimate, equation (20) is given as:

$$\hat{p}_{Ibys}=1-\left(1-\frac{37+1}{375+1+\frac{50.66}{5}}\right)^{\frac{1}{5}}$$

$$= 1 - 0.979494$$

$$= 0.020506$$

In addition, comparison can also be made in terms of relative bias and relative efficiency which are

respectively defined as:

$$RB=\frac{Bias(\hat{p})}{p}$$

and

$$RE=\frac{MSE(\hat{p}_k)}{MSE(\hat{p})}$$

where $\hat{p}_k$ is the estimate for k > 1. The tables below give a summary of the relative bias and the relative efficiency for various values of p and k for g = 10, based on the maximum likelihood, the direct Bayes, and the indirect Bayes estimators.

Table 1. Relative Bias for selected values of p, k and g = 10.

g=10 p	K	$\hat{p}_{mle}$	(α, β)	$\hat{p}_{bys}$	(α^*,β^*)	$\hat{p}_{Ibys}$
0.25			(1,3)			
	1	0.00000		0.00000	(1,3.00)	0.00000
	5	0.21661		0.09552	(1,0.60)	0.01252
	10	1.57583		0.29291	(1,0.30)	0.00192
	15	2.56691		0.37393	(1,0.20)	-0.10853
	20	2.88854		0.35010	(1,0.15)	-0.23565
0.10			(1,9)			
	1	0.00000		0.00000	(1,9.00)	0.00000
	5	0.05731		0.03843	(1,1.80)	0.00311

	10	0.19010		0.08031	(1,0.90)	0.00494
	15	0.90474		0.14572	(1,0.60)	0.01453
	20	2.39111		0.23484	(1,0.45)	0.01712
0.05			(1,19)			
	1	0.00000		0.00000	(1,19.0)	0.00000
	5	0.04851		0.02363	(1,3.80)	-0.00740
	10	0.06713		0.04351	(1,1.90)	-0.00431
	15	0.11444		0.06241	(1,1.27)	-0.00053
	20	0.29962		0.08494	(1,0.95)	-0.00039
0.01			(1,99)			
	1	0.00000		0.00000	(1,99.0)	0.00000
	5	0.04360		0.00452	(1,19.8)	-0.00870
	10	0.05082		0.01180	(1,9.90)	-0.01101
	15	0.05451		0.01821	(1,6.60)	-0.01103
	20	0.05734		0.02374	(1,4.95)	-0.01033

Table 2. Relative Efficiency for selected values of p, k and g = 10.

g=10 p	k	$\hat{p}_{mle}$	(α, β)	$\hat{p}_{bys}$	(α^*, β^*)	$\hat{p}_{I\,bys}$
0.25			(1,3)			
	1	1.00000		1.96000	(1,3.00)	1.96000
	5	1.03260		4.69672	(1,0.60)	7.04301
	10	0.99481		19.03341	(1,0.30)	80.62304
	15	0.99862		35.90983	(1,0.20)	269.94501
	20	0.99971		59.85294	(1,0.15)	147.47321
0.1			(1,9)			
	1	1.00000		4.00000	(1,9.00)	4.00000
	5	1.17922		1.70664	(1,1.80)	1.91413
	10	1.04641		7.82342	(1,0.90)	10.69631
	15	1.00283		35.66633	(1,0.60)	69.54100
	20	0.99924		71.11520	(1,0.45)	210.27562
0.05			(1,19)			
	1	1.00000		9.00000	(1,19.0)	9.00000
	5	1.12490		2.19461	(1,3.80)	2.35772
	10	1.19852		1.89812	(1,1.90)	2.17101
	15	1.07565		5.68040	(1,1.27)	7.04622
	20	1.01584		24.86763	(1,0.95)	34.74474
0.01			(1,99)			
	1	1.00000		121.00000	(1,99.0)	121.00000
	5	1.09484		9.85463	(1,19.8)	10.12575
	10	1.11742		4.47010	(1,9.90)	4.69181
	15	1.13311		3.14221	(1,6.60)	3.35011
	20	1.14780		2.57100	(1,4.95)	2.77764

From the tables, we noted that the biases and the MSE's of the Bayes estimators are smaller than that of MLE especially for low prevalence rate. The indirect Bayes estimator in general performs very well for small k and large g in the sense of having even smaller bias and MSE. This mainly occurs when the experimenter is forced to use smaller group sizes perhaps due to biological considerations involved in test assays.

3.2. Asymptotic Distribution and Interval Estimation

In practice, the population size and the number of groups are fairly large. However, this was such that large sample estimates can be used for inference purposes. The asymptotic distributions of the MLE and that of the Bayesian estimator follow from the general result which obeys the Mann-Wald theorem, given in Rao (1973). For the function h, if

$$h(p')=1-\left(1-\frac{p'+b}{1+c}\right)^{a} \qquad [23]$$

then

$$\sqrt{m}\,\frac{h(\hat{p}')-h(p')}{p'(1-p')}\sim N\left(0,\left[\frac{a}{1+c}\left(1-\frac{p'+b}{1+c}\right)^{a-1}\right]^{2}\right) \qquad [24]$$

For the Bayes estimator, $h(p')=\hat{p}$, with $b=\frac{\alpha}{g}, c=\frac{\alpha+\beta}{g}$ and $a=\frac{1}{k}$. Thus,

$$\text{var}(\hat{p})=\left\{\frac{g}{k(g+\alpha+\beta)}\left[1-\frac{gp^{*}+\alpha}{g+\alpha+\beta}\right]^{\frac{1}{k}-1}\right\}^{2}\frac{p^{*}(1-p^{*})}{g} \qquad [25]$$

From the example 1 above, $p=0.0224 \text{ and } \hat{p}=0.021083$, giving that

$$\text{var}(\hat{p})=\left\{\frac{0.2}{1.13101}\left[1-\frac{0.0224+0.00267}{1.13101}\right]^{-0.8}\right\}^{2}\frac{0.0224(0.9776)}{375}$$

$$=1.89270\times10^{-6}$$

The standard error of $\hat{p}$ is therefore 0.0026965 resulting in a 95% confidence interval of 0.0183865 and 0.023779. For the maximum likelihood estimator, the confidence interval is given by:

$$\hat{p}_{mle}\pm z_{1-\frac{\alpha}{2}}\sqrt{\frac{\text{var}(\hat{p}_{mle})}{g}}$$

Where $\text{var}(\hat{p}_{mle})$ is the asymptotic variance given by $\text{var}(\hat{p}_{mle})=k^{-2}[1-(1-p)^{k}](1-p)^{2-k}$ and $z_{1-\frac{\alpha}{2}}$ denotes $1-\frac{\alpha}{2}$ quantile of the standard normal distribution. Thus, from the above example 1, we get:

$$\text{var}(\hat{p}_{mle})=5^{-2}[1-(1-0.020557)^{5}](1-0.020557)^{2-5}$$

$$=0.004199$$

The standard error is 0.0033466 giving a 95% confidence of 0.01905 and 0.02575. Thus, the indirect Bayes estimator is more precise than the MLE since for the same level of confidence, it gives a narrower interval.

4. CONCLUSION

Group testing is in general economical in the light of reduced average number of units to be tested or samples to be screened since a group is declared defective as soon as an item is found to be defective. Based on a given total cost per unit to be tested, a group size k may be determined in advance and fixed. Next, based on prior knowledge of the population proportion, the group size may be compared to the optimal value of the MLE or that for the Bayes estimator. The direct Bayes method offers a good alternative to the experimenter, as he may have some general ideas about the population proportion which can be used to obtain the value of the optimum k, which can be updated in subsequent testing and estimation. Once k is known, a prior on p may be transformed into a prior on $\hat{p}^*$; and then, the alternative Bayes estimator or the indirect Bayes estimator may be used. This estimator is simple to calculate and hence may be attractive to users. Choice of k may be determined by physical considerations or from the optimal k for the MLE. For practical purposes, a fixed k is desirable unless variability of the prior is very high.

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