

A statistical note on the analysis of the 1948 MRC streptomycin trial

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I was recently asked for my opinion about the statistical analysis likely to have been used by Bradford Hill in analysing the results of the Medical Research Council's celebrated trial of streptomycin for pulmonary tuberculosis.¹ I think he would almost certainly have used the chi-square test. Or, equivalently, he might have taken the ratio of the difference in death rates to its estimated standard error as a standard normal deviate (this being the square root of the chi-square value). Either of these would have seemed ideal examples of the techniques he would have been teaching to his Diploma in Public Health students, and which he included in successive editions of the textbook first published in 1937.²

The chi-square for the differences in mortality in the two groups compared in the streptomycin trial is 7.38. On one degree of freedom, this has a p value between 0.01 and 0.001. The difference in fatality rates is 2.72 times its standard error, 2.72 being $\sqrt{7.38}$. Bradford Hill might have considered a continuity correction to the chi-square (although I would not advocate it and it would not normally be done for the test on the difference in proportions). If this is done, the chi-square goes down to 6.04, with a p value between 0.01 and 0.025, so, on the basis of the information in the paper, I guess he did not do this.

I do not think that, at that time, Bradford Hill would normally have thought in terms of a ratio of

death rates. The ratio observed in the streptomycin trial, 3.70, is very imprecise and I do not think Bradford Hill would have thought it worth estimating. The relative risk came into fashion much more with the analysis of case-control studies, where it became apparent that the population odds ratio can be estimated from case-control data, and that for rare diseases, this will be very close to the relative risk (that is, the ratio of risks).

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