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Estimating the Rate of Defectiveness by Group-Testing in the Presence of Test Errors

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Abstract

Group-testing is a more cost-effective method than individual testing. When estimating the rate of defectiveness in a large population, the group-testing estimator is more efficient than individual-testing estimator. This study constructs maximum likelihood estimators for both group-testing and individual-testing in the presence of test errors and compares their efficiencies for various characteristics.

Keywords and Phrases: Defectiveness; Group; Group-Testing; Individual-Testing; Likelihood; Test Errors.

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1 Introduction

Group-testing refers to the simultaneous testing of more than one sample by one test. Group-testing can provide substantial economies as compared to individual-testing(Dorfman, 1943). Group-testing can be done in two stages starting with the testing of groups followed by the testing of all individuals in groups that test positive. Greater efficiency can be obtained by multistage testing schemes (cf. Nyongesa, 2004; Johnson *et.al.,* 1991, and Brookmeyer, 1999). Apart from greater savings achieved by the Dorfmans' procedure, the procedure is also applicable where the identity of the subject needs to be concealed (Gastwirth and Hammick, 1989), where the identification of the subject will lead to either denial of work permit or insurance as is the case with HIV/AIDS.

Group-testing has two objectives. The first is to test the pools followed by individuals in group that test positive with the aim of identifying the infected individuals. This objective is the most vigorously studied subject in this field since Dorfman (1943). The second objective is to estimate the rate of defectiveness in a population as championed by Thompson (1962). Thompson's work has been extended and generalized by Sobel and Elashoff (1975), Brookmeyer (1999) and Hughes-Oliver and Swallow (1994). Xie *et.al.*, (2001) introduced the idea of blockers in the procedure. This paper will focus on the second objective.

An important issue is that the sensitivity and specificity of assay with grouped samples could depend on the group size. If the group sizes are large, the assays may not be sensitive because of the dilution effect (Hwang, 1976). In order to investigate dilution effect, one might consider the re-testing of pools classified as positive and negative (Nyongesa, 2004). A negative pool that tests positive on re-testing would indicate test errors. It has also been shown that re-testing of pools reduces the misclassification errors (cf. Nyongesa, 2004). Indeed, some lost sensitivity of the procedure is recovered by re-testing pools classified as negative in the initial stage if the tests are imperfect. It is on this background that this paper is developed. This paper proposes a testing scheme with test errors. This is the reality as test kits on the market can not be claimed to be a hundred percent perfect. The proposed estimator is then compared with the individual-testing estimator, and as it will be seen the group-testing estimator is more efficient than individual testing.

The rest of the paper is organized as follows. Section 2, discusses the likelihood estimator in the individual-testing scheme and deriving the asymptotic variance. Section 3 introduces the group-testing procedure and the estimator obtained. The conclusion of the study is presented in Section 4.

2 The Individual Testing Estimator

Suppose we have a finite population of size N and we wish to test this population with the objective of classifying the constituent elements as either defective or non-defective. This is known as the classification problem (Dorfman, 1943). This problem will not be discussed in this study but for further discussion on this subject see Johnson et al (1991). Our objective in this section is to estimate the rate of defectiveness that characterizes the population under investigation by testing each and every element in the population individually.

Firstly, the probability of classifying an item as positive when errors are allowed in the testing procedure is given by

$$\pi(p|\eta, \phi) = \eta p + (1 - \phi)(1 - p), \tag{1}$$

where η is the sensitivity of the test kits in use, by sensitivity we mean the probability of correctly classifying a defective item while ϕ is the specificity of the test kit. Here, specificity means the probability of correctly classifying a negative individual. In practice η and ϕ are close to 100%. The rate p is the prevalence of defectiveness, and is the parameter of interest.

We can characterize population N as consisting of either defective or non-defective items. Therefore, let

$$X_i = \begin{cases} 1 \; if\ the\ i^{th}\ item\ tests\ positive\ on\ the\ test \\ 0 \; otherwise \end{cases}$$

for i=1,2,...,N. This implies that $pr(X_i = 1) = \pi(.)$ and $pr(X_i = 0) = 1 - \pi(.)$. Here, we shall assume that η and ϕ are known. But if they are unknown they can be estimated from the experiment (cf. Nyongesa, 2010). Suppose now that N independent tests are to be performed each of which results in a positive with probability $\pi(.)$ and a negative with probability $1 - \pi(.)$. The likelihood function for this model under construction is

$$L(p|\eta, \phi, N, X) \propto \prod_{i=1}^{N} \pi^{x_i}(.)(1 - \pi(.))^{1-x_i}. \tag{2}$$

Upon utilizing (2), the MLE of the rate of defectiveness in the population under investigation is given by

$$\hat{p} = 1 - \left(\frac{\eta - X/N)}{\eta + \phi - 1} \right) \tag{3}$$

where $X = \sum_{i=1}^{N} x_i$, the number of individuals that test positive in the population. The asymptotic variance of the estimator (3) can be computed from

$$\left\{ -E \left[\frac{d^2}{dp^2} log\ L(.) \right] \right\}^{-1}$$

and can be easily shown to be

$$Var(\hat{p}) = \frac{\pi(.)(1 - \pi(.))}{N(\eta + \phi - 1)^2}. \tag{4}$$

Therefore, the confidence interval for the estimator (3) is

$$\hat{p} \pm Z_{\alpha/2} \sqrt{\frac{\pi(.)(1 - \pi(.))}{N(\eta + \phi - 1)^2}}. \tag{5}$$

One can easily see that for large sample behavior of $\hat{p}$, we have

$$\sqrt{N}(\hat{p} - p) \overset{d}{\rightarrow} N(0, \frac{\pi(.)(1 - \pi(.))}{(\eta + \phi - 1)^2}). \tag{6}$$

In the next section we discuss the estimation of the rate of defectiveness in the presence of errors when group-testing procedure is employed instead of individual testing algorithm.

3 The Group-Testing Estimators

The proportion p, $0 < p < 1$, of individuals in an infinite population who possess a certain trait of defectiveness is to be estimated under the assumptions that the probability of having the trait of defectiveness is the same for all members of the population; and the tests used in this situation are imperfect-i.e., not a hundred percent accurate as it is the case in practice. The first assumption rules out situations where clustering of the trait is possible such as in the case of an infectious defectiveness. The second assumption allows the possibility of incorrectly labeling an individual or a group; that is, there are false negatives and false positives. Now, in this testing procedure, the population N is pooled into n groups of equal sizes, k, such that $N = nk$. Each of the n groups is then tested as if it was individual testing as discussed above.

3.1 The Estimator for Rate of Defectiveness

The usual Dorfman group-testing estimation scheme with imperfect tests of n groups, each of size k, is applied (cf. Thompson (1962)). This estimation scheme labels each of the groups according to whether one or more samples in the group possess the trait of defectiveness. If a group is labeled as possessing the trait of defectiveness, then it can be interpreted that at least one member of the group has the trait of defectiveness.

Under these assumptions the number of groups, say X_1, testing positive for defectiveness has a binomial distribution with parameters n and $\pi(p|\eta, \phi, k)$, the probability of classifying a group as positive. This is equivalent to Equation (1) in the case of group-testing is

$$\pi(p|\eta, \phi, k) = \eta(1 - (1 - p)^k) + (1 - \phi)(1 - p)^k. \tag{7}$$

Note that if $p \in [0, 1]$, then

$$1 - \phi < \pi(.) < \eta.$$

We have already pointed out that $X_1 \sim binomial(n, \pi(p|\eta, \phi, k))$. Thus, the likelihood function is

$$L(p \mid \eta, \phi, k) \propto \pi(p \mid \eta, \phi, k)^{x_1}(1 - \pi(p \mid \eta, \phi, k))^{n-x_1}. \tag{8}$$

Using maximum likelihood estimation method, the estimator of p is

$$\hat{p} = 1 - \left\{\frac{\eta - \frac{x_1}{n}}{\phi + \eta - 1}\right\}^{\frac{1}{k}} \tag{9}$$

if the test were perfect i.e., $\phi = \eta = 1$, then (8) yields

$$\hat{p} = 1 - \left(1 - \frac{x_1}{n}\right)^{\frac{1}{k}}. \tag{10}$$

Clearly, (10) provides a result that is similar to Thompson (1962) among others. For Bayesian estimation see Bilder and Tebbs (2004). Therefore, the estimation model under discussion generalizes the previous results. Notice that Dorfman (1943) studied the classification problem of group-testing. It is Thompson (1962) who introduced estimation problem in group-testing literature and the present study extends the problem to presence of test errors. Setting $k = 1$ in (10), $E(\hat{p}) = p$, implying that $E(\hat{p})$ is unbiased estimator of p. For $k > 1$, $E(\hat{p}) > p$. That is, the proposed estimator over estimates p. This assertion can be shown by the help of Jensen's inequality (Billingsley, 1995: p. 276).

Now, with $L(.) \propto \pi(p|\eta,\phi,k)^{x_1}(1-\pi(p \mid \eta,\phi,k))^{n-x_1}$, the log likelihood function is

$$logL(.) \propto \; x_1 log\pi(p \mid \eta,\phi,k) + (n-x_1)log(1-\pi(p|\eta,\phi,k)) \tag{11}$$

From (11), we compute for

$$\left[-E\left(\frac{\partial^2}{\partial p^2}\log L(.)\right)\right]^{-1}$$

to obtain the asymptotic variance of our group-testing estimator as

$$var(\hat{p}) = \frac{(1-p)^2\pi(p|\eta,\phi,k)(1-\pi(p|\eta,\phi,k))(1-p)^{-2k}}{nk^2(\phi+\eta-1)^2}. \tag{12}$$

Therefore, asymptotically, $\hat{p}$ is normally distributed and is an efficient estimator of the rate of defectiveness in a population. That is, for fixed k and $n \to \infty$, we have

$$\sqrt{n}(\hat{p}-p) \overset{d}{\longrightarrow} normal\Big(0, \frac{(1-p)^2\pi(p|\eta,\phi,k)(1-\pi(p|\eta,\phi,k))(1-p)^{-2k}}{k^2(\phi+\eta-1)^2}\Big). \tag{13}$$

Notice that if the group size is one (i.e. $k = 1$), then individual samples are being tested and (12) reduces to (4) as noted earlier. Equations (4) and (12) can be used to compute the efficiency of this procedure. The confidence interval (CI) for p is given by

$$\hat{p} \pm Z_{\alpha/2}\sqrt{\frac{(1-p)^2\pi(p|\eta,\phi,k)(1-\pi(p|\eta,\phi,k))(1-p)^{-2k}]}{nk^2(\phi+\eta-1)^2}}$$

where Z is distributed as a standard normal distribution.

4 Discussion and Conclusion

We have constructed estimators for both individual testing and group-testing in the presence of test errors as it is the case in practice. We acknowledge that until now this has not been discussed in the group-testing literature with the objective of estimation.

For comparison purposes between individual-testing and group-testing in the presence of test errors, we compute asymptotic relative efficiency (ARE) given by

$$ARE = \frac{k(1-p)^{2k-2}\pi(p|\eta,\phi)(1-\pi(p|\eta,\phi))}{\pi(p|\eta,\phi,k)(1-\pi(p|\eta,\phi,k))}. \tag{14}$$

Utilizing Equation (14), we computed the AREs for various values of p,η,ϕ, and k using MATLAB software, the MATLAB code 'ken' is presented in the Appendix. The computed results are given in Table 1, to help our discussion.

Table 1: AREs for various prevalence rates, group sizes, sensitivity and specificity for imperfect model.

$\eta = \phi = 95\%$

k / p	5	10	15	20	25	30
0.001	0.22	0.12	0.08	0.07	0.06	0.05
0.01	0.33	0.25	0.23	0.22	0.22	0.22
0.10	0.94	1.28	1.90	3.05	5.30	10.03
0.15	1.20	2.17	4.69	12.39	39.66	147.13
0.20	1.52	3.92	14.60	77.12	511.95	3812.40

$\eta = \phi = 99\%$

k / p	5	10	15	20	25	30
0.001	0.27	0.18	0.15	0.14	0.13	0.12
0.01	0.61	0.57	0.57	0.57	0.58	0.60
0.10	1.17	1.58	2.21	3.20	4.82	7.62
0.15	1.37	2.28	4.12	8.30	19.29	53.67
0.20	1.61	3.46	8.96	30.68	148.20	943.63

It is evident from the tabulated results that group-testing is more efficient than individual-testing when the rate of defectiveness is reasonably high. For example, if the rate of defectiveness is 15% and a group-size of 20 is used in screening ($\eta = \phi = 99$). The group-testing estimator is about 8 times more efficient than individual-testing in the presence of test errors. Therefore, even in the presence of test errors, group-testing is more efficient than individual-testing as alluded to by Dorfman (1943) in the case of perfect tests. When the rate of defectiveness is negligible say 0.1%, it can be seen from the simulated results that group-testing is not ideal as compared to individual-testing. A small or negligible rate of defectiveness can be shielded from being detected and this compounded with dilution effect in grouped samples (cf. Hwang, 1976) makes the detection of the defective items difficult. The remedy to this problem in group-testing can be handled by carrying out a re-test see for example Nyongesa (2010). Misclassifications are greatly reduced by re-testing (cf. Nyongesa, 2004), hence more efficient estimator. Also, it can be easily seen from the tabulated results that group-testing estimators' efficiency increases with increase in sensitivity and specificity of the test kits for relatively smaller groups. However, for relatively bigger groups, relative efficiency decreases with increase sensitivity and specificity of the test kits. Thus, this makes the group-testing methodology viable in situations where errors are part of the testing procedure. When the sensitivity and specificity of the test kits are 100% as the case of Thompson (1962), the AREs table is given below.

Table 2: AREs for various prevalence rates and group sizes for perfect model.

$\eta = \phi = 100\%$

k / p	5	10	15	20	25	30
0.001	1.00	1.00	1.01	1.01	1.01	1.01
0.01	1.02	1.05	1.07	1.10	1.13	1.16
0.10	1.25	1.68	2.31	3.25	4.65	6.78
0.15	1.42	2.31	3.95	7.03	12.95	24.56
0.20	1.64	3.33	7.31	17.15	42.19	107.52

Clearly, from Table 2, even in a perfect situation group-testing is more efficient than individual testing. Comparing Table 1 and 2, we observe that in relatively high prevalence population, more efficient results are realized in imperfect situation than in perfect situation when group-testing is used.

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A Appendix

This MATLAB code generates the values in Tables 1 and 2 when the inputs p,k, η and ϕ are fed in the function 'ken'.
function ken(p,k,eta,phi)
A=p*eta+(1-phi)*(1-p);
B=$eta * (1 - (1 - p)^k) + (1 - phi) * (1 - p)^k$;
C=$k * (1 - p)^(2 * k - 2) * A * (1 - A)/(B * (1 - B))$;
ARE=1/C