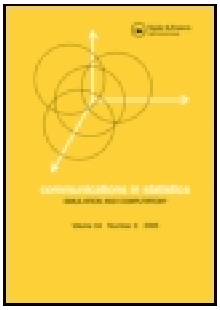

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A comparison of two approaches for power and sample size calculations in logistic regression models

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A COMPARISON OF TWO APPROACHES FOR POWER AND SAMPLE SIZE CALCULATIONS IN LOGISTIC REGRESSION MODELS

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Key words and phrases: Likelihood ratio test; Logistic regression; Maximum likelihood estimate; Power; Sample size.

ABSTRACT

Whittemore (1981) proposed an approach for calculating the sample size needed to test hypotheses with specified significance and power against a given alternative for logistic regression with small response probability. Based on the distribution of covariate, which could be either discrete or continuous, this approach first provides a simple closed-form approximation to the asymptotic covariance matrix of the maximum likelihood estimates, and then uses it to calculate the sample size needed to test a hypothesis about the parameter. Self et al. (1992) described a general approach for power and sample size calculations within the framework of generalized linear models, which include logistic regression as a special case. Their approach is based on an approximation to the distribution of the likelihood ratio statistic. Unlike the Whittemore approach, their approach is not limited to situations of small response probability. However, it is restricted to models with a finite number of covariate configurations. This study compares these two approaches to see how accurate they would be for the calculations of power and sample size in logistic regression models with various response probabilities and covariate distributions. The results indicate that the Whittemore approach has a slight advantage in achieving the nominal power only for one case with small response probability. It is outperformed for all other cases with larger response probabilities. In general, the approach proposed in Self et al.

(1992) is recommended for all values of the response probability. However, its extension for logistic regression models with an infinite number of covariate configurations involves an arbitrary decision for categorization and leads to a discrete approximation. As shown in this paper, the examined discrete approximations appear to be sufficiently accurate for practical purpose.

1. INTRODUCTION

Logistic regression models are frequently used in the analysis of epidemiologic data concerning the relationship between potential risk factors and a disease. In such studies the involvement and cost of living subjects require extra attention, and accurate procedures are needed for determining the sample size to achieve a prescribed power and medical standard.

Whittemore (1981) proposed an approach for determining the sample size needed to test hypotheses with specified significance and power against given alternative for logistic regression with a small response probability. This approach is developed for selected distributions of a single covariate and for a class of exponential type distributions of several covariates. Based on the distribution of the covariates, the Fisher information matrix for the estimated parameters can be approximated by the augmented Hessian matrix of the moment generating function for the covariates. With this matrix one can obtain a simple closed-form estimate of the asymptotic covariance matrix of the maximum likelihood estimates (MLE), and then an approximate sample size needed to test both directional and non-directional hypotheses about a single parameter by treating the MLE as normally distributed. Furthermore, correction factors were provided to enhance the accuracy of sample size calculations. In general, the response probabilities must be less than 4 percent for the sample size approximations to be accurate within 10 percent. By following the Whittemore approach, Hsieh (1989) provided sample size tables for logistic regression for a test of one normally distributed covariate, possibly in the presence of other normally distributed covariates with specified multiple correlation with the covariate of interest. Also, Monte Carlo simulations were performed and they indicated that, when there is only one covariate in the model, the given sample sizes are reasonably accurate for both normal and exponential distributions of the covariate, although they can be inaccurate for some distributions, such as double exponential.

In the framework of generalized linear models, Self et al. (1992) proposed a noncentral chi-square approximation to the distribution of the likelihood ratio test statistic (SMO) and utilized it for the purpose of sample size and power calculations. Their simulation studies, including results for logistic regression models, showed that the approach is accurate over a much wider range of parameter values and data configurations than the method proposed in Self and Mauritsen (1988). As the logistic regression model is a special case of generalized linear models, the SMO approach is directly applicable and becomes an alternative to the Whittemore approach for the logistic regression model. Furthermore, this approach is not only useful for other generalized linear models, but is also more general than the Whittemore approach in terms of no restriction on the response probability and no limitation on the number of parameters being tested simultaneously in the hypothesis. In other words, the SMO approach becomes the natural choice as compared to the Whittemore approach when the response probabilities are not small, or when more than one parameter need to be tested simultaneously. However, some restrictions apply, for example, it is developed solely for models with a finite number of covariate configurations. See Table 1 for a summary of the differences and similarities in the two approaches. From an examination of Table 1, two questions arise that motivate this study. First, is the Whittemore approach really better for logistic regression with small response probability, and if it is, how much better is it than the SMO approach? Second, can the SMO approach be modified in order to extend its use to models with continuous covariates, and how accurate is it? The study of the first question will determine whether there is any advantage to the Whittemore approach for its aim of small response probability. Furthermore, if the advantage is substantial, then it is worth our attention to consult the response probability before we apply the Whittemore approach instead of others, since it will give more accurate results. On the other hand, if the advantage is very limited or does not exist, one may then simply apply the SMO approach for all logistic regression models regardless of the values of response probability. The second question is raised since it is common for both linear and nonlinear regression models to have continuous covariates or regressors. The usual practice for the chi-square goodness of fit test is to group the original values of covariates into finite intervals, as we do here. It results in an approximation of the true covariate distribution so that the SMO approach can be applied. It is obvious that the investigation of this question is not a matter of proposing a new way of extending the use of the SMO approach for accommodating continuous type of covariates. More importantly, the key is to

Table 1. Comparison of two approaches for power and sample size calculations.

	Whittemore (1981)	Self et al. (1992)
Model	*Logistic regression model*	*Generalized linear model*
Test statistic (distribution)	Maximum likelihood estimate (normal)	Likelihood ratio test (chi-square)
Allow directional test	Yes	Yes
Allow to test more than one parameter simultaneously	No	Yes
Flexibility in the value of response probability	No - assume small	Yes
Accommodate both finite and infinite number of covariate configurations	Yes	No - assume finite

examine how it will affect the accuracy by using an approximation for covariates with an infinite number of configurations.

Actually these two questions are intertwined, that is, as compared to the Whittemore approach, how accurate the extension of SMO approach is for logistic regression with small response probability and continuous covariates. The purpose of this paper is to compare both approaches through Monte Carlo simulation studies that cover a wide range of response probabilities and several discrete and continuous covariate distributions. In this investigation we not only present more results to have a better understanding of the Whittemore approach, but we also shed light on the extension of the SMO approach to continuous covariates, which will expedite its use in applied settings.

In Section 2, we describe the details of the two approaches for power and sample size calculations and illustrate the sample size calculations with an example concerning risk factor for coronary heart disease. In Section 3, the designs of the simulation studies are provided. The results of the simulations are presented in Section 4, and Section 5 contains a brief discussion of the findings.

2. POWER AND SAMPLE SIZE DETERMINATION

A logistic regression model can be described as follows. Let Y_i denote the binary response for subject i, i = 1, ..., N. Let $x_i = (x_{i1}, ..., x_{iK})^T$ denote the vector of covariates associated with the i^{th} subject. Also, let ψ_0 and $\psi = (\psi_1, ..., \psi_K)^T$ be the K + 1 unknown regression coefficients and let $p_i = \exp(\psi_0 + x_i^T\psi)/\{1 + \exp(\psi_0 + x_i^T\psi)\}$ denote the conditional probability of $Y_i = 1$ given x_i. Assume without loss of generality that among the K unknown parameters associated with the K covariates, respectively, ψ_1 is of primary interest. We wish to test the null hypothesis of H_0: $\psi_1 = 0$ against the alternative hypothesis H_1: $\psi_1 \neq 0$. We shall now describe the two approaches for power and sample size determination.

2.1 Whittemore Approach

Suppose the vector of K covariates X has a joint pdf f(x) which does not depend on the unknown parameters ψ_0 and ψ. It follows that the maximum likelihood estimate $(\hat{\psi}_0, \hat{\psi})$ is asymptotically normally distributed with mean (ψ_0, ψ) and covariance matrix given by the inverse of the Fisher information matrix. Assume the response probability is small, Whittemore (1981) showed the asymptotic variance of the MLE $\hat{\psi}_1$ of ψ_1 is approximately $v(\psi)/\{N \cdot \exp(\psi_0)\}$, where $v(\psi)$ is the second diagonal element of $H^{-1}(\psi)$ with $H(\psi) = \begin{bmatrix} m & m^{(1)T} \\ m^{(1)} & m^{(2)} \end{bmatrix}$, $m = m(\psi) = E\{\exp(\psi^T X)\}$ is the moment-generating function of X, $m^{(1)} = (m_1, \ldots, m_K)^T$, $m_i = \partial m/\partial\psi_i$, $i = 1, \ldots, K$, and $m^{(2)}$ is the $K \times K$ matrix of second partials of m, $m_{ij} = \partial^2 m/\partial\psi_i\partial\psi_j$, $i, j = 1, \ldots, K$. The test statistic is computed as $N \cdot \exp(\hat{\psi}_0)(\hat{\psi}_1 - \psi_1)^2/v(\hat{\psi})$ and is referred to its asymptotic distribution under the null hypothesis, which is a central chi-square distribution on 1 degree of freedom.

To estimate the sample size needed to test the hypothesis defined above with significance level α and power $1 - \beta$, Whittemore (1981) showed the sample size N_{W0} must satisfy

$$N_{W0} \geq \exp(-\psi_0) \left\{\frac{v^{1/2}(\psi^{(0)})Z_{\alpha/2} + v^{1/2}(\psi)Z_{\beta}}{\psi_1}\right\}^2, \qquad (1)$$

where $\psi^{(0)} = (0, \psi_2, \ldots, \psi_K)^T$ and Z_p is the $100(1 - p)^{th}$ percentile of the standard normal distribution.

In order to give more accurate calculation, corrections were presented. For the univariate case, K = 1, more accurate sample size is calculated as

$$N_{W1} = N_{W0}\{1 + 2\exp(\psi_0)\delta(\psi_1)\}, \tag{2}$$

where $\delta(\psi_1) = \{v^{1/2}(0) + v^{1/2}(\psi_1)R(\psi_1)\}/\{v^{1/2}(0) + v^{1/2}(\psi_1)\}$ and $R(\psi_1) = v(\psi_1)\{m_{11}(2\psi_1) - 2m^{-1}(\psi_1)m_1(\psi_1)m_1(2\psi_1) + m^{-2}(\psi_1)m(2\psi_1)m_1^2(\psi_1)\}$. For the multivariate case, $K \geq 2$, the correction is too complicated, and the author proposed a simple version for routine use:

$$N_{W2} = N_{W0}\{1 + 2\exp(\psi_0)\}. \tag{3}$$

2.2 SMO Approach

Self et al. (1992) studied the power calculations for likelihood ratio test in generalized linear models. Since the logistic regression model is a special case of the generalized linear model, their approach is readily applicable here. However, they made the simplifying assumption that all of the covariates in the model are categorical. It implies that there are a finite number of distinct covariate configurations $x_j^* = (x_{j1}^*, ..., x_{jK}^*)^T$, j = 1, ..., C. Let $p(X = x_j^*) = \pi_j$, j = 1, ..., C, denote the distribution of the C distinct covariate configurations for X. Their approach approximates the distribution of the likelihood ratio test statistic by a noncentral chi-square distribution with one degree of freedom. It follows that the sample size needed for given significance level α and power $1 - \beta$ is calculated as follows. First, find the noncentrality γ_N of a noncentral chi-square distribution with one degree of freedom such that its $100\cdot\beta^{th}$ percentile, $\chi^2_{1,\,1-\beta}(\gamma_N)$, is equal to the $100(1-\alpha)^{th}$ percentile of a central chi-square distribution with one degree of freedom, $\chi^2_{1,\alpha}$. Second, the sample size is computed as

$$N_{SMO} = \frac{\gamma_N - \{K - tr(M)\}}{\Delta^*}, \quad (4)$$

where tr(M) is the trace of M,

$$M = \{\sum_{j=1}^{C} \pi_j b''(\theta_j) x_j^{**} x_j^{**T}\}^{-1} \{\sum_{j=1}^{C} \pi_j b''(\theta_j^*) x_j^{**} x_j^{**T}\},$$

$$\Delta^* = 2 \sum_{j=1}^{C} \pi_j [b'(\theta_j)\{\theta_j - \theta_j^*\} - \{b(\theta_j) - b(\theta_j^*)\}],$$

$x_j^{**} = (1, x_{j2}^*, \ldots, x_{jK}^*)^T$, $b(\theta) = \log\{1 + \exp(\theta)\}$, $b'(\theta) = \exp(\theta)/\{1 + \exp(\theta)\}$, $b''(\theta) = \exp(\theta)/\{1 + \exp(\theta)\}^2$, $\theta_j = \psi_0 + x_j^{*T}\psi$, $\theta_j^* = \psi_0^* + x_j^{*T}\psi^*$, and $\psi^* = (0, \psi_2^*, \ldots, \psi_K^*)^T$. The values $(\psi_0^*, \psi_2^*, \ldots, \psi_K^*)$ represent the limiting values of the MLE for $(\psi_0, \psi_2, \ldots, \psi_K)$ under the null hypothesis H_0: $\psi_1 = 0$ as described in Self and Mauritsen (1988). Note that $(\psi_0^*, \psi_2^*, \ldots, \psi_K^*)$ is generally not a consistent estimate of $(\psi_0, \psi_2, \ldots, \psi_K)$.

The likelihood ratio statistic is given by $2\{L_N(\hat{\psi}_0, \hat{\psi}) - L_N(\hat{\psi}_0^*, \hat{\psi}^*)\}$, where L_N denotes the log-likelihood function based on a sample size N, and $(\hat{\psi}_0, \hat{\psi})$ and $(\hat{\psi}_0^*, \hat{\psi}^*)$ denote the maximum likelihood estimators of (ψ_0, ψ) under the alternative and null models, respectively. The actual test is performed by referring the likelihood ratio statistic to its asymptotic distribution under the null hypothesis, which is a central chi-square distribution on 1 degree of freedom.

As pointed out by the authors, the term K – tr(M) is usually very close to zero. Moreover, Shieh and O'Brien (1998) provided further evidence on this and advocated the simplicity and accuracy of using

$$N_{SMO} = \frac{\gamma_N}{\Delta^*}. \tag{5}$$

In this study we found there are no practical differences between (4) and (5) under a greater variety of different settings than Self et al. (1992) and Shieh and O'Brien (1998). Hence only the sample size calculated with (5) will be reported here.

It is useful to examine the general formula described above in an example. For the purpose of illustration, we continue the sample size calculations in Whittemore (1981) for the problem of testing whether the incidence of coronary heart disease among white males aged 39-59 is related to their serum cholesterol level. Following the study of Hulley et al. (1980), the probability of a coronary heart disease event during an 18-month follow-up period for a subject with the mean serum cholesterol level is 0.07. The cholesterol levels in this population are well represented by a standard normal distribution. According to Whittemore's approach, the approximate response probability is 0.07; it results in an intercept parameter $\psi_0 = -2.6593$. It can be shown that $v(\psi) = \exp(-\psi^2/2)$ and $\delta(\psi_1) = \{1 + (1 + \psi_1^2)\exp(5\psi_1^2/4)\}/\{1 + \exp(-\psi_1^2/4)\}$. To detect the odds ratio of $e^{0.1} = 1.1052$ ($\psi_1 = 0.1$) and $e^{0.5} = 1.6487$ ($\psi_1 = 0.5$) for a subject with a cholesterol level of one standard deviation above the mean with $\alpha = 0.05$ and $1 - \beta = 0.95$, one would need $N_{W1} = 21147$ and $N_{W1} = 839$, respectively. To apply the SMO approach, we first group the range of serum cholesterol levels into classes (categories) with class endpoints defined in Table 2 for a (standard) normal

Table 2. The endpoints for constructing approximations for Poisson, normal, double exponential and exponential covariate distributions

	Poisson
SMO1	(-1, 0, 1, 3, 5, ∞)
SMO2	(-1, 0, 1, 2, 3, 4, 5, 6, 7, ∞)
	Normal
SMO1	(-∞, -1.5, -0.7, 0.0, 0.7, 1.5, ∞)
SMO2	(-∞, -2.0, -1.5, -1.0, -0.5, 0.0, 0.5, 1.0, 1.5, 2.0, ∞)
	Double exponential
SMO1	(-∞, -1.5, -0.7, 0.0, 0.7, 1.5, ∞)
SMO2	(-∞, -2, -1.5, -1.0, -0.5, 0.0, 0.5, 1.0, 1.5, 2.0, ∞)
	Exponential
SMO1	(-1, -0.4, 0.2, 0.8, 1.6, 2.6, ∞)
SMO2	(-1, -0.6, -0.2, 0.2, 0.6, 1.0, 1.5, 2.0, 2.6, 3.5, ∞)

distribution. The numbers of classes for these two class grouping are 6 and 10, respectively. The actual covariate configurations x_j* and corresponding probabilities π_j are listed in Table 3. To detect the same effects, one would need N_{SMO1} = 21883 and N_{SMO1} = 840 for the class grouping with 6 covariate configurations, while N_{SMO2} = 21645 and N_{SMO2} = 825 for the class grouping with 10 covariate configurations, respectively.

All the formulas mentioned above could be used to determine the nominal power for given values of significance level α and sample size. With this power calculation, the more powerful approach can be easily identified. However, there is no guarantee that the one that gives higher power will be always more accurate in achieving the nominal power. Hence we shall continue to compare the accuracy of these formulas in terms of the discrepancy between estimated actual power and nominal power where they are all based on the same value of sample size. This is demonstrated in the following simulation studies.

3. SIMULATION DESIGNS

In order to compare the Whittemore and SMO approaches, computer simulation studies are performed. The designs of our simulation studies are constructed from those used by Hsieh (1989), Self et al. (1992) and Whittemore (1981). They are conducted as follows.

3.1 Covariate Distributions

For a single covariate, we consider Bernoulli, Poisson, normal, double exponential and exponential distributions for $X = X_1$. The parameter π of the Bernoulli distribution is chosen to be 0.05, 0.50 and 0.95. The covariates are standardized with mean 0 and variance 1 for Poisson, normal, double exponential and exponential distributions. The only multivariate distribution for $X = (X_1, X_2)^T$ examined is multinomial with probability $(\pi_1, \pi_2, \pi_3, \pi_4)$, which corresponds to (x_1, x_2) values of (0, 0), (0 ,1), (1, 0) and (1, 1), respectively. Four sets of $(\pi_1, \pi_2, \pi_3, \pi_4)$ are studied to represent different shapes of distributions: (0.76, 0.19, 0.01, 0.04), (0.4, 0.1, 0.1, 0.4), (0.04, 0.01, 0.19, 0.76) and (0.25, 0.25, 0.25, 0.25).

3.2 Regression Coefficients

In all models the parameter of interest ψ_1 is taken to be log(2). The parameter ψ_2 for the multinomial distribution is set to be log(2). The remaining parameter ψ_0 is chosen to satisfy different overall response probabilities to be explained next.

3.3 Response Probabilities

To cover the range of response probabilities μ, its value is chosen to be 0.02, 0.15 and 0.50 for all models. Given ψ and μ, the value of ψ_0 is determined through $\mu = E\{p(X)\}$, where $p(X) = \exp(\psi_0 + X^T\psi)/\{1 + \exp(\psi_0 + X^T\psi)\}$, and the expectation is taken with respect to the distribution of X defined in Section 3.1.

3.4 Approximations of Covariate Distribution

To implement the SMO approach, one needs to adopt some categorization (class grouping) process in order to have finite configurations for covariate distributions with an infinite number of values. Except for Bernoulli and multinomial distributions, we study two approximations for each of Poisson, normal, double exponential and exponential distributions. The exact distributions of both approximations are listed in Table 3. The related calculations of sample size and power using these two approximations are called the SMO1 and SMO2 methods, respectively. They are constructed from the endpoints presented in Table 2. For the sake of easy identification, the related calculations of sample size and power for Bernoulli and multinomial distributions is called the SMO0 method.

3.5 The Estimates of Sample Size

Given the covariate distribution, regression coefficients and response probability, the estimates of sample size required to achieve significance level

Table 3. The approximations for Poisson, normal, double exponential and exponential covariate distributions

	Poisson
SMO1	X* = (−1, 0, 1, 2, 4, 6) with probability (0.3679, 0.3679, 0.1839, 0.0766, 0.0036, 0.0001)
SMO2	X* = (−1, 0, 1, 2, 3, 4, 5, 6, 7, 9) with probability (0.3679, 0.3679, 0.1839, 0.0613, 0.0153, 0.0031, 0.0005, 0.0001, 9×10^{-6}, 10^{-6})
	Normal
SMO1	X* = (−1.9, −1.1, −0.35, 0.35, 1.1, 1.9) with probability (0.0668, 0.1752, 0.2580, 0.2580, 0.1752, 0.0668)
SMO2	X* = (−2.25, −1.75, −1.25, −0.75, −0.25, 0.25, 0.75, 1.25, 1.75, 2.25) with probability (0.0228, 0.0441, 0.0918, 0.1499, 0.1915, 0.1915, 0.1499, 0.0918, 0.0441, 0.0228)
	Double exponential
SMO1	X* = (−1.9, −1.1, −0.35, 0.35, 1.1, 1.9) with probability (0.0599, 0.1259, 0.3142, 0.3142, 0.1259, 0.0599).
SMO2	X* = (−2.25, −1.75, −1.25, −0.75, −0.25, 0.25, 0.75, 1.25, 1.75, 2.25) with probability (0.0296, 0.0304, 0.0616, 0.1250, 0.2535, 0.2535, 0.1250, 0.0616, 0.0304, 0.0296)
	Exponential
SMO1	X* = (−0.7, −0.1, 0.5, 1.2, 2.1, 3.1) with probability (0.4512, 0.2476, 0.1359, 0.0910, 0.0469, 0.0273)
SMO2	X* = (−0.8, −0.4, 0.0, 0.4, 0.8, 1.25, 1.75, 2.30, 3.05, 3.95) with probability (0.3297, 0.2210, 0.1481, 0.0993, 0.0666, 0.0533, 0.0323, 0.0225, 0.0162, 0.0111)

0.05 and three levels of power, 0.80, 0.90 and 0.95, are calculated with Equations (2) or (3) for the Whittemore approach, and Equation (5) for the SMO approach (SMO0, SMO1 and SMO2). These values are listed in the first row of results for each of three response probabilities in Tables 4-14. These estimates provide a comparison of relative efficiency in terms of sample size for obtaining desired significance level and power.

Table 4. Calculated sample sizes and estimates of actual power at specified sample size for Bernoulli covariate (0.05)

	Whittemore			SMO		
Power	0.80	0.90	0.95	0.80	0.90	0.95
$\mu = 0.02$						
Sample size[a]	15674	19804	23577	11871	15892	19654
Nominal power[b] at N_{SMO0}	.6486	.8068	.8973	.8000	.9000	.9500
Estimated power	.8114	.8976	.9366	.7690	.8726	.9228
Error	.1628	.0908	.0393	−.0310	−.0274	−.0272
Percentage error	25.10	11.25	4.38	−3.88	−3.05	−2.86
$\mu = 0.15$						
Sample size[a]	2511	3172	3776	2080	2785	3444
Nominal power[b] at N_{SMO0}	.6996	.8486	.9263	.8001	.9001	.9501
Estimated power	.8816	.9426	.9650	.7814	.8858	.9314
Error	.1820	.0940	.0387	−.0187	−.0143	−.0187
Percentage error	26.02	11.08	4.17	−2.33	−1.59	−1.96
$\mu = 0.50$						
Sample size[a]	1098	1387	1652	1448	1938	2396
Nominal power[b] at N_{SMO0}	.9143	.9776	.9944	.8002	.9001	.9500
Estimated power	.9766	.9920	.9954	.8028	.9098	.9526
Error	.0623	.0144	.0010	.0026	.0097	.0026
Percentage error	6.81	1.47	0.10	0.32	1.08	0.27

[a] The sample sizes needed to achieve power 0.8, 0.9, and 0.95, respectively.
[b] The nominal powers at calculated sample sizes of SMO0 method in [a].

3.6 Nominal Power Calculations

For a meaningful comparison of accuracy in the simulation study, the nominal powers are calculated with the three sample size estimates of SMO0 or SMO2 based on the significance level 0.05 and power 0.80, 0.90 and 0.95 mentioned in Section 3.5. Obviously the nominal powers for SMO0 or SMO2 are very close to 0.80, 0.90 and 0.95 because this is just the inversion of Equation (5). However most of the nominal powers of the SMO1 and Whittemore methods are

Table 5. Calculated sample sizes and estimates of actual power at specified sample size for Bernoulli covariate (0.50)

	Whittemore			SMO		
Power	0.80	0.90	0.95	0.80	0.90	0.95
$\mu = 0.02$						
Sample size[a]	4553	5935	7214	3524	4718	5835
Nominal power[b] at N_{SMO0}	.6802	.8152	.8946	.8000	.9000	.9500
Estimated power	.8092	.9050	.9576	.8088	.9036	.9564
Error	.1290	.0898	.0630	.0088	.0036	.0064
Percentage error	18.96	11.01	7.04	1.10	0.40	0.67
$\mu = 0.15$						
Sample size[a]	642	837	1017	532	712	881
Nominal power[b] at N_{SMO0}	.7133	.8429	.9153	.8002	.9001	.9501
Estimated power	.8698	.9424	.9756	.8082	.9040	.9560
Error	.1565	.0995	.0603	.0080	.0039	.0059
Percentage error	21.93	11.80	6.59	1.00	0.44	0.62
$\mu = 0.50$						
Sample size[a]	224	292	355	266	356	440
Nominal power[b] at N_{SMO0}	.8685	.9505	.9816	.8010	.9007	.9503
Estimated power	.9644	.9882	.9966	.8238	.9034	.9560
Error	.0959	.0377	.0150	.0228	.0027	.0057
Percentage error	11.05	3.97	1.53	2.84	0.30	0.60

[a] The sample sizes needed to achieve power 0.8, 0.9, and 0.95, respectively.
[b] The nominal powers at calculated sample sizes of SMO0 method in [a].

different from 0.80, 0.90 and 0.95 since the SMO1 method uses Equation (5) with different covariate approximation, while the Whittemore approach is based on Equations (2) or (3). The major differences of nominal powers between the SMO and Whittemore approaches are direct consequences of using different asymptotic approximations described in Section 2.

3.7 Evaluation of Estimated Powers

Estimates of the actual power associated with given sample size and

Table 6. Calculated sample sizes and estimates of actual power at specified sample size for Bernoulli covariate (0.95)

	Whittemore			SMO		
Power	0.80	0.90	0.95	0.80	0.90	0.95
$\mu = 0.02$						
Sample size[a]	33297	44469	54910	26194	35066	43367
Nominal power[b] at N_{SMO0}	.6992	.8201	.8927	.8000	.9000	.9500
Estimated power	.7910	.9154	.9640	.8320	.9318	.9716
Error	.0918	.0953	.0713	.0320	.0318	.0216
Percentage error	13.13	11.62	7.99	4.00	3.53	2.27
$\mu = 0.15$						
Sample size[a]	4455	5950	7347	3689	4939	6108
Nominal power[b] at N_{SMO0}	.7214	.8392	.9073	.8000	.9000	.9500
Estimated power	.8548	.9458	.9796	.8250	.9218	.9708
Error	.1334	.1066	.0723	.0250	.0218	.0208
Percentage error	18.49	12.71	7.96	3.12	2.42	2.19
$\mu = 0.50$						
Sample size[a]	1352	1805	2229	1448	1938	2396
Nominal power[b] at N_{SMO0}	.8266	.9192	.9623	.8002	.9001	.9500
Estimated power	.9594	.9868	.9950	.8062	.9056	.9562
Error	.1328	.0676	.0327	.0060	.0055	.0062
Percentage error	16.07	7.35	3.39	0.75	0.61	0.65

[a] The sample sizes needed to achieve power 0.8, 0.9, and 0.95, respectively.
[b] The nominal powers at calculated sample sizes of SMO0 method in [a].

model configurations are then computed by Monte Carlo simulation based on 5,000 replicate data sets. For each data set, the covariate is generated with the selected distribution in Section 3.1. In order to have a finite number of covariate configurations for the cases of Poisson, normal, double exponential and exponential distributions, an extra step is performed to calculate the empirical distribution, namely the percentages of generated covariate values in the categories with endpoints defined in Table 2. The estimated power is the

Table 7. Calculated sample sizes and estimates of actual power at specified sample size for multinomial covariate (0.76, 0.19, 0.01, 0.04)

	Whittemore			SMO		
Power	0.80	0.90	0.95	0.80	0.90	0.95
$\mu = 0.02$						
Sample size[a]	12273	15627	18702	9819	13145	16257
Nominal power[b] at N_{SMO0}	.6844	.8318	.9129	.8000	.9000	.9500
Estimated power	.8304	.9078	.9470	.7926	.8802	.9330
Error	.1460	.0760	.0341	−.0074	−.0198	−.0170
Percentage error	21.33	9.14	3.74	−0.93	−2.20	−1.79
$\mu = 0.15$						
Sample size[a]	1707	2173	2601	1971	2638	3262
Nominal power[b] at N_{SMO0}	.8638	.9530	.9843	.8002	.9001	.9500
Estimated power	.9118	.9590	.9848	.8008	.8942	.9422
Error	.0480	.0060	.0005	.0006	−.0059	−.0078
Percentage error	5.56	0.62	0.05	0.08	−0.65	−0.82
$\mu = 0.50$						
Sample size[a]	593	755	904	1803	2414	2985
Nominal power[b] at N_{SMO0}	.9996	1.0000	1.0000	.8001	.9001	.9500
Estimated power	.9864	.9964	.9988	.8118	.9096	.9572
Error	−.0132	−.0036	−.0012	.0117	.0095	.0072
Percentage error	−1.33	−0.36	−0.12	1.46	1.06	0.75

[a] The sample sizes needed to achieve power 0.8, 0.9, and 0.95, respectively.
[b] The nominal powers at calculated sample sizes of SMO0 method in [a].

proportion of these 5000 replicates whose test statistic values exceed the nominal 0.05-level critical value. Finally, the error = estimated power − nominal power and the percentage error = 100 × error/(nominal power) are calculated. All calculations are performed using programs written with SAS/IML.

4. SIMULATION RESULTS

We shall discuss the results of calculated sample sizes and estimates of

Table 8. Calculated sample sizes and estimates of actual power at specified sample size for multinomial covariate (0.40, 0.10, 0.10, 0.40)

	Whittemore			SMO		
Power	0.80	0.90	0.95	0.80	0.90	0.95
$\mu = 0.02$						
Sample size[a]	7509	9813	11947	5942	7954	9837
Nominal power[b] at N_{SMO0}	.6922	.8242	.9008	.8001	.9000	.9500
Estimated power	.8042	.9034	.9580	.8058	.9038	.9574
Error	.1120	.0792	.0572	.0057	.0038	.0074
Percentage error	16.17	9.61	6.35	0.72	0.42	0.78
$\mu = 0.15$						
Sample size[a]	943	1233	1501	874	1169	1446
Nominal power[b] at N_{SMO0}	.7662	.8829	.9422	.8004	.9000	.9500
Estimated power	.8652	.9470	.9748	.7930	.9068	.9526
Error	.0990	.0641	.0326	−.0074	.0068	.0026
Percentage error	12.92	7.27	3.46	−0.92	0.75	0.27
$\mu = 0.50$						
Sample size[a]	253	330	402	422	564	698
Nominal power[b] at N_{SMO0}	.9590	.9908	.9980	.8007	.9001	.9502
Estimated power	.9674	.9888	.9958	.8002	.8960	.9504
Error	.0084	−.0020	−.0022	−.0005	−.0041	.0002
Percentage error	0.87	−0.21	−0.22	−0.07	−0.45	0.02

[a] The sample sizes needed to achieve power 0.8, 0.9, and 0.95, respectively.
[b] The nominal powers at calculated sample sizes of SMO0 method in [a].

actual power at specified sample sizes for the Whittemore and SMO approaches in Tables 4-14.

4.1 Comparison of Sample Size Estimates

For the covariate distributions considered in these simulations, the estimates of sample size given by the SMO approach, Equation (5), are generally smaller than those calculated from Whittemore approach, Equations (2) and (3).

Table 9. Calculated sample sizes and estimates of actual power at specified sample size for multinomial covariate (0.04, 0.01, 0.19, 0.76)

	Whittemore			SMO		
Power	0.80	0.90	0.95	0.80	0.90	0.95
$\mu = 0.02$						
Sample size[a]	52370	69711	85898	41234	55201	68268
Nominal power[b] at N_{SMO0}	.6982	.8207	.8938	.8000	.9000	.9500
Estimated power	.8056	.9150	.9580	.8414	.9326	.9660
Error	.1074	.0943	.0642	.0414	.0326	.0160
Percentage error	15.38	11.49	7.18	5.17	3.62	1.68
$\mu = 0.15$						
Sample size[a]	6532	8695	10714	5511	7377	9124
Nominal power[b] at N_{SMO0}	.7286	.8464	.9134	.8000	.9000	.9500
Estimated power	.8418	.9402	.9742	.8194	.9268	.9644
Error	.1132	.0938	.0608	.0194	.0268	.0144
Percentage error	15.54	11.09	6.66	2.42	2.98	1.51
$\mu = 0.50$						
Sample size[a]	1616	2151	2651	1803	2414	2985
Nominal power[b] at N_{SMO0}	.8419	.9302	.9692	.8001	.9001	.9500
Estimated power	.9456	.9838	.9938	.8088	.9140	.9548
Error	.0137	.0536	.0246	.0087	.0139	.0048
Percentage error	12.31	5.76	2.54	1.09	1.54	0.50

[a] The sample sizes needed to achieve power 0.8, 0.9, and 0.95, respectively.
[b] The nominal powers at calculated sample sizes of SMO0 method in [a].

In other words, the SMO approach requires less sample size to achieve desired power at prescribed significance level. The only exceptions are the cases of Bernoulli, multinomial, normal and exponential distributions for response probability $\mu = 0.50$, and multinomial (0.76, 0.19, 0.01, 0.04) for response probability $\mu = 0.15$. Furthermore, there are some extraordinary large values for double exponential covariate calculated by the Whittemore approach in Table 13. This is because twice the chosen value of $\psi_1 = \log(2)$ is very close to the upper

Table 10. Calculated sample sizes and estimates of actual power at specified sample size for multinomial covariate (0.25, 0.25, 0.25, 0.25)

	Whittemore			SMO		
Power	0.80	0.90	0.95	0.80	0.90	0.95
$\mu = 0.02$						
Sample size[a]	4484	5844	7104	3531	4727	5845
Nominal power[b] at N_{SMO0}	.6887	.8225	.9000	.8001	.9000	.9500
Estimated power	.8088	.9036	.9540	.8024	.9000	.9518
Error	.1201	.0811	.0540	.0023	.0000	.0018
Percentage error	17.44	9.87	6.00	0.29	0.00	0.19
$\mu = 0.15$						
Sample size[a]	574	748	910	539	722	893
Nominal power[b] at N_{SMO0}	.7719	.8885	.9462	.8001	.9002	.9502
Estimated power	.8732	.9430	.9744	.7964	.9022	.9512
Error	.1013	.0545	.0282	−.0037	.0020	.0010
Percentage error	13.12	6.13	2.98	−0.46	0.22	0.11
$\mu = 0.50$						
Sample size[a]	161	209	254	274	366	453
Nominal power[b] at N_{SMO0}	.9635	.9923	.9984	.8011	.9002	.9503
Estimated power	.9682	.9894	.9968	.8074	.8964	.9450
Error	.0047	−.0029	−.0016	.0063	−.0038	−.0053
Percentage error	0.48	−0.30	−0.16	0.79	−0.42	−0.55

[a] The sample sizes needed to achieve power 0.8, 0.9, and 0.95, respectively.
[b] The nominal powers at calculated sample sizes of SMO0 method in [a].

bound $\sqrt{2}$ for the range of the moment generating function. This result is consistent with the finding in Hsieh (1989) that the reported sample sizes using the Whittemore approach are less accurate for double exponential than normal and exponential covariates.

4.2 The Accuracy of Estimated Power

To compare the accuracy of the two approaches, we examined the percentage errors. Note that the nominal powers of both approximations are

Table 11. Calculated sample sizes and estimates of actual power at specified sample size for Poisson covariate

	Whittemore			SMO1			SMO2		
Power	0.80	0.90	0.95	0.80	0.90	0.95	0.80	0.90	0.95
$\mu = 0.02$									
Sample size[a]	980	1203	1405	710	950	1175	567	758	938
Nominal power[b] at N_{SMO2}	.4470	.6371	.7744	.7069	.8253	.8964	.8007	.9001	.9502
Estimated power	.8078	.8996	.9394	.7374	.8542	.9096	.7442	.8592	.9140
Error	.3608	.2625	.1650	.0305	.0289	.0132	−.0565	−.0409	−.0362
Percentage error	80.71	41.20	21.31	4.31	3.50	1.47	−7.06	−4.54	−3.81
$\mu = 0.15$									
Sample size[a]	242	298	347	129	173	214	113	152	187
Nominal power[b] at N_{SMO2}	.3263	.4978	.6355	.7461	.8603	.9212	.8002	.9015	.9500
Estimated power	.8916	.9518	.9800	.7702	.8730	.9392	.7742	.8782	.9420
Error	.5653	.4540	.3445	.0241	.0127	.0180	−.0260	−.0233	−.0080
Percentage error	99.99[c]	91.20	54.21	3.23	1.48	1.95	−3.25	−2.58	−0.84
$\mu = 0.50$									
Sample size[a]	170	209	244	83	111	137	79	106	131
Nominal power[b] at N_{SMO2}	.3246	.4939	.6346	.7827	.8879	.9418	.8020	.9021	.9512
Estimated power	.9790	.9932	.9994	.7992	.9182	.9564	.8056	.9186	.9592
Error	.6544	.4993	.3648	.0165	.0303	.0146	.0036	.0165	.0080
Percentage error	99.99[c]	99.99[c]	57.49	2.11	3.41	1.55	0.45	1.83	0.84

[a] The sample sizes needed to achieve power 0.8, 0.9, and 0.95, respectively.
[b] The nominal powers at calculated sample sizes of SMO2 method in [a].
[c] The actual percentage error is larger than 99.99.

Table 12. Calculated sample sizes and estimates of actual power at specified sample size for normal covariate

	Whittemore			SMO1			SMO2		
Power	0.80	0.90	0.95	0.80	0.90	0.95	0.80	0.90	0.95
$\mu = 0.02$									
Sample size[a]	998	1307	1593	933	1249	1545	901	1206	1492
Nominal power[b] N_{SMO2}	.7547	.8737	.9358	.7862	.8898	.9433	.8001	.9001	.9501
Estimated power	.8198	.9170	.9580	.7800	.8878	.9388	.7960	.8994	.9498
Error	.0651	.0433	.0222	−.0062	−.0020	−.0045	−.0041	−.0007	−.0003
Percentage error	8.63	4.96	2.37	−0.79	−0.22	−0.48	−0.51	−0.08	−0.03
$\mu = 0.15$									
Sample size[a]	161	211	257	147	196	242	144	193	239
Nominal power[b] N_{SMO2}	.7504	.8710	.9342	.7943	.8961	.9477	.8001	.9004	.9505
Estimated power	.8906	.9538	.9780	.7878	.8914	.9414	.7994	.9004	.9494
Error	.1402	.0828	.0438	−.0065	−.0047	−.0063	−.0007	−.0000	−.0011
Percentage error	18.68	9.51	4.69	−0.82	−0.52	−0.66	−0.09	−0.00	−0.12
$\mu = 0.50$									
Sample size[a]	75	98	120	77	103	127	77	103	128
Nominal power[b] N_{SMO2}	.8110	.9140	.9621	.8018	.9011	.9516	.8014	.9008	.9514
Estimated power	.9730	.9928	.9980	.7834	.8990	.9472	.7976	.9090	.9544
Error	.1620	.0788	.0359	−.0184	−.0021	−.0044	−.0038	.0082	.0030
Percentage error	19.98	8.62	3.73	−2.29	−0.23	−0.46	−0.47	0.91	0.32

[a] The sample sizes needed to achieve power 0.8, 0.9, and 0.95, respectively.
[b] The nominal powers at calculated sample sizes of SMO2 method in [a].

Table 13. Calculated sample sizes and estimates of actual power at specified sample size for double exponential covariate

	Whittemore			SMO1			SMO2		
Power	0.80	0.90	0.95	0.80	0.90	0.95	0.80	0.90	0.95
$\mu = 0.02$									
Sample size[a]	211333	258664	301352	1105	1479	1830	1010	1352	1672
Nominal power[b] at N_{SMO2}	.0013	.0015	.0017	.7639	.8727	.9314	.8001	.9000	.9500
Estimated power	.9220	.9664	.9874	.8516	.9274	.9728	.8696	.9392	.9778
Error	.9207	.9649	.9857	.0877	.0547	.0414	.0695	.0392	.0278
Percentage error	99.99[c]	99.99[c]	99.99[c]	11.48	6.27	4.44	8.69	4.36	2.93
$\mu = 0.15$									
Sample size[a]	210628	257801	300347	172	230	284	163	218	270
Nominal power[b] at N_{SMO2}	.0007	.0008	.0008	.7802	.8850	.9403	.8005	.9001	.9503
Estimated power	.9294	.9750	.9884	.8230	.9110	.9552	.8414	.9242	.9648
Error	.9287	.9742	.9876	.0428	.0260	.0149	.0409	.0241	.0145
Percentage error	99.99[c]	99.99[c]	99.99[c]	5.49	2.94	1.58	5.11	2.68	1.53
$\mu = 0.50$									
Sample size[a]	210558	257715	300247	92	123	152	90	121	149
Nominal power[b] N_{SMO2}	.0007	.0007	.0007	.7936	.8966	.9469	.8010	.9019	.9505
Estimated power	.9598	.9874	.9952	.8042	.9108	.9542	.8228	.9238	.9646
Error	.9591	.9867	.9945	.0106	.0142	.0073	.0218	.0219	.0141
Percentage error	99.99[c]	99.99[c]	99.99[c]	1.34	1.58	0.77	2.72	2.43	1.48

[a] The sample sizes needed to achieve power 0.8, 0.9, and 0.95, respectively.
[b] The nominal powers at calculated sample sizes of SMO2 method in [a].
[c] The actual percentage error is larger than 99.99.

Table 14. Calculated sample sizes and estimates of actual power at specified sample size for exponential covariate

	Whittemore			SMO1			SMO2		
Power	0.80	0.90	0.95	0.80	0.90	0.95	0.80	0.90	0.95
$\mu = 0.02$									
Sample size[a]	679	747	806	616	824	1019	488	653	807
Nominal power[b] at N_{SMO2}	.2985	.7474	.9507	.7036	.8227	.8940	.8006	.9003	.9501
Estimated power	.8438	.9144	.9544	.7864	.8832	.9280	.8050	.8922	.9384
Error	.5453	.1670	.0037	.0828	.0605	.0340	.0044	−.0081	−.0117
Percentage error	99.99[c]	22.34	0.39	11.77	7.35	3.80	0.55	−0.90	−1.23
$\mu = 0.15$									
Sample size[a]	74	82	88	116	155	192	106	142	175
Nominal power[b] at N_{SMO2}	.9954	1.0000	1.0000	.7647	.8736	.9313	.8014	.9012	.9501
Estimated power	.7832	.8522	.8940	.7654	.8698	.9270	.7750	.8810	.9304
Error	−.2122	−.1478	−.1060	.0007	−.0038	−.0043	−.0264	−.0202	−.0197
Percentage error	−21.32	−14.78	−10.60	0.09	−0.43	−0.46	−3.29	−2.24	−2.07
$\mu = 0.50$									
Sample size[a]	19	21	23	95	127	157	92	122	151
Nominal power[b] at N_{SMO2}	1.0000	1.0000	1.0000	.7891	.8892	.9430	.8039	.9001	.9502
Estimated power	.8158	.8488	.8884	.8112	.9034	.9558	.8222	.9174	.9592
Error	−.1842	−.1512	−.1116	.0221	.0142	.0128	.0183	.0173	.0090
Percentage error	−18.42	−15.12	−11.16	2.80	1.60	1.36	2.28	1.92	0.95

[a] The sample sizes needed to achieve power 0.8, 0.9, and 0.95, respectively.
[b] The nominal powers at calculated sample sizes of SMO2 method in [a].
[c] The actual percentage error is larger than 99.99.

essentially different and are derived from the sample size estimates based on SMO0 or SMO2 method. This is different from the simulation study in Self et al. (1992) where same value of nominal power was set for all competing approaches. Since both of the methods are based on the asymptotic approximations, the magnitude of sample size is a significant factor of accuracy in achieving the nominal power. Our assessment tries to control for its effects that may confound these results.

First, we focus on the results of small response probability $\mu = 0.02$. Although the Whittemore approach is proposed for small response probability, there is only one case that shows its advantage. For exponential covariate with power 0.95 in Table 14, the percentage error of the Whittemore approach is 0.39, while the percentage errors for SMO1 and SMO2 are 3.80 and −1.23, respectively.

Now we turn to the results of larger response probability. When the overall response probability μ is 0.15, in all but the multinomial (0.76, 0.19, 0.01, 0.04) distribution, the SMO0, SMO1 and SMO2 methods have smaller absolute percentage errors than the Whittemore method for all three levels of power. When the overall response probability μ is 0.50, the Whittemore approach is dominated in all but the cases of Bernoulli (0.05), multinomial (0.76, 0.19, 0.01, 0.04), multinomial (0.40, 0.10, 0.10, 0.40) and multinomial (0.25, 0.25, 0.25, 0.25) in Tables 4, 7, 8 and 10, respectively. We believe that these are due to the ceiling effects because the nominal powers are nearly one for the Whittemore approach. Despite the fact that the Whittemore method is designed solely for small response probability, however, it is somehow surprising to see that there is no degradation in the performance of Whittemore's approach for high response probabilities. In fact, our simulation results in Tables 4-10 show that it is more accurate for higher response probabilities.

Next, we examine the performance of the SMO1 and SMO2 methods with discrete approximations of Poisson, normal, double exponential and exponential distributions in Tables 11-14, respectively. Due to the approximation of true covariate distribution, these absolute percentage errors tend to be larger than those of Bernoulli and multinomial covariates. Both the SMO1 and SMO2 methods perform extremely well for the normal covariate. However the absolute percentage errors of SMO1 may be as large as 4.31, 11.48 and 11.77 for Poisson, double exponential and exponential covariates, respectively. For the SMO2 method, the absolute percentage errors are all smaller than 7.06, 8.69 and 3.29 for Poisson, double exponential and exponential covariates, respectively. Note that the covariate distribution approximation of SMO2 is a refinement of SMO1. Hence SMO2 should be at least as accurate as SMO1. The numerical outcomes do not completely agree with this assertion, which reminds us that using an arbitrary categorization of true distribution is indeed a delicate subject. For the Poisson case, SMO1 is better for small response probability 0.02 and is as accurate as SMO2 for larger response probability 0.15. However SMO1 becomes worse than SMO2 when the response probability is 0.50. The SMO2 method is more accurate for both normal and double exponential situations. However there is no dominance in the case of exponential case, since SMO2 is better for small response probability 0.02, while SMO1 becomes more accurate for the large response probability 0.15.

5. CONCLUSION

This study compares the two approaches in Whittemore (1981) and Self et al. (1992) for the calculations of power and sample size in logistic regression models. The major distinction of these two approaches is in the overall response probability and covariate distribution of logistic regression models. The Whittemore approach is designed just for small response probability, while the Self et al. (1992) approach is proposed for a finite number of covariate configurations. Hence either approach has its limitations which will confine its applicability. In the simulation studies, we cover a wide range of data configurations in terms of three different values of response probability and 14 different covariate distributions. Among them, the Poisson, normal, double exponential and exponential distributions represent those with an infinite number of covariate configurations. Overall, the results indicate that the approach of Self, et al. (1992) outperforms the Whittemore approach, even for small response probability. Hence the Self et al. (1992) approach is recommended regardless of the magnitude of the response probability. In order to apply this approach to models with an infinite number of covariate configurations, however, it involves arbitrary categorization decisions. Despite this, it appears to be acceptable over the range of conditions considered here.

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