As the joint distribution of sample means of normal populations is a function of the ratio of their unknown variances, tests based on the difference between sample means of normal populations with unknown unequal variances are inexact, and not a *t*-test.[4]

This problem is not removed by meaninglessly[5] testing for the equality of variances, or avoiding normality with its nuisance unknown variances with nonparametric rank tests such as the Wilcoxon test. Being a comparison of distributions, these rank tests say nothing specifically about the mean, median, or any moment of the distributions if significant. They are moreover biased[6] to one side in a two-sided test.

Tsakok[7] has solved this Behrens–Fisher problem of comparing the means of normal distributions with unknown variances at exact significance levels, showing that the Tsakok solution is more effective in detecting significant mean differences even with unknown equal variances. There is an indication[8] that the Tsakok technique applies to dependent samples. Its exposition[9] is available.

The software GSP implements the Tsakok technique. It is now used for mean comparisons at 0.02 significance level (one significant figure) per pair.

Unfortunately, it is not possible to apply GSP to the article by Loukovaara *et al*[3] because, ignoring baseline characteristics, they did not publish the sufficient statistics for ANOVA (sample means and standard deviations), obstructing the minimum requirement of facilitating independent verification.

For Table 3,[1] there are significant mean differences between phakic and pseudophakic patients in their total number of breaks (preoperative and intraoperative), best-corrected visual acuity (BCVA) 6 months after scleral buckling and BCVA 6 months after vitrectomy.

For Table 2,[2] there is a significant mean difference between basal and after cyclopentolate for the resistive index (RI) of pseudoexfoliation syndrome (PXS).

There is little or no overlap, well below 95% with at least population, between the 99% confidence intervals of the clinical groups concerned.

The care taken with the data means that they deserve correct analysis, which they were denied.

The Tsakok technique is extended to the nonparametric problem of comparing samples using the article on constructing exact unconditional Uniformly Most Powerful Unbiased tests by Tsakok,[10] superseding the χ^2 test or the Wilcoxon test. The Tsakok articles are reprinted[11] with further results.

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Sir,

Reply to Dr AD Tsakok

We highly appreciate Dr AD Tsakok's interest in our recently published paper.[1] In his letter,[2] he suggests a different approach to the statistical problem which we solved using either Student's two-sample *t*-test or analysis of variance (ANOVA). Dr Tsakok argues that the shortcoming of our statistical approach lies in the assumption of equal variances between groups (Behrens-Fisher problem[3,4]). In his opinion, this assumption renders the applied tests unsuitable for the purposes to which they were put. Dr Tsakok advocates a statistical test that he himself has developed to compare quantitative data between multiple groups,[5] and which is already available as commercial software.

Dr Tsakok endeavoured to prove his point by applying his test to data that appears in several publications.[1,6,7] According to his findings, we failed to detect significant differences in the total number of breaks and in the best-corrected visual acuity between scleral buckling and vitrectomy 6 months after surgery (Table 3[1]).

We used the widely applied statistical package SPSS 11.5 (Chicago, IL, USA). The data were tested for normality of distribution using the Shapiro-Wilks test, and the equality of variance was confirmed using Levene's test. SPSS computes two-test statistics for the two-sample *t*-test: one for cases in which the variances in both groups are equal, and the other for cases in which they differ. If the variances differed significantly, we implemented the latter test in conjunction with the relevant significance values. Furthermore, due to the retrospective nature of our study, we stressed that the findings might not be generally applicable.[1] According to currently widely accepted standards,[8,9] we are still convinced that the statistical methodology employed in our study was appropriate.

We agree with Dr Tsakok respecting the importance of the Behrens-Fisher problem. According to our literature search, the Tsakok test has as yet neither generally been recognized within the scientific community nor widely applied for the solution of comparable statistical problems. It may well prove to be superior to the statistical tests currently applied to clinical data, but it must first be validated by independent statisticians.

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Sir,

Response

In the Tables of our article, we gave the values of CRP, IL-6, and VCAM-1 as medians and interquartile ranges due to the skewed distribution of these markers. Giving the values in actual serum concentrations enables other investigators to compare their findings to ours. After log transformation to correct skewness, these variables conformed in a satisfactory manner to Normal distribution and were therefore analysed with parametric tests. We did not give the values of the means and standard deviations of the log transformed values because it would not be clinically useful. We trust the medians and interquartile ranges are enough to describe the levels and variances of the measured values.

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Sir,

Advantages of modular phacoemulsification training

Modernising Medical Careers will require rapid and effective training of tomorrow's ophthalmologists, but a