On Alternative Methods for Measuring Visual Field Decay: Tobit Linear Regression

We read with interest the article by Caprioli et al.1 in the June 2011 issue. In this article, the authors propose a novel method of measuring and predicting the rate of visual field (VF) decay in glaucoma patients. This is an important and clinically relevant topic. Of particular interest was the authors’ application of an exponential fit for threshold sensitivity (in decibels) against time, which was found to be the best-fitting model compared against a linear and a quadratic regression—according to the Akaike information criterion (AIC)—in 96.8% of the 21,006 of the data series investigated. This contradicts the idea that point-wise VF decay is best modeled and predicted using simple ordinary least-squares linear regression (OLSLR); previous research investigating other more complex models has shown these to be less accurate than OLSLR for predicting VF progression.2 In response to this article, we would like to suggest possible statistical reasons why the exponential regression is shown to be a better-fitting model than simple OLSLR.

Standard VF threshold measurements from the Humphrey Visual Field Analyzer (Carl Zeiss Meditec, Dublin, CA) are limited to the range of 0 to 50 dB. Consequently, VF thresholds are vulnerable to floor (left-censoring) and ceiling (right-censoring) effects. Caprioli et al.1 state that “exponential fits for individual locations seem to work well for advanced damage because values usually approach 0 dB in an asymptotic fashion”; conversely, we argue that VF progression may occur linearly throughout the disease but the exponential model is more robust than OLSLR to the floor effects of VF threshold data. Floor effects are pertinent to the VF data investigated by Caprioli et al.,1 since the models were applied to patients with moderate to advanced glaucomatous damage. Furthermore, in Figure 9 of their study, it is apparent that for “actual thresholds” above approximately 20 dB, the predicted thresholds from the exponential regression greatly underestimate the VF thresholds.

In circumstances in which the dependent variable is censored (such as threshold sensitivity), the assumptions of the OLSLR model are not strictly valid. However, there are statistical prescriptions that may provide a solution. The Tobit linear regression model3 employs a latent (unobservable) dependent variable that respects left- and/or right-censoring and predicts this variable only within the specified range. To illustrate the usefulness of Tobit regression as well as support the hypothesis that VF progression may occur linearly, even in advanced disease, we synthetically created the example shown in Figure 1, which is akin to Figure 2 in Caprioli et al.1 The Tobit linear regression model is fitted to the synthetic data in Figure 1 (blue line) and compared with the exponential regression (red line) and OLSLR (black line). Different models can be contrasted using the AIC, with the lowest AIC indicating the best model. Specifying appropriate candidate models is imperative, because if only poor models are compared, then the AIC will simply select the best of a bad bunch. Models can be further evaluated using the formula:

\[ \exp \left( \frac{\text{AIC}_{\text{min}} - \text{AIC}_i}{2} \right) \]

where \( \text{AIC}_{\text{min}} \) represents the AIC of the best-fitting model and \( \text{AIC}_i \) is the AIC of the model to be compared.4 For the example in Figure 1, the AICs of the Tobit and exponential models were −388.1 and 37.6, respectively. This result suggests that the exponential model is roughly a googol times less probable than the Tobit model for these particular data! In contrast, the AIC of the standard linear regression was 46.4, suggesting that this model is approximately 100 times less probable than the ex-

Figure 1. Example of regression fits for a single synthetic VF test location progressing at a rate of −2 dB/yr. Black: the standard linear regression; red: the exponential; blue: the Tobit.
ponential fit. Of course, this is only a single synthetic example, but it illustrates the relevance of the Tobit linear regression for VF threshold data.

Undoubtedly, not all the data investigated by Caprioli et al.\textsuperscript{1} will be affected as significantly by a threshold floor effect; however, in the absence of pronounced floor effects, the exponential regression could still outperform OLSLR for other reasons. One hypothesis is that an exponential fit better models medical interventions than linear regression. In the Advanced Glaucoma Intervention Study (AGIS), patients received one of two sequences of surgical treatments, yet all VF data (pre- and post-surgery) were included in the regression models investigated by Caprioli et al.\textsuperscript{1} Consequently, an exponential model may better represent the expected change in the rate of VF progression pre- and postsurgery compared against OLSLR. To account for therapeutic interventions, a segmented linear fit could be compared to the exponential regression, or, pre-surgery VF data could be discarded from the models. We would be greatly interested to see forecast results for the exponential regression compared with the linear and Tobit regressions for the authors’ postsurgery VF data and to see forecast results for all test locations, declining or not. We hope our remarks are considered as positive suggestions rather than direct criticism of the paper, perhaps stimulating other researchers to think of appropriate statistical prescriptions that might improve the estimation of rates of VF decay in glaucoma.

Richard A. Russell
David P. Crabb

Department of Optometry and Visual Science, City University London, United Kingdom.
E-mail: david.crabb.1@city.ac.uk

References


Citation: Invest Ophthalmol Vis Sci. 2011;52:9539–9540. doi:10.1167/iovs.11-8948