A decision criterion for the application of the Rogan-Gladen estimator in prevalence studies

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Summary

It is considered good epidemiologic practice to adjust the apparent prevalence estimate of a disease for diagnostic misclassification (Rogan-Gladen estimator). This estimator is a non-linear function of three stochastic parameters (sensitivity and specificity of the diagnostic test and apparent prevalence). A second order Taylor series linearisation can be used to derive estimates of the bias and variance of the adjusted estimator. Monte-Carlo and bootstrap simulations confirmed the theoretical results concerning bias and variance of the Rogan-Gladen estimator. In this context, an improved parameterisation of the beta distribution as a model for empirical proportions was developed and validated. Variance and bias together determine the overall "quality" of the estimator and can be expressed as mean square error. The ratio of the mean square errors of the adjusted estimate and the crude estimate is proposed as a criterion for the usefulness of the adjustment. The review of published applications of the Rogan-Gladen estimator in veterinary epidemiology and other areas revealed that the ratio criterion is often not fulfilled. It is concluded that the recommendation for an adjustment for diagnostic misclassification in prevalence studies is not appropriate under all circumstances.

Introduction

The parameter of interest in prevalence studies is often the true prevalence (P) rather than the serological -- or in general terms -- the apparent prevalence (AP). If reliable estimates of the diagnostic sensitivity (Se) and specificity (Sp) are available, the crude estimate AP can be adjusted for misclassification probabilities using the Rogan-Gladen estimator (RGE) as described by Marchevsky (1974) and Rogan and Gladen (1978). However, bias correction is often obtained at the cost of increased variance. RGE is a non-linear combination of three stochastic parameters. Taylor series linearisation, also known as delta method, can be used to derive expected values (and therefore bias) and variance of complex estimators. A quality criterion for estimators is the mean square error (MSE), which can be derived from the bias and variance.

Objectives

The objective of the study is (a) to establish a combined quality measure for the bias and variance of the Rogan-Gladen estimator (RGE), (b) to derive a decision criterion for the use of RGE versus the crude estimator and (c) to re-analyse published prevalence studies as an illustration of the concept.

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Materials and Methods

Mean square error: The expected value (and bias) of RGE based on a second order Taylor series approximation is known from the literature (Rogan and Gladen, 1978). The second order approximation of the variance was derived in a closed form using computer-assisted algebra (Maple, Waterloo Maple Inc., version 5.1). The variance of all simple estimators (Se, Sp, AP) is established under assumption of simple random sampling. The bias of AP is B=AP–RGE. The mean square error is MSE = Variance + B^2.

Validation of the asymptotic distribution: For empirical validation, the mean and variance of RGE for all 96 combinations of AP={5/100, 50/100, 95/100, 50/1000, 500/1000, 950/1000} and Se, Sp={80/100, 95/100, 800/1000, 950/1000} were computed and compared to values obtained by bootstrap (Stata, Stata Corp., version 7.0) and Monte-Carlo integration of three beta distributions (@Risk, Palisade, version 4.5.0). For the latter, the standard parameterisations a=k+1, b=n–k+1 for the fraction k/n and an alternative a'=k–k/n and b'=n–k–1+k/n were used.

Derivation and application of a decision criterion: The ratio R=MSE(RGE)/MSE(AP) was established using first and second order approximation as criterion with the rule “use AP if R>1 and use RGE else”. A macro for numerical and graphical analyses of R was developed (“msergei”; StataCorp, version 7.0). Under the conservative assumption that the Se and Sp are known values, a 95% confidence interval for the bias reduction was constructed as $B \pm 1.96\sqrt{[Var(AP)(Se+Sp-2)^2/(Se+Sp-1)^2]}$. The criterion R and the confidence interval for the bias correction was established for 25 published applications of the RGE that were obtained by systematic literature search.

Results

An improved approximation of the variance of RGE was obtained by second order Taylor series approximation. Monte-Carlo and bootstrap simulations confirmed the theoretical results concerning bias and variance of the RGE. The alternative parameterisation of the beta distribution as a model for empirical proportions was superior compared to the standard form in terms of the mean values and variances of the simulated sampling distribution. The results were used to establish the criterion R.

The study by Lunden et al. (2002) is an illustration for a useful application of RGE according to the criterion R=0.03 for AP=0.05 (Fig. 1 a). This means, MSE(RGE) is only 3% of the MSE(AP). In the hypothetical scenario described by Greiner and Gardner (2000) the criterion R=1.5 at AP=0.77 suggests that AP can be used without adjustment (Fig. 1 b). In 16 out of 25 published studies the bias reduction through application of RGE was negligible or not significant (95% confidence intervals include zero; results not shown).

Discussion

This study indicates that an adjustment for diagnostic misclassification in prevalence studies is not appropriate under all circumstances. The expected bias is often used as the only quality criterion of estimators in epidemiology. From a practical viewpoint, this notion should be questioned. Even unbiased or approximately unbiased estimates can be practically non-informative, if the form of the estimator entails a large standard error. For biased estimators, as for example RGE, the MSE is a suitable combined quality measure of the bias and variance.

A second order approximation of the RGE function was used here as a compromise between a first order approximation (standard for most complex estimators in epidemiology) and higher-order approximations, which are mathematically intractable. The results were confirmed with distribution-free resampling techniques (Monte-Carlo and bootstrap). An improved parameterisation of the beta sampling distribution was derived and used. The closed form expression of the variance of RGE presupposes simple random sampling processes of all stochastic parameters. If evidence for extra-binomial variation or parameter heterogeneity exists, this should be accounted for. In such cases, the distribution of RGE can be found by Monte-Carlo integration.

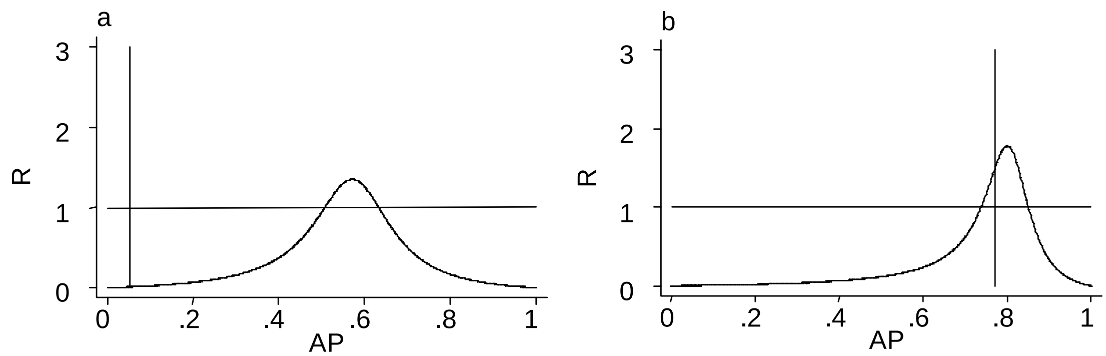

Fig. 1. Plot of the criterion R (assuming known values for Se and Sp) against the apparent prevalence for (a) AP=42/807, Se=0.94, Sp=0.92 (data from Lunden et al., 2002) and (b) AP= 270/350, Se=0.95, Sp=0.8 (hypothetical data from Greiner and Gardner, 2000).

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