Asymptotic efficiency: Conceptualization of the general, weighted noniterative estimators of common relative risk

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Theorem on the asymptotic efficiency of general, weighted noniterative point estimators of the common relative risk (risk ratio, RR, or odds ratio, OR) was formalized by Nurminen (1981), based on the regularity conditions defined by Gart (1962). However, Nurminen gave a formal proof only for the case of nonrandom weights. Pigeot (1990) presented a theorem on a new class of asymptotically optimal (consistent, normally distributed and efficient) noniterative estimators of a common odds ratio, allowing empirical weights.

In general, when dealing with valid (mean unbiased) weighted estimators, efficiency is considered to be an issue of choosing appropriate weights. All of these estimators were asserted to be asymptotically efficient. The maximum likelihood (ML) method yields an asymptotically efficient estimator of RR, but the method requires an iterative solution. Also, the ML estimators are usually biased in small samples. Bjerre (1995) noted, "Weighted estimation has to with the situation in which there is presumed to be a single, unknown parameter value and more than one independent estimate of this single value is available; it is a matter of averaging the available estimates, of computing their mean – with a set of chosen weights involved in the averaging."

In epidemiologic research practice, we are often faced with the problem of combining and stratifying or pooling independent estimates of a parameter obtained from different samples (Nurminen, 1988). In such cases, a problem arises: If the estimates are aiming at the same quantity, what is the optimal way of combining them to obtain a single estimate?

While differences between separate studies could be of interest on their own, the paper by Nurminen (1981) was concerned with the method of combining homogeneous relative risk estimates from independent samples to arrive at a quantitative estimate of the assumed common value of the effect parameter. Thus, in the derivation of the asymptotic variance we directly aimed at a system of weights that would converge to that of the efficient ML estimator of relative risk.

Gart (1962) questioned the applicability of the noniterative weighting method only to data which either are assumed to have equal relative risks or have been selected by having passed tests as to the homogeneity of the relative risk. Mantel, Brown and Byar (1977) advised that tests of for homogeneity be conducted with care and that primary concern should be given to trying to determine, by inspection of the data, how to make studies homogeneous rather than to demonstrate their heterogeneity. Tarone, Gart and Hauck (1983) recommend that, "in most instances it would seem reasonable to follow the traditional course of searching for the 'best' estimator in finite samples among those
which are asymptotically efficient." The choice of an estimator to use in a particular case should not be determined by asymptotic efficiency alone.

The choice among the various point estimators of relative risk can be made in two stages. The first choice is determined by the study design, i.e., whether the marginal total of the individual contingency tables can be regarded as random or fixed. The paper by Nurminen (1981) dealt only with the problem of estimation in the mathematically unrestricted sample space. The asymptote considered is the one where the sizes of a fixed number of strata increase to very large (infinity) – the other (unrealistic) course being that where the number of fixed-size strata grows unboundedly. Computational aspects and applicability to small samples (to be verified by simulation studies) affect the final choice.

Application of the theorem to epidemiologic studies has been considered in terms of the Mantel-Haenszel (1959) estimator and its analogues. The original MH summary odds ratio (OR) is applicable in case-referent studies and is formed as a ratio of summed numerator and denominator study-specific cross-products with shared weights 1/n_i:

\[
OR_{MH}^* = \frac{\sum x_{1i}(n_{0i} - x_{0i})/n_i}{\sum x_{0i}(n_{1i} - x_{1i})/n_i},
\]

where \(x_{1i}\) (index series) and \(x_{0i}\) (referent series) are independent binomial variates with parameters \(p_{1i}\) and \(p_{0i}\) and sample sizes \(n_{1i}\) and \(n_{0i}\): \(x_i = x_{1i} + x_{0i}\), \(n_i = n_{1i} + n_{0i}\). This estimator can be obtained as the first iteration in the calculation of the unconditional ML estimator of a common odds ratio (Tarone, 1981).

Bjerre (1995) explicated that the MH estimator can be interpreted as having a dual purpose: \(OR_{MH}^*\) is an estimate of the underlying parameter value when there is a common value \(OR\), and an estimate of the importance-weighted average of the stratum-specific estimates when there isn’t. Tarone (1981) presents the MH weights as approximately equal to precision weights (i.e. the inverse of the asymptotic variances of the stratum-specific estimates of odds ratio) when the common OR parameter is close to one.

For estimating a common risk ratio for application in cohort studies, from binomial data, Tarone (1981) proposed an analogue of the MH estimator given by

\[
RR_{B}^* = \frac{\sum n_0 x_{1i}/(n_i - x_i)}{\sum n_1 x_{0i}/(n_{1i} - x_{0i})},
\]

Nurminen (1981) proposed another common risk ratio or prevalence ratio estimator for cohort follow-up or cross-sectional studies that takes the form (see also Miettinen, 1985, expression 17.4)

\[
RR_{P}^* = \frac{\sum n_0 x_{1i}/n_i}{\sum n_1 x_{0i}/n_{1i}}.
\]

Formally this can be interpreted as a weighted average of the individual risk ratios (Hauck, 1979), with \(RR_i^*\) the estimate of \(RR_i\):

\[
RR_{P}^* = \sum w_i^* RR_i^*/w^*, \quad RR_i^* = R_{1i}^* / R_{0i}^*, \quad w_i^* = R_{0i}^*/(1/n_{1i} + 1/n_{0i})
\]

The asymptotic variance is given by \((RR)^2/w\), where \(w\) is the sum of study-specific weights \(w_i\). The weighting can thus be said to weigh the study-specific risk ratios according to their precision and importance, importance being measured by the occurrence rate in the population selected for reference, \(R_{0i}^*\). This estimator can be
obtained as the first iteration in the calculation of the ML estimator for Poisson variates (Tarone, 1981). In this sense, $RR^*_P$ is a natural analogue of the MH estimator for obtaining a summary risk ratio from Poisson data.

Tarone et al. (1983) published a paper in which they showed that the $OR_{MH}^*$ estimator is asymptotically inefficient, except when the common OR is equal to one, or in the degenerate case when the proportion of exposed cases and referents is respectively the same across strata. In the latter situation, stratification is not needed, for the sake of confounding, since the stratum-specific estimates $OR_i^*$ and the overall estimate will necessarily be the same. Nevertheless, the asymptotic relative efficiency of $OR_{MH}^*$ is very high over a wide range of parameters (Donner and Hauck, 1986).

Tarone et al. (1981) further explained that the $RR_B^*$ estimated in binomial sampling is asymptotically efficient if and only if the common risk ratio $RR=1$, i.e., under the null hypothesis. Thus this 'inefficient' estimator is not recommended.

Nurminen (1981) applied his theorem only to the estimator of $RR_P^*$ assuming a common risk ratio; he did not consider the asymptotic (in)efficiency of the $OR_{MH}^*$ and $RR_B^*$ estimators. It turns out that only for the balanced Poisson sampling design with equal sampling fraction for the index category of the exposure variate in each stratum, $RR_P^*$ is fully efficient, because then the estimate $RR_P^*$ equals the ML estimate of $RR_P$ for Poisson data, as proven by Tarone et al. (1983). The discrepancy between their and Nurminen's conclusions may be due to his focus on weighted average formulation of the MH estimator. Further, Nurminen gave a formal proof of the asymptotic efficiency of $RR_P^*$ only for the case of unvarying weights (cf. Gart, 1962). He did allude to the more general situation in which the change in $RR_P$ reflects the amount of sampling variability in the $w_i$s; then the partial derivative of $RR_P$ with respect to $RR_i$ may be defined as

$$D_i(RR_P) = \partial RR_P/\partial RR_i + (\partial RR_P/\partial w_i)(dw_i/dRR_i),$$

where the empirical, estimated weight is $w_i^* = w_i(RR_i^*)$, say.

Finally, given that the computational burden of finding an iterative solution for an common relative risk estimator is today not that severe, asymptotic efficiency should not be the only property in choosing the 'best' estimator. Performance in small sample situations should also be considered. Asymptotic, iterative estimators of relative risk, based on theoretical principles and with applicable properties, were suggested by Miettinen and Nurminen (1985).

References


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