4 Bardhan KD, Macsdal J, Bianchi-Porro G, *et al.* Omeprazole in the treatment of refractory peptic ulcer. [Abstract] *Gastroenterology* 1988; **94:** A22.
5 Bianchi-Porro G, Parente F. Duodenal ulcers resistant to H_2 blockers: an emerging therapeutic problem. *Scand J Gastroenterol* 1988; **23:** [suppl 153]: 81–8.
6 Crowe JP, Wilkinson SP, Bate CM, Willoughby CP, Peers EM, Richardson PDI. Symptom relief and duodenal ulcer healing with omeprazole of cimetidine. *Aliment Pharmacol Ther* 1989; **3:** 83–91.

Processing gastric pH measurements

SIR,—The paper by Chiverton *et al*[1] not only provides stimulating clinical pharmacological results, but also uses a non-traditional approach for processing gastric pH measurements.

For each subject, a working file was obtained by averaging raw fast acquired pH recordings of each minute (1440 points/24 h). The average acidity during a given time window was expressed as the arithmetic mean of pHs. This acidity index was normally distributed on the basis of the assessment of skewness and kurtosis among their 15 subjects, and therefore it could be handled using parametric statistics for assessing differences, if any, between treatments. The 0·01 probability threshold was used and mean circadian pH profiles were drawn to describe the average behaviour of each treatment.

This work contains several interesting innovations. The use of one minute averaged working files reduces the reading noise and provides tracings which are comparable with those obtained with higher frequency scanning rates, without loss of relevant information.[2] Such a standardisation is necessary, as the value of acidity indexes is function of the working sampling rate.[2] The mean of pHs is an index of average acidity during a predefined time window which is more reliable than the median, particularly when drug related events are concerned.[3] Where appropriate, parametric statistics allow the use of numerous powerful techniques which are more robust than equivalent non-parametric methods[4] or exist only in the parametric form. The 0·01 probability threshold is five times more severe than the commonly adopted 0·05, thus making it possible to arrive at firmer clinical conclusions.

The demonstration that means of pHs are normally distributed among the whole population is a crucial point of this paper. The authors calculated skewness and kurtosis to assess the normality of this acidity index, but, as the distribution of these moments of the mean 'does not approach the normal closely until the sample size is over 1000',[5] the results they obtained from 15 subjects must be confirmed on larger samples.

In the Figure are reported the frequency distributions of both 24 h means and medians of pHs calculated from one minute averaged 259 pH profiles we obtained with bedtime and twice daily doses of various H_2 blockers (famotidine 40 and 20 mg; ranitidine 300 and 150 mg, nizatidine 300 and 150 mg, cimetidine 800 mg). As one can see, the individual 24 h means of pHs are normally distributed, whereas the medians are far from having a gaussian distribution.

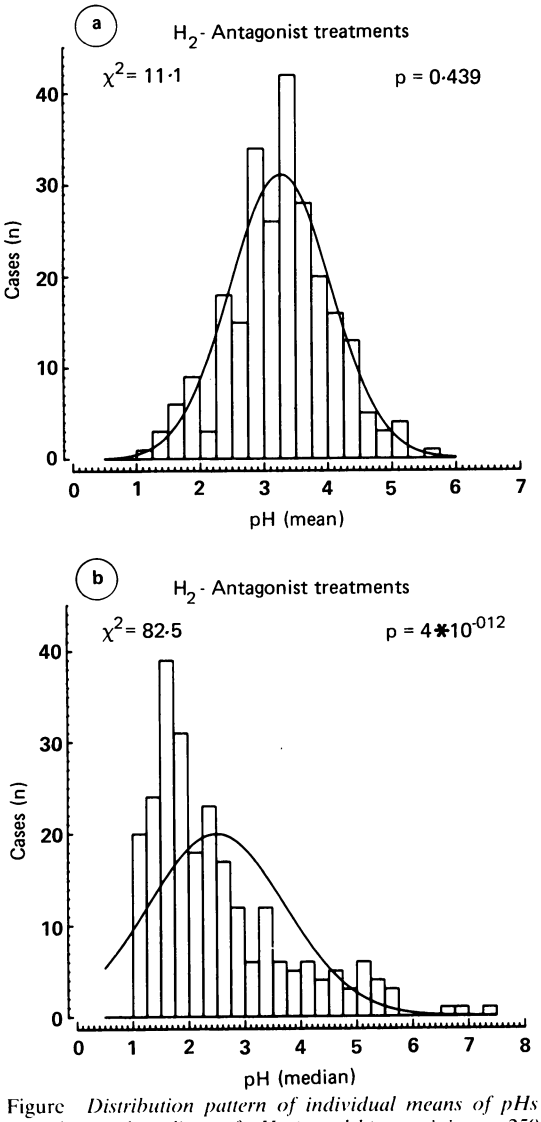

Figure *Distribution pattern of individual means of pHs (panel a) and medians of pHs (panel b) pertaining to 259 circadian pH profiles obtained with various H_2 antagonists. χ^2 values refer to the assessment of agreement of the two distributions with the normal one.*

These data corroborate those of Chiverton and colleagues, and, in our opinion, this processing method should be used routinely, at least when dealing with 24 hour gastric acidity studies on antisecretory drugs.

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References

1 Chiverton SG, Burget DW, Hunt RH. Do H_2 receptor antagonists have to be given at night? A study of the antisecretory profile of SKF 94482, a new H_2 receptor antagonist which has a profound effect on daytime acidity. *Gut* 1989; **30:** 594–9.
2 Mela GS, Savarino V, Moretti M, Bonifacino G, Sumberaz A, Zentilin P. Clinical relevance of sampling rate in the characterization and analysis of 24-hour gastric acidity. A report on 413 cases. *Scand J Gastroenterol* (In press).
3 Mela GS, Savarino V, Moretti M, Bonifacino G, Zentilin P. Mean and median of pH values, characterizing average intragastric acidity. *Am J Gastroenterol* 1989; **84:** 444–5.
4 Armitage P, Berry G. *Statistical methods in medical research.* Oxford: Blackwell, 1987: 419.
5 Snedecor GW, Cochran WG. *Statistical methods.* Ames, Iowa: The Iowa State University Press, 1967: 88.

Reply

SIR,—We should like to thank Drs Mela and Savarino for their kind comments which relate to the methods which we used for the analysis of pH data, and they raise several important points. The collection of pH data, whether obtained by aspiration at hourly intervals and measured *ex vivo*, or by continuous recording at six second intervals by intragastric pH electrode, provides more pH data than should be used in an assessment of overall acidity. This requires that a summary variable be calculated across time for each subject studied. This summary variable should provide a physiologically relevant measure of gastric acidity, and is not to be confused with the statistical concept of 'central tendency'. Furthermore, as total exposure to acid concentration is likely to be of greatest physiological consequence, any attempt to use statistics to compensate for non-normal distribution of raw pH data over time, may well obscure important fluctuations in intragastric pH. Drs Mela and Savarino have drawn attention to our observation that the means of pH across time appear to be normally distributed. It is worth emphasising that this refers to the distribution of the summary variable itself and not the underlying raw pH data. They are quite correct that skewness and kurtosis estimates require much larger sample sizes, but this is a practical impossibility in a single study.

We have also compared the mean and median as summaries of pH over time in a prospective series of six studies with 25 treatment arms, and involving a total of 296 individual 24 hour studies. Our results show that while the mean and median are highly correlated, the relationship is not linear, with the median significantly skewed to lower pH ($p<0{\cdot}00001$). The median 24 hour pH showed a greater skew in 20 of the 25 treatment arms, a higher variance in 21 of 25 treatment arms, and greater heterogeneity of variance in five of the six studies. These characteristics of the median result in a decreased sensitivity for detecting differences among drugs in all of the six studies. These results therefore confirm, in a prospective study, that the mean is a more robust summary of pH changes over time than is the median.

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Books

Statistics with confidence – confidence intervals and statistical guidelines. By M J Gardner and D G Altman. (Pp. 140; illustrated; £7·95.) London: *British Medical Journal*, 1989.

The use of confidence intervals in the presentation of data derived from clinical research is now required 'when appropriate' by a number of journals. This book is a compilation of articles, written for the *British Medical Journal*, that is intended as guidance and assistance for research workers with the new statistical orthodoxy. As one in need of guidance, I had two expectations from this book. First, a clear exposition of the benefits of confidence intervals, and second, an easily comprehensible demonstration of the methodology.

On the first point, I was looking for firm evidence that this shift in opinion does not merely represent the hijacking of the research community by a group of trendy statisticians, but I found myself not much the wiser. Certainly I agree that the abolition of the plus or minus sign for standard errors or deviation would be helpful because this sign is not usually found on computer keyboards and is not a standard