Relating Change to Initial Value

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Dear Sir,

A recent exchange of letters illustrates some important problems regarding the use of statistics in medical research.

Musso et al [1] analysed the change in free norepinephrine concentration after hemodialysis in relation to the predialysis levels. They found a correlation of $r = -0.98$ ($p < 0.0001$). Boer [2] pointed out that this was a spurious correlation, and in fact there was no association between pre- and postdialysis levels of free norepinephrine concentration ($r = -0.06$). Musso et al [3] rejected these criticisms. There is a danger that readers of your journal will either be confused by this disagreement, or will believe that Musso et al. have validly refuted Boer's criticisms. I am therefore writing as an independent statistician to explain why Boer [2] is correct.

The relation between change and initial value is often of clinical interest. However, examination of the simple correlation between these quantities will give a spurious high negative correlation because they are not independent. We can see this by expressing the quantities as $X_2 - X_1$ and X_1 . In other words, we expect a strong negative correlation between initial value and change for any measurements. For high X_1 we expect $X_2 - X_1$ to be low on average and vice versa. In fact, if X_1 and X_2 are random numbers we expect on average to get a correlation of -0.71 .

A proper analysis of such data is complex [4], and it is unlikely that such a small sample would yield useful answers. However, the simple plot of pre- and postdialysis values [Boer's fig. 1, 2] does not suggest that there is anything interesting in these data.

The reply by Musso et al. [3] beautifully illustrates two phenomena. Firstly, they use the specious argument that the methods used are 'widely accepted in important scientific journals'. All the references cited are from the same research group, but it is true that many such papers are published. Indeed, at least one further example has subsequently appeared in Nephron [5]. This does not make the method correct. Rather, it illustrates my second point, which is that scientific journals should use statistical referees to try to reduce (if not eliminate) the misuse of statistics in medical journals.

References

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