

Comparing methods of measurement: why plotting difference against standard method is misleading

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Summary

When comparing a new method of measurement with a standard method, one of the things we want to know is whether the difference between the measurements by the two methods is related to the magnitude of the measurement. A plot of the difference against the standard measurement is sometimes suggested, but this will always appear to show a relation between difference and magnitude when there is none. A plot of the difference against the average of the standard and new measurements is unlikely to be misled in this way. We show this theoretically and by a practical example.

Lancet 1995; **346**: 1085-87

Introduction

In earlier papers^{1,2} we discussed the analysis of agreement between methods of clinical measurement. We had two issues in mind: to demonstrate that the analyses then in use were incorrect and misleading, and to recommend a more appropriate method. We saw the aim of such studies as to determine whether two methods agreed sufficiently well for them to be used interchangeably. This led us to suggest that the analysis should be based on the differences between measurements on the same subject by the two methods. The mean difference would be the estimated bias, the systematic difference between methods, and the SD of the differences would measure random fluctuations around this mean. We recommended 95% limits of agreement, mean difference plus or minus 2 (more precisely, 1.96) SDs which would tell us how far apart measurements by the two methods were likely to be for most individuals.

Figure 1 shows a typical data set, the measurement of systolic blood pressure by a test method, finger pressure, and a standard method, arm blood pressure. This is a random subsample of 200 observations from a larger data set.^{3,4} The subsample was taken to avoid cluttered graphs. The mean difference, finger minus arm, is 4.3 mm Hg and the SD is 14.6. Hence the lower 95% limit is $4.3 - 1.96 \times 14.6 = -24$ mm Hg and the upper 95% limit is $4.3 + 1.96 \times 14.6 = 33$ mm Hg. Thus we estimate that for 95% of subjects the finger measurement will be between 24 mm Hg below the arm measurement and 33 mm Hg above it.

For the mean and SD of the differences to be meaningful estimates we must assume that they are reasonably constant throughout the range of measurement. We suggested checking this assumption graphically.^{1,2} The usual plot, method one versus method two, is inefficient because the points tend to be clustered

along the line of equality (figure 1), especially if the two methods give closely related measurements. We therefore proposed that the difference be plotted against the average of the measurements by the two methods (figure 2). In figure 2 we have also added the 95% limits of agreement and the regression line of difference on average. The main departure from assumptions we were expecting was an increase in variability, shown by an increase in the scatter of the differences, as the magnitude of the measurement increased. There may also be a trend in the bias, a tendency for the mean difference to rise or fall with increasing magnitude. Either would show that the methods did not agree equally through the range. In figure 2, for example, there is an increase in bias with magnitude, shown by the positive slope of the regression line. Such deviations from assumptions can often be dealt with by a suitable transformation, usually logarithmic.⁵ In particular, this approach will be effective if the differences are proportional to the magnitude of the measurement.

The 95% limits of agreement approach has been widely adopted and *The Lancet* paper¹ widely cited.⁶ However, it is sometimes argued that when one method may be regarded as a gold standard, it is presumably more accurate than the other method and so we should plot the difference against the gold standard.^{6,7} We think that this idea is misguided and is likely to lead to misinterpretation. Here we will show why, and that the plot of difference against average is almost always preferable.

Plotting difference against average

We denote our standard measurement by S , the new or test measurement by T , their variances by σ_S^2 and σ_T^2 , and their correlation by ρ . If the study includes a wide range of measurements, and unless the two methods of

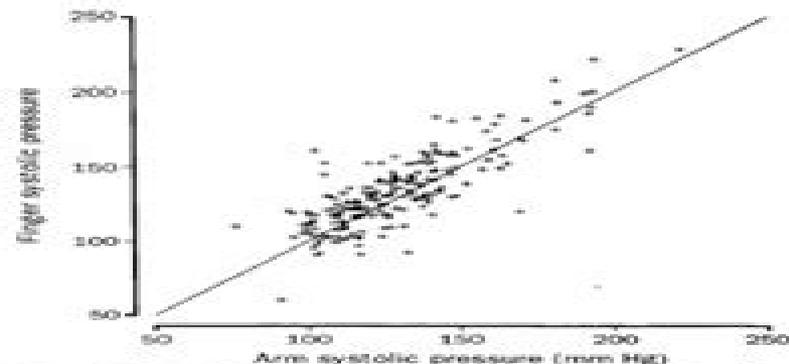


Figure 1: Test and standard measurements, with line of equality

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