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Comments on

"AN ALTERNATE METHOD FOR CALCULATING AN ODDS RATIO"
(J. Medicine, 6 (1975), pp. 15-26)

by Sister Rosalie Bertell

This paper is offered as an improvement on the Woolf-Haldane analysis of epidemiological retrospective studies. Even though we have not had sufficient time to dig deeply into this article, we have some doubts about its value and correctness.

In discussing this paper, it is helpful to refer to the following 2 × 2 contingency table:

	cases	controls
exposed	n_{11}	n_{12}
not exposed	n_{21}	n_{22}

(1)

where, in the present context, "cases" refers to cases of leukemia and "exposed" refers to exposure to a sick pet bird. "Not exposed" means no exposure to a pet bird, sick or otherwise. The n_{ij}'s are the numbers of subjects falling into each category.

Basically, the Woolf method is to calculate the log odds ratio:

$$\hat{\gamma} = \ln\left(\frac{n_{11}\, n_{22}}{n_{21}\, n_{12}}\right) \tag{2}$$

and its variance, which is approximately

$$V(\hat{\gamma}) \sim \frac{1}{n_{11}} + \frac{1}{n_{12}} + \frac{1}{n_{21}} + \frac{1}{n_{22}} \tag{3}$$

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When several tables of the form (1) exist (e.g., one for each age group), Woolf's estimate of the log of the common odds ratio γ is the weighted average of the $\hat{\gamma}_i$ given by (2), with weights inversely proportional to the variances given by (3).

Haldane's modification of this procedure is simply to add 0.5 to each cell before going through the calculation. This not only reduces the bias in the estimated log odds ratio, but it avoids the problems caused by empty cells in the calculations (2) and (3).

As Sister Bertell points out, the Woolf-Haldane method can be unsatisfactory if any of the n_{ij}'s are small, but she seems to have dwelled almost entirely on the influence of Haldane's modification, i.e., the addition of 0.5 to each cell. The effect of this modification is negligible, however. For example, note in Table IV on p. 20 that the greatest disparity between the two methods seems to occur for males 65 and over. Here the Bertell estimate of relative risk (which for a single 2 × 2 table is just the straightforward odds-ratio) is 3.16 as compared with 2.23 for the Woolf-Haldane estimate. Using Woolf's approximation (3) for the variance of the log odds ratio, the approximate 95% confidence interval for the odds ratio turns out to be (0.48, 20.70). In view of this wide range of "acceptable" values for the odds ratio, the effect of Haldane's correction is of no consequence.

Sister Bertell correctly observes, however, that there is a difference between her "constructed population" estimate of the relative risk and the Woolf-Haldane estimate when the data from several subpopulations (e.g., age groups) are combined. This difference is a consequence of the fact that her method does not estimate relative risk in any well defined sense. Consider, for example, the data below, which is exaggerated to make the point.

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	Cases	Controls
Exposed	93	25
Not exposed	907	975
	1000	1000

Males

	Cases	Controls
Exposed	973	900
Not exposed	27	100
	1000	1000

Females

(4)

The odds ratios are 4.00 for both males and females. Using the Woolf-Haldane method, we calculate an estimate of 1.37 for the log odds ratio in each table. Taking the appropriate weighted average, we obviously get 1.37 for the estimate of the common log odds ratio, from which the estimated odds ratio is $e^{1.37} = 3.95$.

Sister Bertell's "constructed population" method, if we understand it correctly, would be applied to the same data as follows.

Expected cases exposed (males) $= \frac{25}{1000} \times 1000 = 25$

Expected cases not exposed (males) $= \frac{975}{1000} \times 1000 = 975$

Expected cases exposed (females) $= \frac{900}{1000} \times 1000 = 900$

Expected cases not exposed (females) $= \frac{100}{1000} \times 1000 = 100$

These expected numbers are calculated on the basis of the observed frequencies in the control population. Note that for males (or females) alone, the "relative risk" defined by Sister Bertell is

$$\frac{\text{observed cases exposed}}{\text{expected cases exposed}} \; \frac{\text{expected cases not exposed}}{\text{observed cases not exposed}} = 4.00$$

That is, for a single table, Sister Bertell's relative risk is exactly the usual odds-ratio. In combining the two tables, however, she sums before going through the odds-ratio calculations, so she obtains a table like the one on

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page 19. The corresponding table for the data in our example is

	With exposure	Without exposure
Cases	1066	934
Expected numbers	925	1075

The relative risk defined by Sister Bertell is 1.33. The deviation of this value from the Woolf-Haldane estimate certainly cannot be ascribed to a "bias" in the Woolf-Haldane technique. It is difficult to see how Sister Bertell's method can possibly be a "meaningful summary estimate of the relative risk," as is claimed in the abstract.

Sister Bertell also seems to be assuming (on p. 19) that the summed number of cases exposed has a Poisson distribution under the null hypothesis. We suspect this is not true in general; at any rate she should state the assumptions under which it holds.

Incidentally, when Mantel's and Haenszel's suggested estimate of the common odds ratio is applied to the data of our example, we get

$$\hat{\gamma} = \frac{\frac{(93)(975)}{2000} + \frac{(973)(100)}{2000}}{\frac{(907)(25)}{2000} + \frac{(27)(900)}{2000}} = 4.00$$

which, like the Woolf-Haldane result, is sensible. Sister Bertell apparently views her method as an extension of Mantel-Haenszel, but it seems to be an extension in the wrong direction.

Numerous other methods exist for estimating a common odds ratio. (See, for example, Gart's 1970 article in Biometrika, p. 471.) These estimates can be considered summary statistics even though the odds ratio may not in

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fact be constant. However, there are many dangers involved in pooling heterogeneous odds ratios.

With respect to the originality of the method, Sister Bertell's "constructed population" appears to be the same as the "indirect age adjustment" often used by epidemiologists in comparing disease incidences among populations with different mortality rates.

In summary, we feel that although Sister Bertell's effort to bring statistical techniques to the attention of medical researchers is commendable, it would be better for all concerned if her work were first subjected to the scrutiny of the editors and referees of a statistical journal.

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