Estimating Differences in Variance when Comparing Two Methods of Assay

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Morgan’s test for the relative precision of two assays compared in the same set of samples is extended to the case where the underlying distribution may not be bivariate normal and where the units of the two assays may differ. The jackknife is also suggested for computing confidence intervals on the differences in variance or coefficients of variation.

Key Words
Comparative assay
Testing equality of two correlated variances
Jackknife

1. Introduction
It is common practice, when two methods of assay are to be compared, to collect pairs of data taken from individual samples assayed first by one method, then by the other. The first method might be a widely used procedure and the second a simpler or a “more accurate” method proposed to replace it; or, the first method might be an exhaustive but expensive procedure while the second method might be a less expensive substitute which is hoped to be “sufficiently accurate.” It is a simple matter to compare the means of the two methods or to regress one method’s estimates on the other’s with tolerance bounds on the predicted regressant. Other questions that can be legitimately asked of the data concern the relative precision of the two methods. Which has the smaller variance? How can one construct confidence bounds on the difference in variance between the two? If the two methods result in measurements of different units, how can one compare the coefficients of variation?

2. Morgan’s Test
One approach to this problem is due to W. A. Morgan [6]. If we denote the two correlated measures as X and Y, then

\[ \text{Cov}(X + Y, X - Y) = \text{Var}(X) - \text{Var}(Y), \]

and a test for zero correlation between the sum and difference of the measures is equivalent to a test for equal variance. Morgan derived this test as a monotone function of the likelihood ratio test for equal variances and showed that if the measures are bivariate normal, it was as powerful as a generalization of the usual F test for a ratio of sample variances due to Finney [1]. That is, this test is as good as the usual ratio test when there is a zero correlation between the two measures and, as a monotone function of the likelihood ratio, it can be looked upon as a uniformly most powerful test against the hypothesis of unequal variances within the class of all bivariate normal distributions.

Although Morgan derived the test from normality assumptions, it can be applied in a more general context. The identity between the variances of X and Y and the covariance of (X + Y) and (X - Y) holds without normality assumptions. Thus, any robust test on the hypothesis that the underlying correlation is zero will hold. Fisher [2] has shown that normal theory tests on the hypothesis of zero correlation are robust in the face of moderate deviations from normality. For readers who do not trust such vague statements about robustness, a distribution free test on the Spearman Rank correlation between (X + Y) and (X - Y) can be used (see Olds [7]).

There is still another extension of the Morgan test. It may happen that the two methods of assay yield values in different units of measure. In that case, we make use of a first order approximation

\[ \text{Var}(\log(X)) = \text{Var}(X)/E(X)^2 \]

which is the square of the coefficient of variation. Then, if we let

\[ W = \log(X) \]
\[ V = \log(Y), \]

a test on the correlation of \((W + V) = \log(XY)\) and \((W - V) = \log(X/Y)\) will be a test on the equality of the squares of the coefficients of variation.

Thus, the Morgan test is a powerful omnibus test that can be applied with some confidence over almost the entire range of comparative assays, in spite of suspected non-normality or the use of differing units of measurement.
3. Estimating Differences in Variance

There are times when it is useful to estimate the difference in variance and confidence bounds on that difference. It is, of course, possible to compute confidence bounds on the correlation between \( (X + Y) \) and \( (X - Y) \) or between \( \log (XY) \) and \( \log (X/Y) \). However, the correlation between \( (X + Y) \) and \( (X - Y) \) involves the (usually unknown) correlation between \( X \) and \( Y \). A procedure which does not involve knowledge of the between-measure correlation would be to jackknife the sample covariance between the two derived variables. Miller [5] has a good survey of the current state of the jackknife.

To illustrate its use in this case, we consider the data shown in Table 1. Here 13 samples were split and assayed first by a radioactive method and then by a much simpler visual estimate based on a color code from a less expensive assay. The two measures are in different units, and so it is appropriate to compare the coefficients of variance. The sample correlation between \( \log (XY) \) and \( \log (X/Y) \) is \(-0.090\), which is not significantly different from zero.

We now apply the jackknife to estimate confidence bounds on the difference between squared coefficients of variation. The sample covariance between \( \log (XY) \) and \( \log (X/Y) \) is \(-0.0169\); for notational simplicity, we label this \( \hat{\theta} \). Next, we eliminate the first pair and recalculate the sample covariance of \( \log (XY) \) and \( \log (X/Y) \) from the remaining twelve, yielding a value of \(0.0247\), we label this \( \hat{\theta}' \), indicating that it was calculated from all but the first observation. Then, the first “pseudo-variate”, labeled \( \hat{\theta}_1 \), is calculated as

\[
\hat{\theta}_1 = \frac{n}{n-1} \hat{\theta} - (n - 1) \hat{\theta}'
\]

yielding a value of \(-0.516\). This first pseudo-variate can be thought of as the contribution of the first observation pair to the overall estimate of covariance. We continue this way, eliminating one pair at a time, and replacing the previously eliminated pairs, yielding the 13 pseudo-variates, displayed in Table 1. The sample covariance is a U-Statistic, and it has been shown (see Miller [5]) that jackknifed U-Statistics have the property that their pseudo-variates are asymptotically independent and that we can apply the usual \( t \)-statistic bounds using the mean of the pseudo-variates and their sample variance. Here, the overall mean

\[
\hat{\theta} = \frac{1}{n} \sum \hat{\theta}_i = -0.0169
\]

and the sample variance

\[
S^2 = \sum (\hat{\theta}_i - \hat{\theta})^2/(n - 1) = 0.0443
\]

yielding 90% confidence bounds on the difference of the squared coefficients of variation of

\[
\hat{\theta} \pm 1.783 S/\sqrt{n} = [0.121, 0.087].
\]

4. Concluding Remarks

The referee has pointed out that this discussion deals entirely with the variance due to assay. The variance of a specific measure consists of two components, that due to the inherent variability of the material being assayed and that due to the method. If the inherent variance is small in comparison to the assay variance, then Morgan’s test will be a useful tool for discrimination. If, however, the inherent variance is much greater than the variance due to method of assay, it may swamp this second component and Morgan’s test (dealing as it does with the difference of two variances) will miss what might be a ratio of the smaller components that is considerably greater than one. Grubbs [3] and Maxwell [4] represent an attempt to get at this problem within the framework of analysis of variance.

I would also like to thank the same referee for calling my attention to Morgan’s work after an earlier version of this paper had derived a small part of Morgan’s work independently.

References