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EFFICIENCIES AND SURROGATE VARIABLES IN LOGISTIC REGRESSION

Leonard A. Stefanski
Department of Statistics
North Carolina State University
Raleigh, NC 27695

Raymond J. Carroll
Department of Statistics
Texas A&M University
College Station, TX 77843

ABSTRACT

We study logistic regression with response y when the true predictor x is measured with error and the observable data consist of pairs (y, w), where w is correlated with x. Two approaches to estimation are studied. In the first, integrated likelihood estimates are obtained from the conditional distribution of y given $E(x \mid w)$. In the second approach, the calibration curve for (x, w) is used to construct unbiased estimates of x and then errors in variables estimation techniques are employed. When (x, w) has a bivariate normal distribution, the two approaches yield consistent and asymptotically normally distributed parameter estimates. The intergrated likelihood estimates are more efficient here, although the errors in variables estimates are shown to be nearly efficient for many choices of the parameters. Our results also apply to the problem of assessing the loss of efficiency in semiparametric regression models, where in this context it is shown that there is often little potential gain for specifying the distribution of x completely.

KEY WORDS: Asymptotic relative efficiency; Conditional score; Errors in variables; Logistic regression; Measurement error models; Semiparametric regression; Surrogate variables.

1: INTRODUCTION

Consider the ordinary logistic regression model:

$$\text{pr}(y = 1 \mid x) = \text{F}(\alpha + \beta^t x); \qquad \text{F}(v) = \{1 + \exp(-v)\}^{-1}. \tag{1.1}$$

Suppose that x is not observable, but a variable w is observed with the property that $\text{pr}(y = 1 \mid x, w) = \text{pr}(y = 1 \mid x)$. When this holds, w is said to be a *surrogate* for x. Under various assumptions on the joint distribution of x and w it is possible to estimate $\theta = (\alpha, \ \beta^t)^t$ given only independent observations (y_i, w_i) for $i = 1, ..., n$.

One approach, which we call the controlled variable approach, is to base estimation of θ on the transformation $z_p = z_p(w) = E(x \mid w)$. If, for example, it is assumed that conditional on z_p, x is normally distributed with mean z_p and variance σ_p^2, then it follows that

$$\text{pr}(y_i = 1 \mid z_{ip}) = E\Big\{F(\alpha + \beta^t x_i) \mid z_{ip}\Big\} = G(z_{ip}, \theta, \sigma_p). \tag{1.2}$$

The right hand side of (1.2) involves a logistic normal integral and must be evaluated numerically. When z_{ip} and σ_p are known, the integrated likelihood estimate of θ can be computed numerically.

A second approach, which we call the calibration/measurement error approach, assumes that there is a transformation $z_c = z_c(w)$ which, given x, is normally distributed with mean x and variance σ_c^2. When both z_c and σ_c are known, the observable pairs (y_i, z_{ic}) follow the logistic regression measurement error model of Stefanski and Carroll (1985, 1987). For a given function $t(\Delta)$, conditional score estimators of θ can be obtained by solving the conditional score equations

$$0 = \sum_{i=1}^{n} \psi_{ct}(y_i, z_{ic}, \theta, \sigma_c), \qquad \text{with} \tag{1.3}$$

$$\psi_{ct} = \Big\{y - F(\alpha + \beta^t \Delta)\Big\}\Big\{1 \ \ t(\Delta)\Big\}^t, \ \ \Delta = z_c + (y - 1/2)\sigma_c^2 \beta.$$

When the (x_i) are independent and identically distributed, taking $t(\delta) = E(x \mid \Delta = \delta)$ results in asymptotically efficient estimators in the absence of any assumptions on the distribution of x, see Lindsay (1983) and Stefanski and Carroll (1987).

The fundamental difference between the two approaches lies in the distributional assumptions on x and w. In the controlled variable approach, the distribution of x given w is specified, while in the measurement error approach, the distribution of w given x is specified. Provided both specifications are correct, either method yields consistent estimates of θ under simple random sampling. The controlled variable approach is appropriate when the surrogates are controlled via the sampling design, but not when the x_i are fixed constants, and vice–versa.

In practice, (z_p, σ_p) and/or (z_c, σ_c) will be unknown, although estimates of these quantities may be derived from additional data, e.g., independent validation data on (x, w). Since z_p is the regression of x on w, it can be estimated from simple random samples of (x, w) or from samples stratified on w; this assumes that the conditional distribution of x given w is the same for the main data set and the validation data set. If we have the classical measurement error model for which $w = x + \epsilon$, and if the distribution of ϵ given x is the same across data sets as it often is, then the controlled variable approach assumes that the marginal of x is the same across data sets.

Since z_c is typically obtained by inverting the regression of w on x, it can be estimated either from simple random samples or from samples stratfied by x. In the absence of simple random sampling of either (y, w) or (x, w), sample design will frequently dictate which of the two estimation strategies is appropriate. However, when data are obtained by simple random sampling, the choice between the two approaches is not so clear cut and we are led to consider statistical properties of the two estimation methods.

In this paper, we assume that the measurement error model holds with simple random sampling. In this context, the conditional score estimator can be applied without knowledge of the underlying distribution of x. We address two questions:

(1) How much can be gained by correctly specifying the marginal distribution of x, thus using the controlled variable model instead of the conditional score approach?

(2) How much does one lose by replacing the controlled variable model when appropriate by a calibration/measurement error model with unknown marginal distribution for x?

We also address the potential loss of efficiency incurred by an estimator of Stefanski and Carroll (1987), relative to the semiparametric information bound. This is interesting because estimators which achieve the information bound are typically complex computationally and rely of nonparametric score estimates. In our examples, we find that the simpler estimator can be used without much loss of efficiency.

The underlying model chosen for this comparison is when (x, w) has a bivariate normal distribution, see Section 2. Asymptotic relative efficiencies are computed in Section 3, first under the assumption that (z_p, σ_p) and (z_c, σ_c) are known and then under the assumption that these parameters are estimated from independent data. The parameterizations in the calculations are taken from two epidemiology studies, Gordon and Kannel (1968) and Jones, et al. (1987).

2: THE DISTRIBUTION OF (X,W)

We assume that (x, w) has a bivariate normal distribution with means (μ_x, μ_w), standard deviations (σ_x, σ_w) and correlation ρ. This means that $z_p = a_p + b_p w$ and $\sigma_p^2 = \sigma_x^2(1-\rho^2)$, where $a_p = \mu_x - \rho\sigma_x\mu_w/\sigma_w$ and $b_p = \rho\sigma_x/\sigma_w$. Further, $z_c = a_c + b_c w$ and $\sigma_c^2 = \sigma_p^2/\rho^2$, where $a_c = (\rho\sigma_w\mu_x - \sigma_x\mu_w)/(\rho\sigma_w)$ and $b_c = \sigma_x/(\rho\sigma_w)$.

3: ASYMPTOTIC RELATIVE EFFICIENCIES

3.1: Parameters Known

Suppose that $z_p, \sigma_p, z_c, \sigma_c$ are known, and let $\hat{\theta}_p$ be the integrated likelihood estimate of θ. Since this is the maximum likelihood estimate in this case, from standard asymptotic theory,

$$n^{1/2}(\hat{\theta}_p - \theta) \Rightarrow \text{Normal}(0, V_p), \tag{3.1}$$

where $V_p^{-1} = E(\psi_p\psi_p^t)$, $\psi_p = (y-G)G_\theta/(G-G^2)$, $G = G(z_p, \theta, \sigma_p)$ and G_θ is the gradient of G with respect to θ.

Asymptotic distribution theory for the solutions to (1.3) are discussed by Stefanski and Carroll (1987). Let ψ_c and ψ_{cL} denote the scores corresponding to the choices $t(\delta) = E(x \mid \Delta = \delta)$ and $t(\delta) = \delta$ respectively. Then

$$n^{1/2}(\hat{\theta}_c - \theta) \Rightarrow \text{Normal}(0, V_c), \tag{3.2}$$

where $V_c^{-1} = J_c = E(\psi_c\psi_c^t)$. The matrix J_c is the conditional information matrix (Lindsay, 1982; Stefanski and Carroll, 1987), so that V_c is a lower bound for the covariance of all estimators solving equations of the form (1.3). The efficient score ψ_c depends on the distribution of x given Δ, which is unknown. In principle, this can be estimated (Lindsay, 1985; Bickel and Ritov, 1987), but the result is complex computationally and there is less than adequate documentation of the small sample behavior of the result. This suggests study of the estimator $\hat{\theta}_{cL}$, for which it can be shown under appropriate regularity conditions that

$$n^{1/2}(\hat{\theta}_{cL} - \theta) \Rightarrow \text{Normal}(0, V_{cL}), \tag{3.3}$$

where $V_{cL} = A_{cL}^{-1} B_{cL} (A_{cL}^t)^{-1}$, $B_{cL} = E(\psi_{cL}\psi_{cL}^t)$ and $A_{cL} = E\{(\partial/\partial\theta^t)\psi_{cL}\} = E(\psi_{cL}\psi_c^t)$.

In the sense of positive definiteness, $V_p \le V_c \le V_{cL}$. Measures of the relative magnitude of V_p to V_c are given in Table 1 for a set of parameter values known to include a case of practical importance (Stefanski and Carroll, 1985). The efficiency measures used were treff(V_1,V_2) = trace(V_1)/trace(V_2); effU(V_1,V_2) = $\sup_\lambda \left(\lambda^t V_1 \lambda / \lambda^t V_2 \lambda\right)$; effL($V_1$,$V_2$) = $\inf_\lambda \left(\lambda^t V_1 \lambda / \lambda^t V_2 \lambda\right)$. These measures satisfy effL $\le$ treff $\le$ effU, and the extremes provide bounds on the scalar efficiencies of estimators of linear combinations of θ. The efficiencies are invariant to the choice of σ_w and μ_w for fixed $\theta, \mu_x, \sigma_x, \rho$.

Except in the case of a poor surrogate and a strong relationship between y and x ($\rho^2 = 0.25$, $\beta = 2.8$), all efficiencies in Table 1 exceed 0.8. The case $\beta = 1.4, \rho^2 = 0.75$ matches a cohort of males aged 45–54 from the Framingham Heart study (Gordon and Kannel, 1968), where y indicates heart disease and the predictor is the centered form of $\log_e\{$(systolic blood pressure - 75)/3$\}$, i.e., the variable minus its overall mean in the population.

Measures of the asymptotic relative efficiency of V_c to V_{cL} were calculated for the entries in Table 1. In all cases, these exceeded 1 - 10^{-4}. Thus, for the particular model under consideration, there is an inconsequential loss of efficincy for using $\hat{\theta}_{cL}$ instead of $\hat{\theta}_c$. The explanation for this lies in the fact that Δ and $E(x \mid \Delta)$are strongly correlated, being at least 1 - 10^{-3} for the models used in Table 1.

The measures of relative efficiency were also calculated for a second set of parameters, with one entry ($\alpha = -4.42, \beta = -0.5670$, $\rho^2 = 0.25$) matching approximately a subset of the data used by Jones, et al. (1987) in a study of diet and breast cancer. We took as the parameters $\alpha = -4.42, -2.21, 0$; $\beta = -.2835, -.5670, -1.1340$ and $\rho^2 = 0.25, 0.50, 0.75$. These efficiencies were uniformly high and are not listed here.

These results and Table 1 suggests that the efficiencies are often reasonably high. To support this observation, we refer to Table 2. For this table, x has a standard normal distribution and θ was chosen so that $\text{corr}(y, x) = \rho_{yx}$ and $\text{pr}(y = 1) = p_y$. The correlation cannot exceed 0.80 in absolute value for this model. Cell entries in Table 2 are effL(V_p, V_c) for $\rho^2 = 0.75, 0.50, 0.25$.

The point biserial correlation ρ_{yx} is generally small for the epidemiologic studies with which we are familiar; in these cases the difference between the controlled variable and measurement error approaches is not great.

3.2: Parameters Estimated

In this section, we investigate the additional effect of estimating the parameters $z_p, \sigma_p, z_c, \sigma_c$. We assume that there is independent validation data which give rise to these estimates. Specifically, to the main data set consisting of the n pairs $(y_i,\ w_i)$, we append an independent data set of size k, consisting of the pairs $(x_i,\ w_i)$ for $i = n+1, ..., n+k$. Suppose that as $n \to \infty$, $n/k \to \lambda$; the case that $\lambda = 0.0$ is equivalent to the nuisance parameters all known. Let $\hat{a}_p, \hat{b}_p, \hat{\sigma}_p$ and $\hat{a}_c, \hat{b}_c, \hat{\sigma}_c$ be the maximum likelihood estimates using the validation data. For the latter, note that $a_c = -c/d, b_c = 1/d, \sigma_c^2 = \tau^2/d^2$, where w given x follows a normal linear regression with intercept c, slope d and variance τ^2. Using standard asymptotic theory, after considerable algebra we find that

$$n^{1/2}(\hat{a}_p - a_p, \hat{b}_p - b_p, \hat{\sigma}_p^2 - \sigma_p^2) \Rightarrow \text{Normal}(0, \lambda\Omega_p); \tag{3.4}$$

$$n^{1/2}(\hat{a}_c - a_c, \hat{b}_c - b_c, \hat{\sigma}_c^2 - \sigma_c^2) \Rightarrow \text{Normal}(0, \lambda\Omega_{cL}); \tag{3.5}$$

where $\Omega_{cL} = \Omega_{c2}\Omega_{c1}\Omega_{c2}^t$ and

$$\Omega_p = \sigma_x^2(1-\rho^2)\begin{pmatrix} (1+\mu_w^2/\sigma_w^2) & -\mu_w/\sigma_w^2 & 0 \\ -\mu_w/\sigma_w^2 & \sigma_w^{-2} & 0 \\ 0 & 0 & 2\sigma_x^2(1-\rho^2) \end{pmatrix};$$

$$\Omega_{c1} = \sigma_w^2(1-\rho^2)\begin{pmatrix} (1+\mu_x^2/\sigma_x^2) & -\mu_x/\sigma_x^2 & 0 \\ -\mu_x/\sigma_x^2 & \sigma_x^{-2} & 0 \\ 0 & 0 & 2\sigma_w^2(1-\rho^2) \end{pmatrix};$$

$$\Omega_{c2} = \begin{pmatrix} -\sigma_x/(\rho\sigma_w) & \sigma_x^2(\mu_w - \rho\sigma_w\mu_x/\sigma_x)/(\rho^2\sigma_w^2) & 0 \\ 0 & -\sigma_x^2/(\rho^2\sigma_w^2) & 0 \\ 0 & -2(1-\rho^2)\sigma_x^3/(\sigma_w\rho^3) & \sigma_x^2/(\rho^2\sigma_w^2) \end{pmatrix}.$$

In this subsection, the estimates $\hat{\theta}_p$ and $\hat{\theta}_{cL}$ are obtained by replacing the unknown nuisance parameters $a_c, b_c, \sigma_c, a_p, b_p, \sigma_p$ by their estimates. Because these parameter estimates are independent of the (y_i, w_i) pairs for $i = 1, ..., n$, we can readily compute the asymptotic distribution of $\hat{\theta}_p$ and $\hat{\theta}_{cL}$ as follows. Write ψ_p for $\psi(y, z_p, \alpha, \beta, \sigma_p^2)$ and ψ_{cL} for $\psi(y, z_{cL}, \alpha, \beta, \sigma_{cL}^2)$. Define the (2 by 3) matrices

$$D_p = E\left\{\frac{\partial \psi_p}{\partial z_p}(1,\ w),\ \ \frac{\partial \psi_p}{\partial \sigma_p^2}\right\}; \qquad D_{cL} = E\left\{\frac{\partial \psi_{cL}}{\partial z_c}(1,\ w),\ \ \frac{\partial \psi_{cL}}{\partial \sigma_c^2}\right\}.$$

Then, by delta method arguments,

$$n^{1/2}(\hat{\theta}_p - \theta) \Rightarrow \text{Normal}(0, V_p^*); \qquad n^{1/2}(\hat{\theta}_{cL} - \theta) \Rightarrow \text{Normal}(0, V_{cL}^*);$$

$$V_p^* = V_p + \lambda V_p D_p \Omega_p D_p^t V_p^t; \qquad V_{cL}^* = V_{cL} + \lambda A_{cL}^{-1} D_{cL} \Omega_{cL} D_{cL}^t (A_{cL}^{-1})^t.$$

Table 3 contains efficiencies of V_{cL}^* to V_p^* for the same set of parameters employed in Table 1 and for $\lambda = 0.00, 0.50, 1.00, 2.00$. The same trends apparent in Table 1 manifest themselves in Table 3. The performance of $\hat{\theta}_{cL}$ relative to $\hat{\theta}_p$ deteriorates as ρ^2 decreases and/or β increases. However, for cases close to the parameter values of known interest, namely $\beta = 1.4, \rho^2 = 0.75$, no efficiencies are unacceptably low. Table 1 is a subset of Table 3 with $\lambda = 0$. As λ increases all efficiencies decrease, indicating that the effect of estimating nuisance parameters is greater for the calibration–measurement error approach than for the integrated likelihood estimator.

DISCUSSION

If the assumptions underlying the measurement error model are known to hold, we may be willing to entertain a normality assumption for x for the purpose of increasing efficiency. Our calculations indicate that there are many cases for which the potential increase in efficiency is small. Of course, if the normality assumption for x is violated, then $\hat{\theta}_p$ need not be consistent in general. The relationship between $\hat{\theta}_p$ and $\hat{\theta}_c$ or $\hat{\theta}_{cL}$ is similar to the relationship between logistic regression and normal discriminant analysis (Efron, 1975). Although the measurement error model estimators are less efficient than $\hat{\theta}_p$ when x is normal, they maintain consistency for all choices of the distribution of x and for nonrandom x as well.

When the assumptions underlying the integrated likelihood approach are known to hold, our results indicate that $\hat{\theta}_c$ and/or $\hat{\theta}_{cL}$ are less efficient than $\hat{\theta}_p$ and maintain consistency only when z_c given x is normal with mean x.

Additional information on the joint distribution of (w, x) is not always of the type described in Section 3.2 For example, it may be that x is observed on a subset of the main data set (y_i, w_i), in which case the information for estimating the nuisance parameters will not be independent of the primary data set and the asymptotic covariance matrices of $\hat{\theta}_p$ and $\hat{\theta}_c$ will differ from what we have discussed. We would be surprised if this type of additional data severely affected our calculations.

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TABLE 1

Efficiencies of V_p to V_c. Cell entries are, from top to bottom, effU(V_p,V_c), treff(V_p,V_c) and effL(V_p,V_c). In this example, $\mu_x = 0, \sigma_x^2 = 0.1$. All efficiencies equal 1.0 for $\beta = 0.0$ or $\rho^2 = 1.0$.

$\alpha = -2.1$

β	ρ^2 0.75	0.50	0.25
	1.000	0.998	0.990
0.7	0.999	0.995	0.977
	0.999	0.995	0.975
	0.999	0.991	0.962
1.4	0.996	0.976	0.894
	0.995	0.972	0.877
	0.993	0.961	0.843
2.8	0.981	0.893	0.620
	0.975	0.867	0.548

$\alpha = -1.4$

β	ρ^2 0.75	0.50	0.25
	0.999	0.996	0.984
0.7	0.999	0.992	0.965
	0.999	0.992	0.963
	0.998	0.986	0.940
1.4	0.995	0.968	0.865
	0.994	0.964	0.850
	0.990	0.945	0.787
2.8	0.978	0.883	0.599
	0.974	0.864	0.550

$\alpha = -0.7$

β	ρ^2 0.75	0.50	0.25
	0.999	0.995	0.977
0.7	0.998	0.990	0.955
	0.998	0.989	0.953
	0.997	0.980	0.917
1.4	0.993	0.962	0.845
	0.993	0.960	0.838
	0.987	0.928	0.733
2.8	0.977	0.877	0.588
	0.975	0.869	0.568

$\alpha = 0.0$

β	ρ^2 0.75	0.50	0.25
	0.999	0.994	0.974
0.7	0.998	0.989	0.950
	0.998	0.988	0.950
	0.996	0.977	0.905
1.4	0.993	0.960	0.838
	0.993	0.959	0.836
	0.985	0.920	0.707
2.8	0.977	0.876	0.584
	0.976	0.874	0.582

TABLE 2

Lower bound efficiencies of V_p to V_c. Cell entries are, from top to bottom, effL(V_p,V_c) for $\rho^2 =$ 0.75,0.50,0.25 respectively; ρ_{yx} is the point biserial correlation between y and x, while $p_y = pr(y = 1)$.

	ρ_{yx}						
p_y	0.01	0.02	0.04	0.08	0.16	0.32	0.64
	0.999	0.999	0.999	0.996	0.938	-	-
0.0125	0.999	0.999	0.997	0.974	0.701	-	-
	0.999	0.998	0.986	0.852	0.221	-	-
	0.999	0.999	0.999	0.998	0.975	0.644	-
0.0250	0.999	0.999	0.998	0.986	0.861	0.154	-
	0.999	0.998	0.990	0.924	0.496	0.002	-
	0.999	0.999	0.999	0.998	0.988	0.888	-
0.0500	0.999	0.999	0.998	0.990	0.929	0.549	-
	0.999	0.998	0.991	0.952	0.703	0.108	-
	0.999	0.999	0.999	0.999	0.993	0.950	-
0.1000	0.999	0.999	0.998	0.992	0.957	0.758	-
	0.999	0.998	0.992	0.964	0.815	0.331	-
	0.999	0.999	0.999	0.999	0.995	0.974	0.549
0.2000	0.999	0.999	0.998	0.993	0.970	0.859	0.089
	0.999	0.998	0.993	0.970	0.871	0.536	0.000
	0.999	0.999	0.999	0.999	0.996	0.983	0.849
0.4000	0.999	0.999	0.998	0.994	0.975	0.905	0.461
	0.999	0.998	0.993	0.972	0.897	0.665	0.062

Non-entries correspond to numerically unstable cases.

TABLE 3

Efficiencies of V_p^* to V_{cL}^*. Cell entries are, from top to bottom, effU(V_p^*,V_{cL}^*), treff(V_p^*,V_{cL}^*) and effL(V_p^*,V_{cL}^*). In this example, $\alpha = -1.4, \mu_x = 0, \sigma_x^2 = 0.1$. The ratio of the sample size for the main data set to the validation data set is λ; the case $\lambda = 0.0$ occurs when all nuisance parameters are known, see Table 1. All efficiencies equal 1.0 for $\beta = 0.0$ or $\rho^2 = 1.0$.

		λ			
ρ^2	β	0.0	0.5	1.0	2.0
		0.999	0.999	0.999	0.998
	0.7	0.999	0.998	0.997	0.996
		0.999	0.998	0.997	0.996
		0.998	0.996	0.995	0.993
0.75	1.4	0.995	0.992	0.990	0.986
		0.994	0.991	0.989	0.984
		0.990	0.986	0.983	0.977
	2.8	0.978	0.972	0.965	0.953
		0.974	0.965	0.957	0.941
		0.996	0.994	0.978	0.989
	0.7	0.992	0.986	0.985	0.978
		0.991	0.988	0.984	0.977
		0.986	0.979	0.973	0.961
0.50	1.4	0.968	0.955	0.943	0.920
		0.964	0.950	0.936	0.910
		0.945	0.927	0.911	0.883
	2.8	0.883	0.853	0.827	0.781
		0.864	0.826	0.793	0.738
		0.983	0.976	0.968	0.953
	0.7	0.961	0.950	0.934	0.907
		0.960	0.947	0.931	0.902
		0.939	0.915	0.893	0.852
0.25	1.4	0.863	0.822	0.783	0.719
		0.849	0.801	0.758	0.687
		0.787	0.741	0.705	0.648
	2.8	0.599	0.546	0.505	0.445
		0.549	0.486	0.440	0.376