

## Derivation of the weights for the Miettinen-Nurminen method for constructing confidence intervals of risk difference in the case of stratified data

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In the context of stratified data we have, for the chi-square statistic  $X_{RD}^2$  in expression 4 of Miettinen & Nurminen (1985), the variance estimator of

$$\tilde{V}_j = [\tilde{R}_{1j}(1-\tilde{R}_{1j})/S_{1j} + \tilde{R}_{0j}(1-\tilde{R}_{0j})/S_{0j}]S_j/(S_j-1)$$

(Miettinen (1985), equation 12.15). Note the use of the factor  $S_j/(S_j-1)$  which yields an unbiased estimator of the Bernoulli variance in the unconditional approach (Miettinen (1985), equation 11.3). When the stratum-specific data are quite sparse this factor becomes important. (In case of matched pairs this factor equals 2.) For a simulation study in the case of unstratified data, see Newcombe and Nurminen (2011).

The assumed unvarying weights ( $W_j$ 's) should be chosen proportional, as closely as possible, to the amount of comparative information in the  $j^{\text{th}}$  stratum; that is, to the inverse of  $\tilde{V}_j$ , obtained as the negative of the expected value of the second derivative of the log-likelihood function (Fisher information) evaluated at  $R_{ij}$ , whose estimator may be recast as

$$\tilde{V}_j = \{1/S_{1j} + \tilde{R}_{0j}(1-\tilde{R}_{0j})/[\tilde{R}_{1j}(1-\tilde{R}_{1j})S_{1j}]\}\tilde{R}_{1j}(1-\tilde{R}_{1j})S_j/(S_j-1).$$

On the assumption that  $\tilde{R}_{0j}(1-\tilde{R}_{0j})$ , and hence  $\tilde{R}_{1j}(1-\tilde{R}_{1j})$ , is constant over the strata, and given that the factor  $S_j/(S_j-1)$  equals unity in large samples, the weights may be taken as (analogously with the Cochran weights; for the derivation in the case of a general comparative parameter, see Nurminen (1988), p. 180)

$$W_j = [1/S_{1j} + \tilde{R}_{0j}(1-\tilde{R}_{0j})/(\tilde{R}_{1j}(1-\tilde{R}_{1j})S_{0j})]^{-1}.$$

However, this expression still involves the data-dependent, unstable ratio of the estimated unit variances. The problem may be alleviated by assuming constancy of those variances over the strata and by using an overall estimate of that ratio, that is, by taking the weights as (Miettinen (1985), equation 12.16)

$$W_j = \{1/S_{1j} + \tilde{R}_0^* (1-\tilde{R}_0^*)/[\tilde{R}_1^* (1-\tilde{R}_1^*)S_{0j}]\}^{-1},$$

with  $\tilde{R}_i^* = \sum_j W_j \tilde{R}_{ij} / \sum_j W_j$ ,  $i = 1, 0$ . The factor  $\tilde{R}_1^* (1-\tilde{R}_1^*)$ , a constant over the strata, is omitted as inconsequential in the above equation.

An alternative formulation is (M&N (1985), equation 16)

$$W_j = \{\tilde{R}_1^* (1-\tilde{R}_1^*)/[\tilde{R}_0^* (1-\tilde{R}_0^*)S_{1j}] + 1/S_{0j}\}^{-1}.$$

As admitted in the paper, this definition of the weights is somewhat circular. The proposed weighting strategy requires an iterative procedure to implement, which is nested within another procedure for finding the confidence limits. The initial weights might be  $(1/S_{1j} + 1/S_{0j})^{-1}$ ; these imply initial values for  $\tilde{R}_1^*$  and  $\tilde{R}_0^*$ , and the latter the first improved values for  $W_j$ ; etc. For a computational example, see Miettinen (1985), Section 12.1.2; Nurminen (1988), p. 181-3.

#### References (updated 13.6.2016)

For a list of publications on the topic of Comparative Rate Analysis, see:  
<http://www.markstat.net/en/research/interests> -> Comparative Rate Analysis

In particular, the stratified analysis of rate/risk difference in 2x2 tables is addressed in the following publications:

Kaifeng Lu. Cochran-Mantel-Haenszel weighted Miettinen & Nurminen method for confidence intervals of the difference in binomial proportions from stratified 2x2 samples. American Statistical Association, Alexandria, VA: *ASA Proceedings of the Joint Statistical Meetings*, 2008;3888-93.

This paper examines first the Miettinen-Nurminen method, which is nested within another iterative procedure for finding the confidence limits. The M&N weights are defined through the weighted averages of constrained MLEs, which in turn, are specified using the M&N weights. It next suggests to use the Cochran-Mantel-Haenszel weighting strategy that does not require an iterative procedure to implement. Finally, Lu compared the performance of the M&N method with the CMH weighting strategy to that of the M&M method with the M&N weights. The evaluation yielded identical results with respect to bias, coverage probability and Type 1 error. The CMH weighting strategy produced slightly wider confidence intervals while significantly reduced the computing time (although the computational burden is not that severe).

Klingenberg B. A new and improved confidence interval for the Mantel-Haenszel risk difference. *Statistics in Medicine* 2014;33:2968-83. DOI: 10.1002/sim.6122  
This paper proposes and discusses a new score-type interval in terms of Cochran weights reflecting the amount of information provided by each stratum as it is done in the Mantel-Haenszel estimator of the common risk difference. This interval can be expressed in closed form. Secondly, it suggests an approach based on a statistic which is essentially the same statistic that Miettinen and Nurminen proposed for the stratified 2x2 case, although they used different weights. Simulation studies proved that Klingenberg's new confidence interval estimator and the Miettinen-Nurminen type interval outperform the other interval estimators under all considered scenarios.

Nurminen M. *Comparative Analysis of Two Rates. Some New Approaches*. (Doctoral dissertation). Helsinki: University of Helsinki, 1984.

Miettinen O, Nurminen M. Comparative analysis of two rates. *Statistics in Medicine* 1985;4(2):213 - 226. DOI: 10.1002/sim.4780040211

Miettinen OS. *Theoretical Epidemiology. Principles of Occurrence Research in Medicine*. Part II. *Data Analysis*. NY: Wiley, 1985.

Nurminen M. On pooled and stratified analysis of epidemiologic rates, *Public Health Reviews* 1988. Pages 179-183.

Newcombe RG, Nurminen MM. In defence of score intervals for proportions and their differences. *Communications in Statistics – Theory and Methods* 2011;40(7):1271-1282.

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MarkStat Consultancy Commentary 1.9.2012 © Markku Nurminen

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