Power Analysis for Mixed-Effects Logistic Regression Models. Y. Li1, L. A. Escobar2 & D. T. Scholl1.3.* 1Dept. of PathoBiological Sciences, School of Veterinary Medicine. 2Dept. of Experimental Statistics, Louisiana State University, Baton Rouge, LA. 3Canadian Bovine Mastitis Research Network, Faculty of Veterinary Medicine, University of Montreal, Quebec, Canada.

Abstract: Motivated by the need in veterinary epidemiological research, we developed a power analysis/sample size estimation method for mixed-effects logistic regression models based on a noncentral chi-square approximation to the likelihood ratio statistic distribution. When the random effect is present in the study population but is ignored at the planning stage, the sample size calculated from the method for fixed effect model is too small to achieve the desired power in many circumstances.

Introduction: Logistic regression models with random effects have been used frequently in veterinary epidemiological studies to analyze clustered binary data (1, 2). However, sample size/power analysis corresponding to such models are not available. We propose a sample size/power analysis method for logistic-normal models. The proposed method extends the sample size method developed by Self, Mauritsen and Ohara (3) for likelihood ratio tests in fixed-effects generalized linear models to the mixed-effects model proposed by Stiratelli et al (4).

Methods: Let $\boldsymbol{y}_i$ denote a n_i- vector of responses for the ith cluster, $i = 1, 2, \ldots, M$. Each element y_{ij} is assumed to be a binary response. Let $p_{ij} = \Pr(y_{ij} = 1)$, $\lambda_{ij} = \text{logit}(p_{ij})$, and $\boldsymbol{\lambda}_i = (\lambda_{i1}, \lambda_{i2}, \ldots, \lambda_{in_i})'$. Let $\boldsymbol{X}_i$ denote the $n_i \times p$ matrix of the fixed-effects covariates, and $\boldsymbol{Z}_i$ denote the $n_i \times k$ matrix of the random-effects covariates. Let $\boldsymbol{\beta}$ and $\boldsymbol{b}_i$ be the p-vector of fixed regression coefficients and k-vector of random effects, respectively. At stage 1, let $\boldsymbol{\lambda}_i = \boldsymbol{X}_i\boldsymbol{\beta} + \boldsymbol{Z}_i\boldsymbol{b}_i$ as the regular fixed-effects logistic model, and at stage 2 assume that $\boldsymbol{b}_i$ is distributed as multivariate normal, i.e., $\boldsymbol{b}_i \sim \text{MVN}(0, \boldsymbol{\Psi})$. The likelihood function is

$$L(\boldsymbol{\beta}, \boldsymbol{\Psi}; \boldsymbol{y}) = (2\pi)^{-Mk/2} \prod_{i=1}^{M} \int_{\mathcal{R}^k} \prod_{j=1}^{n_i} p_{ij}^{y_{ij}} (1 - p_{ij})^{1-y_{ij}} \exp(-\frac{1}{2}\boldsymbol{b}_i'\boldsymbol{\Psi}^{-1}\boldsymbol{b}_i)|\boldsymbol{\Psi}|^{-1/2} d\boldsymbol{b}_i. \quad (1)$$

Let $\boldsymbol{\alpha}$ be the model parameters of interest and $\boldsymbol{\phi}$ be the nuisance parameters including $\boldsymbol{\Psi}$. For testing null hypothesis of $\boldsymbol{\alpha} = \boldsymbol{\alpha}_0$, the likelihood ratio statistics $2\left[\ell_n(\hat{\boldsymbol{\alpha}}, \hat{\boldsymbol{\phi}}) - \ell_n(\boldsymbol{\alpha}_0, \hat{\boldsymbol{\phi}}_0)\right]$ can be decomposed into three terms in a way similar to Self et al(3)

$$2\left[\ell_n(\hat{\boldsymbol{\alpha}}, \hat{\boldsymbol{\phi}}) - \ell_n(\boldsymbol{\alpha}, \boldsymbol{\phi})\right] - 2\left[\ell_n(\boldsymbol{\alpha}_0, \hat{\boldsymbol{\phi}}_0) - \ell_n(\boldsymbol{\alpha}_0, \boldsymbol{\phi}_0^*)\right] + 2\left[\ell_n(\boldsymbol{\alpha}, \boldsymbol{\phi}) - \ell_n(\boldsymbol{\alpha}_0, \boldsymbol{\phi}_0^*)\right], \quad (2)$$

where $\boldsymbol{\phi}_0^*$ are the limiting value of $\hat{\boldsymbol{\phi}}_0$ evaluated under null model. Using asymptotic expansion and taking only the lead term, the approximate expected value for the first term is $(p + q)$ and the approximate expected value for the second term is the trace of the matrix $\boldsymbol{A}$, where the matrix $\boldsymbol{A}$ is given as

$$\left\{E\left[-\frac{\partial^2 \ell_n(\boldsymbol{\alpha}, \boldsymbol{\phi})}{\partial\boldsymbol{\phi}\partial\boldsymbol{\phi}'}|(\boldsymbol{\alpha}_0, \boldsymbol{\phi}_0^*)\right]\right\}^{-1} E\left[-\frac{\partial \ell_n(\boldsymbol{\alpha}, \boldsymbol{\phi})}{\partial\boldsymbol{\phi}}|(\boldsymbol{\alpha}_0, \boldsymbol{\phi}_0^*)\right]^{\otimes 2},$$

where for a vector $\boldsymbol{a}, \boldsymbol{a}^{\otimes 2} = \boldsymbol{a}\boldsymbol{a}'$ and $E(.)$ denotes expectation taken with respect to the true value of $(\boldsymbol{\alpha}, \boldsymbol{\phi})$. The evaluation of the expectation for the third term is impractical when n_i are large, which is common in veterinary epidemiologic studies. We only consider categorical covariates (continuous covariates can be grouped into small number of categories). Let C_i denote the number of distinct covariate configurations of all possible covariates within the

i^{th} cluster, and the proportion of subjects of certain covariate configuration be π_{is} subject to the constrain of $\sum_{s=1}^{C_i} \pi_{is} = 1$, where $s = 1, 2, \ldots, C_i$, and let n_{is} be the number of subjects in cluster i with s^{th} covariate configuration and u_{is} be the number of total success out of n_{is} subjects, u_{is} is then binomial random variable with event probabilities p_{is}. Furthermore, u_{is} are also independent of each other for given i. The joint density of $(u_{i1}, \ldots, u_{iC_i})$ conditioning on $(n_{i1}, \ldots, n_{iC_i})$ is then given by the product of the binomial density of each u_{is} for all s. The unconditional joint density is the product of conditional density and the density function of $(n_{i1}, \ldots, n_{iC_i})$, i.e.,

$$\Pr(u_{i1}, \ldots, u_{iC_i}) = \left(\prod_{s=1}^{C_i} \binom{n_{is}}{u_{is}} p_{is}^{u_{is}} (1 - p_{is})^{n_{is} - u_{is}} \right) \frac{n_i!}{\prod_{s=1}^{C_i} n_{is}!} \prod_{s=1}^{C_i} \pi_{is}^{n_{is}}.$$

The expectation of $\ell_n(\boldsymbol{\alpha}, \boldsymbol{\phi})$ and $\ell_n(\boldsymbol{\alpha}_0, \boldsymbol{\phi}_0^*)$ in the third term with respect to $\boldsymbol{y}_i$ is equivalent to the expectation with respect to the joint distribution of $(u_{i1}, \ldots, u_{iC_i})$. The likelihood functions are at first evaluated at $(\boldsymbol{\alpha}, \boldsymbol{\phi})$ and $(\boldsymbol{\alpha}_0, \boldsymbol{\phi}_0^*)$, respectively, before the expectation is taken.

The likelihood ratio statistic is approximately distributed as noncentral χ^2 with p degree of freedom and its expectation is therefore $p + \gamma$. Equating this to the approximation of the decomposed terms yields $\gamma_n = [q - \text{tr}(\boldsymbol{A})] + \Delta$.

Self et al (3) and Shieh (5) demonstrated that the term $[q - tr(\boldsymbol{A})]$ is very close to zero in the generalized linear model, therefore it can be ignored in the power analysis. It is reasonable to argue that this term should also be small in the mixed logistic regression model under study. When the term $[q - tr(\boldsymbol{A})]$ is ignored, the calculation of power can be greatly simplified as in equation 3.

$$\gamma_n \approxeq \Delta. \tag{3}$$

For given covariate configurations and planning values for $(\boldsymbol{\alpha}, \boldsymbol{\phi})$, we can approximate the power of the likelihood ratio test by computing γ_n and then referring to non-central χ^2 tables for the probability of exceeding the critical value.

Results: We use a study assessing the effect of BIV on the risk of mastitis in Louisiana dairy herds as an example to illustrate the power analysis method. For different sampling schemes, slightly different approaches should be considered. Here we only consider equal size sampling, i.e., the same number of cows are sampled from each herd. From M herds of cows, n cows from each herd are randomly selected into the study. Therefore the total number of subjects required to achieve the desired power is $M \times n$. The model is $\boldsymbol{\lambda}_i = \mathbf{1}\beta_0 + \boldsymbol{X}_i\beta_1 + b_i$, where $\mathbf{1}$ is a n_i-vector of ones, β_0 is the intercept, $\boldsymbol{X}_i$ is a n_i-vector indicating the BIV status of cows within ith herd, β_1 is the regression coefficient for BIV effect, which is the logarithm of odds ratio, and b_i is the cluster random effect on the intercept. The power for given sample size n can be calculated approximately using formula 3. Power is calculated for total sample sizes of 100 to 1200 in an increments of 100. The planning values are $(\pi = 0.3; p_0 = 0.3; OR = 2; \psi^2 = 1)$ with the number of herds of $3, 4, 5, 6, 8, 10, 12$, and 20.

When no random cluster effect is present, i.e., fixed-effects model, the number of herds is labelled as 100 for convenience in presenting the graphs. In all cases, the power increases as the total sample size gets larger (Fig, 1A). In contrast, the effect of the number of herds on power is not monotone. As shown in figure 1B, power is lowest when the number of herds is 5. As the number of herds increases, the power increases and levels off at about 12 herds.

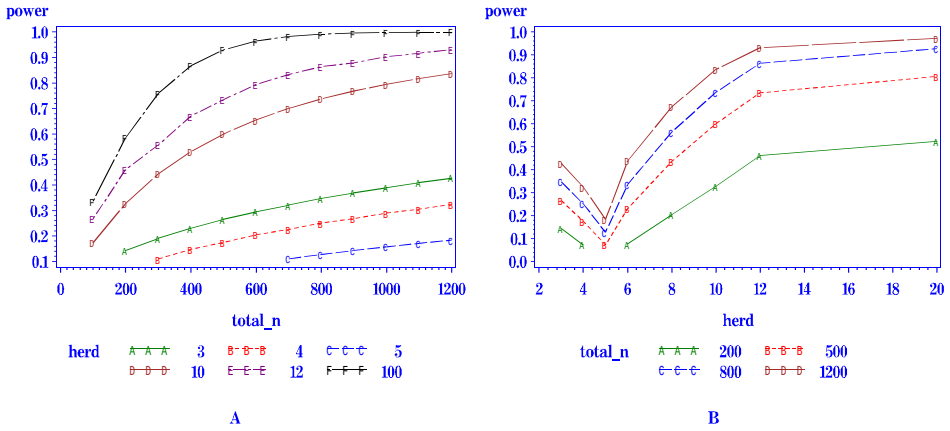

Figure 1: Panel A. Power curves for $OR = 2$, $\pi = 0.3$, $p0 = 0.3$ and $\psi^2 = 1$. Panel B. Relationship between power and the number of herds.

In most cases the power for given total sample size is consistently lower than with the fixed effect model where each individual cow can be considered as a cluster. When the number of herds is as large as 20, the power using the proposed method is very close to the method for the fixed-effects model when the variance of the random effect is 1. In some cases when the variance of the random effect (ψ^2) is larger than 1, eg. 2 and 4, the power for random effect model is some times higher than that for their corresponding fixed-effects model (figures not shown). Such results are contradictory to our theoretical intuition. One possible reason is the errors of approximation in this method. There are two types of approximation errors in this method. One is from the decomposition of the likelihood ratio statistics where only the first-order expansions are used. The second error source is the omission of the term $[q - \mathrm{tr}(\boldsymbol{A})]$ in the sample size calculation step. This term is very close to zero in fixed models. For our mixed-effects model, more evaluation of this term is needed in future studies.

References:

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