

0.1 Regression Methods

Conventional regression models are estimated using the ordinary least squares (OLS) technique, and are referred to as ‘Model I regression’ (Cornbleet and Cochrane, 1979; Ludbrook, 1997). A key feature of Model I models is that the independent variable is assumed to be measured without error. As often pointed out in several papers (Altman and Bland, 1983; Ludbrook, 1997), this assumption invalidates simple linear regression for use in method comparison studies, as both methods must be assumed to be measured with error.

The use of regression models that assumes the presence of error in both variables X and Y have been proposed for use instead. (Cornbleet and Cochrane, 1979; Ludbrook, 1997), These methodologies are collectively known as ‘Model II regression’. They differ in the method used to estimate the parameters of the regression.

Regression estimates depend on formulation of the model. A formulation with one method considered as the X variable will yield different estimates for a formulation where it is the Y variable. With Model I regression, the models fitted in both cases will entirely different and inconsistent. However with Model II regression, they will be consistent and complementary.

Deming regression

The Deming regression line is estimated by minimizing the sums of squared deviations in both the x and y directions at an angle determined by the ratio of the analytical standard deviations for the two methods. This ratio can be estimated if multiple measurements were taken with each method, but if only one measurement was taken with each method, it can be assumed to be equal to one.

0.1.1 Deming's Regression

The most commonly known Model II methodology is known as Deming's Regression, (also known as Ordinary Least Product regression). Deming regression is recommended by Cornbleet and Cochrane (1979) as the preferred Model II regression for use in method comparison studies. As previously noted, the Bland Altman Plot is uninformative about the comparative influence of proportional bias and fixed bias. Deming's regression provides independent tests for both types of bias.

For a given λ , Kummel (1879) derived the following estimate for the Deming regression slope parameter. (α is simply estimated by using the identity $\bar{Y} - \hat{\beta}\bar{X}$.)

$$\hat{\beta} = \frac{S_{YY} - \lambda S_{XX} + [(S_{YY} - \lambda S_{XX})^2 + 4\lambda S_{XY}^2]^{1/2}}{2S_{XY}} \quad (1)$$

As with conventional regression methodologies, Deming's regression calculates an estimate for both the slope and intercept for the fitted line, and standard errors thereof. Therefore there is sufficient information to carry out hypothesis tests on both estimates, that are informative about presence of fixed and proportional bias.

A 95% confidence interval for the intercept estimate can be used to test the intercept, and hence fixed bias, is equal to zero. This hypothesis is accepted if the confidence interval for the estimate contains the value 0 in its range. Should this be, it can be concluded that fixed bias is not present. Conversely, if the hypothesis is rejected, then it is concluded that the intercept is non zero, and that fixed bias is present.

Testing for proportional bias is a very similar procedure. The 95% confidence interval for the slope estimate can be used to test the hypothesis that the slope is equal to 1. This hypothesis is accepted if the confidence interval for the estimate contains the value 1 in its range. If the hypothesis is rejected, then it is concluded that the slope is significant different from 1 and that a proportional bias exists.

For convenience, a new data set shall be introduced to demonstrate Demings regres-

sion. Measurements of transmitral volumetric flow (MF) by doppler echocardiography, and left ventricular stroke volume (SV) by cross sectional echocardiography in 21 patients withour aortic valve disease are tabulated in Zhang et al. (1986). This data set features in the discussion of method comparison studies in ?, p.398 .

Patient	MF (cm^3)	SV (cm^3)	Patient	MF (cm^3)	SV (cm^3)	Patient	MF (cm^3)	SV (cm^3)
1	47	43	8	75	72	15	90	82
2	66	70	9	79	92	16	100	100
3	68	72	10	81	76	17	104	94
4	69	81	11	85	85	18	105	98
5	70	60	12	87	82	19	112	108
6	70	67	13	87	90	20	120	131
7	73	72	14	87	96	21	132	131

Table 1: Transmitral volumetric flow(MF) and left ventricular stroke volume (SV) in 21 patients. (Zhang et al 1986)

Deming’s Regression suffers from some crucial drawback. Firstly it is computationally complex, and it requires specific software packages to perform calculations. Secondly it is uninformative about the comparative precision of two methods of measurement. Most importantly Carroll and Ruppert (1996) states that Deming’s regression is acceptable only when the precision ratio (λ , in their paper as η) is correctly specified ,but in practice this is often not the case, with the λ being underestimated.

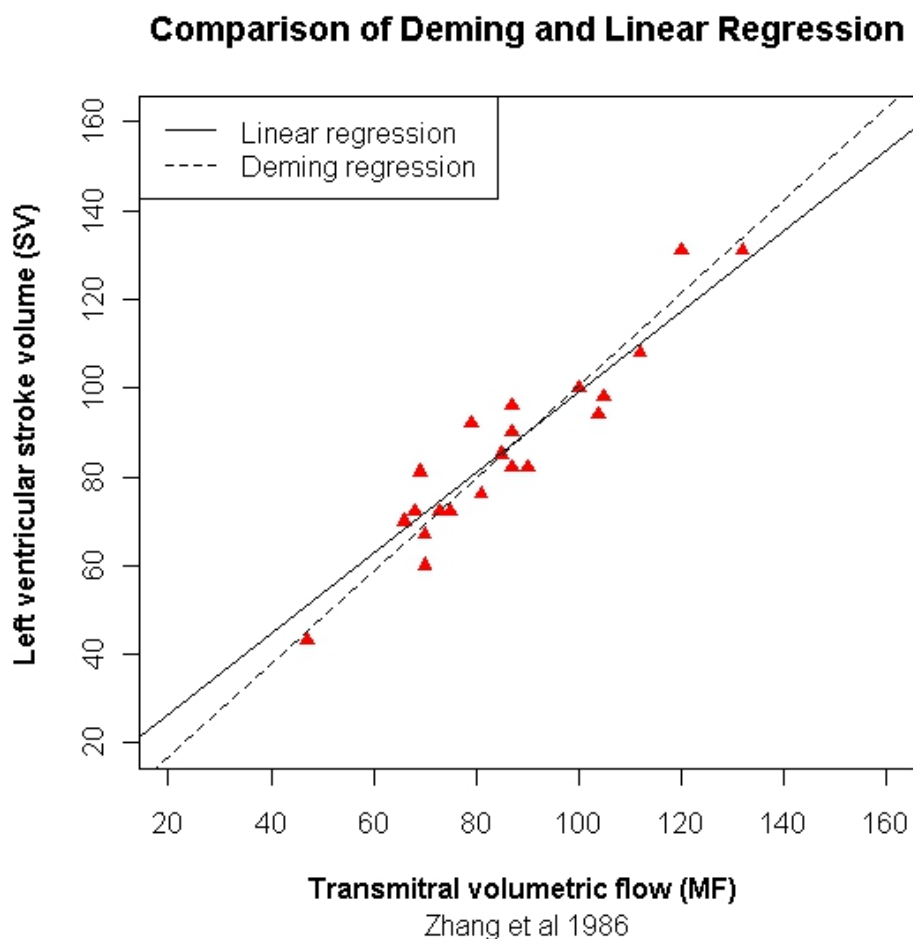


Figure 1: Deming Regression For Zhang's Data

Deming Regression

Performance of Deming regression analysis in case of misspecified analytical error ratio in method comparison studies

Application of Deming regression analysis to interpret method comparison data presupposes specification of the squared analytical error ratio (λ), but in cases involving only single measurements by each method, this ratio may be unknown and is often assigned a default value of one.

On the basis of simulations, this practice was evaluated in situations with real error ratios deviating from one. Comparisons of two electrolyte methods and two glucose

methods were simulated.

In the first case, misspecification of λ produced a bias that amounted to two-thirds of the maximum bias of the ordinary least-squares regression method. Standard errors and the results of hypothesis-testing also became misleading. In the second situation, a misspecified error ratio resulted only in a negligible bias.

Thus, given a short range of values in relation to the measurement errors, it is important that λ is correctly estimated either from duplicate sets of measurements or, in the case of single measurement sets, specified from quality-control data. However, even with a misspecified error ratio, Deming regression analysis is likely to perform better than least-squares regression analysis.

This paper presents an approach for making inferences about the intercept and slope of a linear regression model when both variables are subject to measurement errors. The approach is based on the principle of fiducial inference. A procedure is presented for computing uncertainty regions for the intercept and slope that can be used to assess agreement between two instruments. Computer codes for performing these calculations, written using open-source software, are listed.

EQUIVALENCE REGION

The equivalence region is specified by the user. It can be an ellipse, parallelogram, rectangle, or a region of some other appropriate shape. The way we use the fiducial region in this method is as follows. If the 1γ fiducial region that we construct is completely inside the equivalence region then we have established agreement.

maximum allowable difference of the two equivalent methods.

In this paper we have provided an approach for making inference on the intercept β_0 and slope β_1 of a linear regression model with both X and Y subject to measurement errors. Specifically, we have provided procedures for constructing uncertainty regions for (β_0, β_1) that can be used to assess agreement between two methods. The approach is based on fiducial inference.

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Use of deming regression in method comparison studies. Henk Konings

- Accuracy is closeness to the true value, or alternatively, having a low measurement error.
- The determination of a true value for a biological specimen is difficult and sometimes impossible.
- Precision is expressed in terms of standard deviation, coefficient of variance or variance.
- In Deming regression, the errors between methods are assigned to both methods in proportion to the variances of the methods.

0.2 Linnet - References

The statistical procedures are described in: Linnet K. Necessary sample size for method comparison studies based on regression analysis. Clin Chem 1999; 45: 882-94. Linnet K. Performance of Deming regression analysis in case of misspecified analytical error ratio in method comparison studies. Clin Chem 1998; 44: 1024-1031. Linnet K. Evaluation of regression procedures for methods comparison studies. Clin Chem 1993; 39: 424-432. Linnet K. Estimation of the linear relationship between measurements of two methods with proportional errors. Stat Med 1990; 9: 1463-1473.

0.3 Lewis Conversion

While regarding a comparison of two pump meters under operational conditions

..It is suspected that the various assumptions made by each method are weak under operational conditions Lewis listed several sources of variation that relate to the practical aspects of each measurement method.

There is little reasons to believe that the laboratory conditions of the devise provide a suitable basis for the conversion of data gathered under operational conditions.

Latent variables are variables that are not measured (i.e. not observed) but whose values is observed from other observed variables. One advantage of using latent variables is that it reduces the dimensionality of data. A large number of observable variables can be aggregated in a model to represent an underlying concept, making it easier for humans to understand the data. [wikipedia]

Bibliography

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