bility of recruiting so many patients the demonstration of such a small difference does not seem to us really important from the theoretical or clinical point of view.

M QUATRINI, G BASILISCO AND P A BIANCHI
Cattedra di Patologia Medica III
Istituto di Clinica Medica I
University of Milan, Italy

References

- 1 Linton M, Gallo PS Jr. *The practical statistician*. Monterey, California: Brooks Cole Publishing Company, 1975: 330-3.
- 2 Bardhan KD. Non-responders to cimetidine treatment, part 2. In: Baron JH, ed. *Cimetidine in the 80s*. Edinburgh: Churchill Livingstone, 1981: 42-57.

Appropriate statistical test in comparative ulcer healing studies

SIR,—The recent paper by Lam *et al*¹ draws attention to the possible value of tripotassium dicitrato bismuthate (TDB) in the treatment of cimetidine-resistant duodenal ulcers and, in the process, highlights an important aspect of the burgeoning problem of medical statistics. In the study 25 patients whose ulcers had not healed after four weeks of treatment with cimetidine (1 g/day) were randomised to a further four weeks of treatment with either TDB (four tablets/day) or cimetidine (1.6 g/day). Ulcer healing occurred in 10 of 12 patients receiving TDB and five of 13 patients receiving cimetidine. These results are tabulated below, with expected frequencies in brackets:

	Healed	Unhealed
TDB	10 (7.2)	2 (4.8)
Cimetidine	5 (7.8)	8 (5.2)

The χ^2 -test with Yates' correction for continuity² was allegedly used to assess the difference in healing between the two groups, and this was claimed to be significant at the 2% level. Scrutiny of the data, however, suggests that this significance was achieved using the χ^2 -test ($\chi^2 = 5.24$, $p < 0.02$ as in the text) and not the χ^2 -test with Yates' correction ($\chi^2 = 3.53$, $p > 0.05$). Fisher's test of exact probability for the data gives a p value of 0.0286 (one tail). As there is, *a priori*, no reason to suspect that TDB is necessarily better than cimetidine the two-tailed value of 0.057 applies, which is again not significant at conventional levels.

In view of these findings, and because 2×2 tables are so commonly used in gastroenterology to analyse the results of comparative ulcer healing studies, review of the criteria for choosing when to

use the χ^2 -test, Yates' correction, and Fisher's exact test seemed warranted. There was no consensus as to what constitutes the smallest expected frequency or number of observations which will provide reliable results using the χ^2 -test.³ On the use of Yates' correction or Fisher's test for 2×2 tables the most frequently quoted authority is the time-honoured Cochran, who stated:⁴ 'Use Fisher's exact test (i) if the total N of the table is < 20 , (ii) if $20 > N < 40$ and the smallest expectation is less than 5. If $N > 40$ use χ^2 corrected for continuity if the smallest expectation is less than 500'. Now that tables of significance levels for Fisher's test have been published for N up to 60⁵, however, it has been considered preferable to use these for all sample sizes up to 60 irrespective of the values of the individual cells, and to use Yates' correction for all other 2×2 tables with expected frequencies of 5 or more in each cell.^{6,7} There would appear to be no place for an unmodified χ^2 test in analysis of 2×2 tables in comparative clinical trials as carried out at present.

It seems, therefore, that however one interprets the above criteria Lam *et al*¹ have used inappropriate methods to analyse their data. This in no way detracts from the interest of their paper, however, or the conclusion drawn from the later cross over part of the study which achieved significance at the 2% level with both Fisher's test and the χ^2 -test with Yates' correction.

E BOYD AND I N MARKS

Gastrointestinal Clinic,
Department of Medicine,
University of Cape Town,
Cape Town, South Africa

References

- 1 Lam SK, Lee NM, Koo J, Hui WM, Fok FH, Ng M. Randomised crossover trial of tripotassium dicitrato bismuthate versus high dose cimetidine for duodenal ulcers resistant to standard dose cimetidine. *Gut* 1984; **25**: 703-6.
- 2 Snedecor GW, Cochran WG. *Statistical methods*. Ames, Iowa: Iowa State University Press, 1967.
- 3 Roscoe JT, Byars JA. An investigation of the restraints with respect to sample size commonly imposed on the use of the Chi-square statistic. *J Am Statist Ass* 1971; **66**: 755-9.
- 4 Cochran WG. The χ^2 -test of goodness of fit *Ann Math Statist* 1952; **23**: 315-45.
- 5 Documenta Geigy. *Scientific Tables*, 7th ed. Macclesfield: Geigy Pharmaceuticals, 1970.
- 6 Langley R. *Practical statistics*. New York: Drake Publishers Inc, 1971.
- 7 Armitage P. *Statistical methods in medical research*. Oxford: Blackwell Scientific Publications, Oxford, 1971.