Ophthalmic statistics note 9: parametric versus non-parametric methods for data analysis

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INTRODUCTION/SCENARIO

Distributions of measured data are often well modelled by known probability distributions, which provide a useful description of their underlying properties such as location (average), spread (variation) and shape. Statisticians use probability distributions to interpret and attribute meaning, draw conclusions and answer research questions using the measurements or data that researchers gather during their studies. Different types of data follow different probability distributions, and these distributions are characterised by certain features called parameters. Even the most statistically averse of researchers is likely to have heard of the normal distribution, which is often used to approximate the distribution of continuous or measurement data such as intraocular pressure, central retinal thickness and degree of proptosis. The normal distribution follows a 'bell-shaped curve' (although with a rim stretching to ±infinity) the shape of which is specified by the mean and SD, with different values of each, giving rise to different bell-shaped curves (see figure 1).

Other distributions such as the binomial and Poisson probability distributions are less commonly reported in ophthalmic research and are characterised by different parameters. The binomial distribution is used for dichotomous data and is characterised by the probability of success, that is, the number of 'successes' out of a total number of observed events, for example, the proportion of graft transplants that fail within 6 months of transplantation. The Poisson distribution is used for counts data and is characterised by the mean number of events, for example, endophthalmitis rates.

The assumption that the observed data follow such probability distributions allows a statistician to apply appropriate statistical

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tests, which are known as parametric tests. The normal distribution is a powerful tool provided the data plausibly arise from that distribution or can be made to reasonably approximate this following a suitable transformation such as by taking natural logarithms to reduce asymmetry. The normal distribution also serves as an approximating distribution to the Poisson or binomial distribution under certain circumstances or can be used for large samples to approximate the distribution of the sample mean via the central limit theorem. Tests based on the normal distribution are therefore extremely useful and form the basis of many analyses, the usual tests being z tests or t tests, which rely on approximate normality or normality, respectively. If we can assume a normal distribution, then we expect 95% of values to lie within 1.96 SDs of the mean.

Parametric tests make assumptions about the distribution of the data and sometimes it may be impossible to assess these assumptions, perhaps because the sample size is small or because that data do not follow any of the more common probability distributions. Alternatively, we may be interested in making inferences about medians rather than means or about ordinal or ranked data. In such circumstances, statisticians may adopt an alternative class of statistical tests, which are known as non-parametric or distribution-free methods. These methods work by ranking the data in numerical order and analysing these ranks rather than the actual measurements observed. Two of the most well-known non-parametric methods are the Mann-Whitney test (or U test) and the Wilcoxon matched-pairs signed-rank test, which are suitable for data from two unpaired samples or two paired samples, respectively.^{2 3}

The Wilcoxon matched-pairs signed-rank test calculates the differences between each matched pair in the two samples and replaces their absolute values with their ordered ranks (1, 2, 3, etc), ignoring zeros. Under the null hypothesis of no difference between samples, the sum of the positive and negative ranks should be similar. The test statistic is usually taken to be the smaller of the two sums, and exact p values can be found using statistical software or by comparison with statistical tables.

The Mann-Whitney U test effectively considers all pairs of observations from two independent samples and calculates the number of pairs for which an observation in one sample is preceded by an observation from the other. Again, the U statistic can be calculated from the summed ranks within each sample, found by ordering the pooled observations.

Such tests depend only on the rank ordering of the observed values and not on any assumptions about their underlying distributions, so that there are no associated parameters to be estimated, and in that sense such methods are considered non-parametric or distribution-free. These are easily implemented in standard statistical software packages such as R, Stata, SAS or SPSS.

Scenario 1

A colleague has conducted an exploratory randomised controlled clinical trial evaluating a novel treatment for ocular trauma in 40 patients, 20 of whom received standard care and 20 of whom received the novel treatment. The primary outcome measure is visual acuity in the treated eye 6 months surgery, measured using Early Treatment Diabetic Retinopathy Study charts at a starting distance of 4 m. In the analysis of the trial, a decision has to be made between using parametric and nonparametric methods, and she asks me for advice. A histogram of visual acuity is highly asymmetric, that is, the distribution is skewed, so that these data appear to violate the assumption of approximate normality. I decide therefore to propose the Mann-Whitney test, and a p value of 0.76 leads to the conclusion that there is little evidence of any difference between the medians in the two groups. My colleague asks me to see an estimate of the treatment effect. While the t test would have provided me with an estimate of the mean difference with a CI, no such result is directly forthcoming from the Mann-Whitney test, although it is possible to calculate the difference in medians and a 95% CI for the difference.⁴

DISCUSSION

Non-parametric tests can be useful, but careful thought should be given on a case-by-case basis as to whether they are the most appropriate method of analysis. Where an assumption of normality is tenable, parametric tests will be more powerful, offering greater opportunity to detect differences where they exist, and have the advantage that they provide useful information about the size of treatment effect and CIs directly. The relative loss of power (the probability of finding statistically significant results



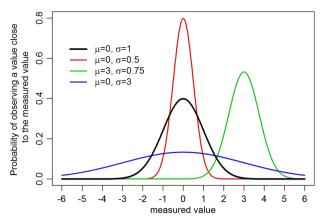


Figure 1 Examples of the normal N (μ, σ) distributions parameterised by different values of mean (μ) and SD (σ) .

differences exist) when adopting nonparametric methods, even where these are appropriate, is well known. It is not unusual to inflate sample sizes by 10% or more to accommodate possible nonparametric analyses resulting in poorer efficiency (ie, a larger sample size is required to identify a given difference between treatment groups).

It is important to note that, in contrast to what is stated in certain statistical text books, non-parametric tests are not a solution to the problem of small sample sizes. ⁶ ⁷ In fact, for comparative samples with less than four per group, the Mann-Whitney test cannot produce a significant p value (<0.05) whatever the values of observations in the samples. For small samples where normality is difficult to assess, it may be reasonable to assume a normal distribution, or to use a transformation, based on the distribution of data from previous larger studies. Nonparametric methods are themselves not free of assumptions, for example, the Mann-Whitney test assumes that samples arise from the same underlying distribution and differ only in location.

Scenario 2

My colleague brings me results of her comparison of the visual acuity data captured in an exploratory randomised controlled clinical trial. She has used a non-parametric test to compare visual acuity 6 months post surgery. She states that she has used this test because the data were highly skewed. She shows me histograms of the data from each group, and looking at this, I realise that she herself has violated an assumption used by the non-parametric test. The distributions differ by central location and in the spread of the data. Examination of the data in both groups suggests that patients either

respond greatly or not at all—average change is misleading in this instance.

SUMMARY

With highly skewed or otherwise awkward data, the median may be more robust than the mean as a measure of central tendency and is used with non-parametric methods of analysis. However, it should be noted that this approach separates the p value from the effect size since the Mann-Whitney test, for example, tells us only whether there is a shift in location between samples and is by design divorced from the actual estimation of effect. CIs for the difference in medians should be presented to give an indication of the size of the effect. An alternative to nonparametric methods is given by bootstrapping or resampling,³ but such methods should not be considered without reference to a statistician. Where assumptions of normality are plausible, possibly following a transformation, parametric methods are preferable providing extra power and allowing adjustment for other factors such as differences between treatment groups at baseline in the case of clinical trials.8

LESSON LEARNT

- ▶ If the data appear to follow a probability distribution, use the appropriate parametric test. This will maximise power and interpretation.
- ▶ If data are highly skewed, see whether a simple transformation will achieve normality but do not forget to backtransform when presenting results.
- ▶ If data appear not to follow any common distribution and there are no reports of these data elsewhere to allow you to assume normality, you should consider a non-parametric test.
- ▶ If in doubt, analyse your data both ways and see whether the conclusions agree.

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