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References

The need for confidence intervals in reporting clinical trials
Sir,—At first glance Lucey et al’s randomised controlled trial of bran in irritable bowel syndrome (*Gut* 1987; 28: 221–5) appears to show that this treatment amounts to no more than trial by bran. Before accepting their conclusion that the beneficial effects of bran are due to a placebo response, however, it is instructive to calculate the confidence interval on which they base this conclusion.

According to Figure 1 of their paper, 10 (70%) of 14 patients had a reduction in symptom score of greater than 2 after three months on bran biscuits, compared with 8 (57%) of 14 patients on placebo biscuits for three months. Using conventional methods for calculating the standard error of the difference between two sample proportions, the 95% confidence interval around the 14% difference in response, runs from −20% to +50%.1 In other words, the trial result is compatible with the true proportion of subjects responding to bran being 50% more than the proportion responding to placebo. This is a difference I think most clinicians would regard as worth obtaining. Indeed, considering the lack of efficacy of drugs and other measures in irritable bowel syndrome, a difference of only 20% might be regarded as worth obtaining.

Similar considerations apply to Chapman et al’s trial of metronidazole in acute ulcerative colitis (*Gut* 1986; 27: 1210–2). In that study 14 (74%) of 19 patients receiving metronidazole recovered without colectomy compared with 14 (70%) of 20 patients not receiving metronidazole. The 95% confidence interval on this difference extends from −24% to +32%. Again, this interval includes a potential benefit many clinicians might regard as worth having, as well as the potential for harm.

The authors of both these papers may well be right about their conclusions, but equally, these two small trials are open to considerable risk of Type 2 errors—that is, they may falsely accept the null hypothesis of there being no difference when important clinical differences do exist.3 Some may argue as to whether a 50% benefit from taking bran or a 32% benefit from metronidazole are clinically important but at least by stating a confidence interval, referees and readers can judge for themselves. Surely *Gut* should now adopt the policy of other leading journals and ask authors to state the relevant confidence intervals?

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References

Reply
Sir,—Thank you for the opportunity to respond to Dr Logan’s letter. In our study of the efficacy of bran in irritable bowel syndrome, on comparing the initial response to bran or to placebo in two groups of 14 subjects; or on comparing in a crossover fashion the responses to bran and placebo in all 28 subjects; or finally on stratifying the subjects according to the effect of bran on stool weight, no therapeutic advantage of bran over placebo could be demonstrated.1 Thus we could not reject the null hypothesis that bran and placebo are similar. The possibility of a Type 2 error exists in any study which does not reject the null hypothesis. In studies such as ours, however, given the relatively small numbers, a confidence interval based on either data from the initial treatment period or the crossover analysis is likely to contain zero, be fairly wide and include both positive and negative values. Therefore this is not an appropriate setting for this form of analysis as the result always will be too diffuse to be meaningful. Confidence intervals are of value in larger studies in which the null hypothesis is rejected because they allow the reader to judge whether a statistical significant observation is of clinical significance.2

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References

IgA protease-producing bacteria in patients with ulcerative colitis

Sir,—We have studied the relationship between IgA protease producing bacteria and the pathogenesis of inflammatory bowel disease for several years. We read with great interest the study by Barr et al (Gut 1987; 28: 186–9) concerning IgA1 protease activity of the colonic bacterial flora obtained from five patients with ulcerative colitis. They concluded that colonic bacterial IgA1 protease production was unlikely to contribute to the pathogenesis of ulcerative colitis, on the basis that any isolate from patients with ulcerative colitis was unable to provide IgA1 protease activity.

In our studies, four bacterial strains (three strains of Bifidobacterium spp and one strain of Clostridium sp) capable of releasing IgA proteases were isolated from faecal material of three of 17 patients with inflammatory bowel disease.1 Interestingly, the extracellular enzyme produced by Clostridium ramosum from an ulcerative colitis patient was specific to not only IgA1, but also to IgA2 (A2m(1) allotype).2–3 The isolate frequency of C1 ramosum producing IgA protease was no more than 3%, although IgA protease negative C1 ramosum was indigenous (approximately 80% detected) in the human intestinal tract.4 So far, we have no evidence supporting that IgA protease played a role in the pathogenesis of inflammatory bowel disease.

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Colorectal carcinoma in ulcerative colitis

Sir,—The Swedish study1 of the accompanying editorial2 in a recent issue of your journal has reiterated the need for cancer surveillance in patients with long standing ulcerative colitis. The Swedish study does not clarify the referral pattern of their centre. Two other recent editorials3 4 have pointed out that most of the cases of carcinoma complicating ulcerative colitis have been reported from tertiary referral centres. Another interesting comment in some of the recent articles is that this complication may have some geographical basis as well.5 6 Studies from Czechoslovakia,7 Denmark8 and Israel9 have failed to show the higher risk of cancer reported from other countries.6 10 The Czechoslovakian study was from a centre which was getting referrals of all patients with ulcerative colitis over a period of 40 years.1 Thus the bias of a referral centre reporting an exaggerated incidence of cancer in such patients was excluded. The authors pointed out that colorectal cancer is not uncommon in the general population. The study from Denmark accounted for more than 99% of the patients with ulcerative colitis in the region.6

Although ulcerative colitis is not uncommon in India, the complication of cancer has been rarely reported among Indians.11 This observation has led some of the gastroenterologists to proclaim that surveillance in Indian patients may not be warranted.1 We do not agree with this but feel that there is a strong geographical basis for the development of colitis carcinoma. At our centre, which is a referral hospital for five of the north Indian states, we have encountered four cases of carcinoma complicating ulcerative colitis in the last 10 years. In the same period about 400 cases of ulcerative colitis have been managed by us.

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