Minimising sample size for glaucoma neuroprotection trials by recruiting patients with low visual field test variability | IOVS

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Abstract

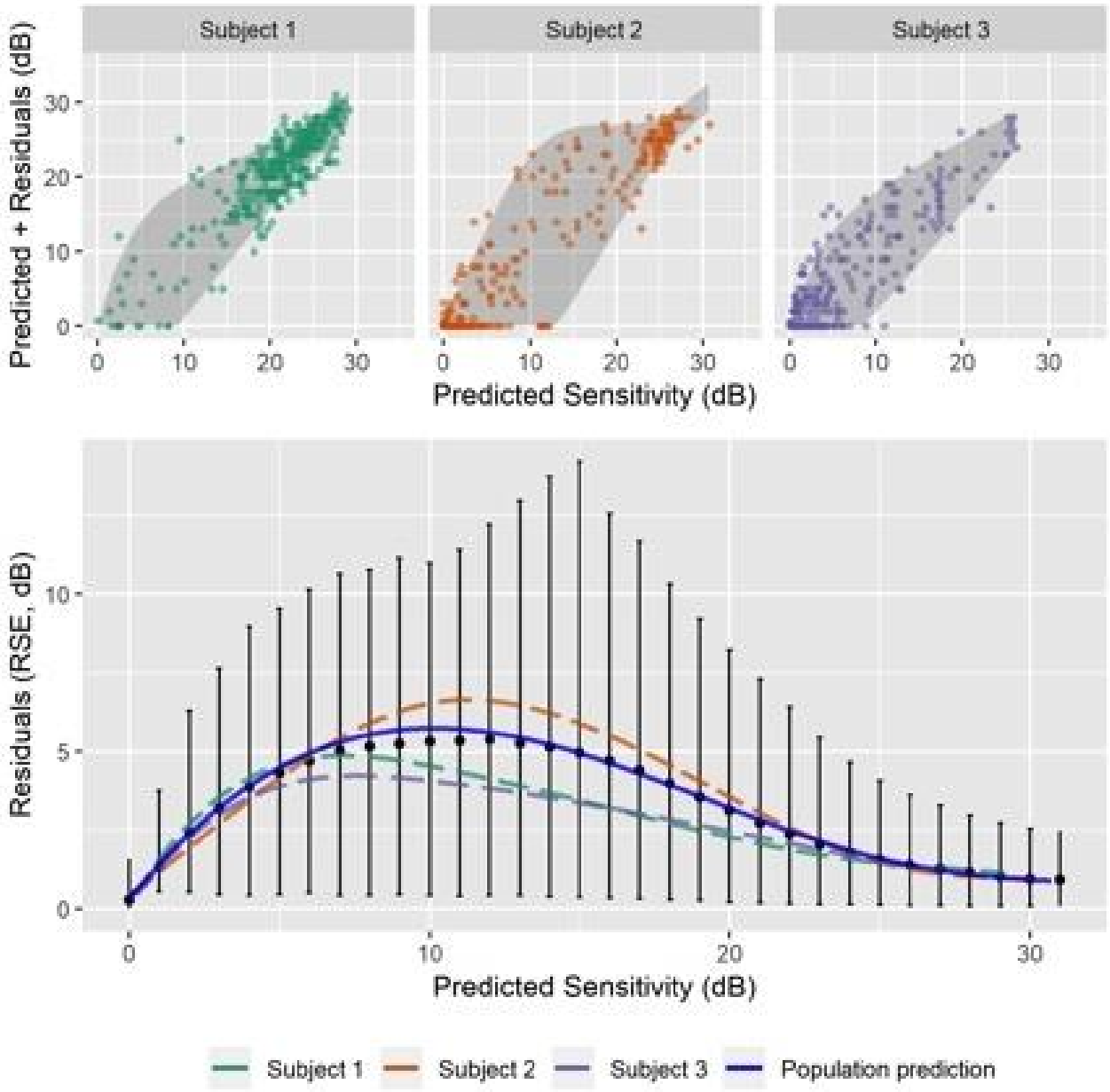
Purpose : Selecting reliable visual field (VF) test takers with a history of low inter-test variability has been proposed as a way to improve power for glaucoma neuroprotection trials. We test this hypothesis via simulations using a large real world dataset.

Methods : Patients under standard clinical treatment with at least 10 VFs were extracted from electronic records from five different English glaucoma clinics. A variability index (VI) for each subject was calculated using residuals of the regression line of the mean deviation over time for the first six VFs in a series. A random effect spline model on the remaining tests (4 or more) of each series estimated the individual pointwise inter-test variability (Figure 1). This was used to simulate VFs at regular intervals for two years, as in the UK Glaucoma Treatment Study. We simulated the effect of a neuroprotective agent by reducing the observed progression rate by 20%, 30% or 50%. Subjects were ranked by VI values. In the simulation, patients were recruited from the smallest (best) to progressively largest VI and randomly allocated to either arm of the trial, until predefined sample size (N) was reached. This strategy was compared to random selection of patients at the same Ns. We calculated the power to detect a significant difference ($p < 0.05$; power 80%) for increasing Ns.

Results : Simulations were based on 2702 treated patients (>1.5 million pointwise VF data points). We could not reach 80% power for the low neuroprotective effect with the maximum available number of patients, but the sample size was reduced by 32% and 62% for the 30% and 50% neuroprotective effect respectively (Figure 2).

Conclusions : Recruitment of participants with lower inter-test VF test measurement variability is an efficient way to maximise the power and minimize sample size of a trial for a new treatment for glaucoma.

This is a 2020 ARVO Annual Meeting abstract.



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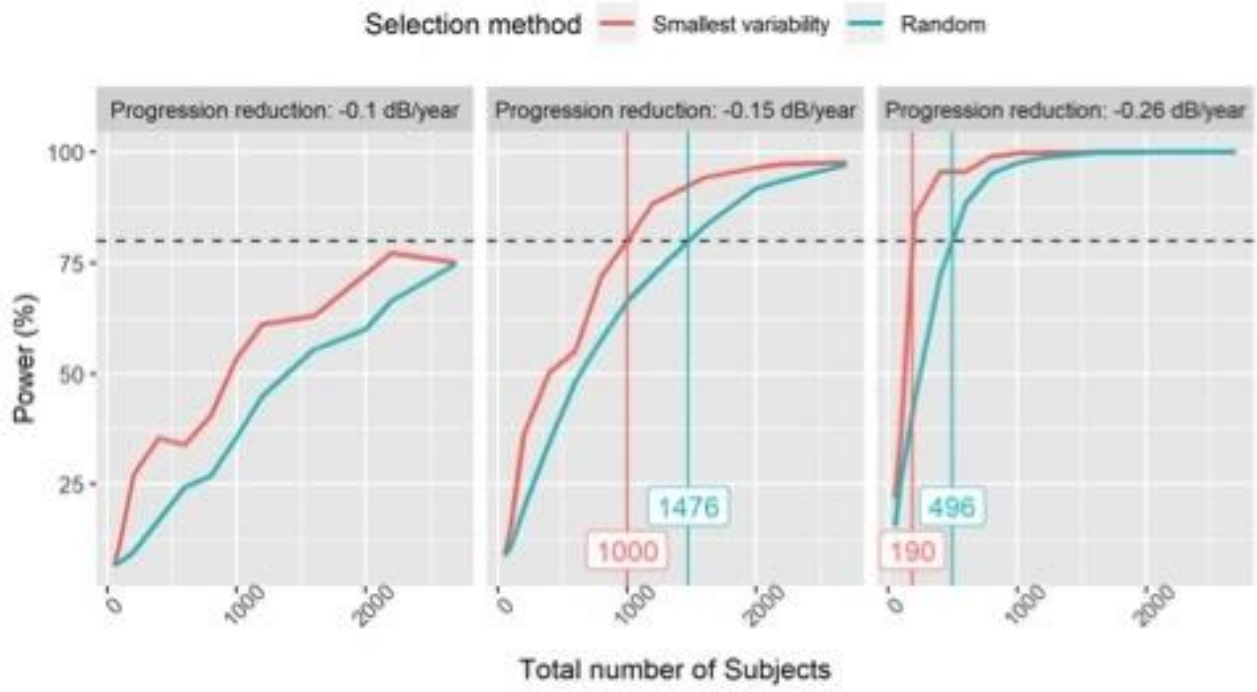
Bottom panel shows the predicted average point-wise variability (Root Squared Error, RSE, blue line). Dashed lines represent the random effect predictions for the three individuals in the top panel (colour matched). Black dots and vertical error bars = raw population mean and 5 - 95% quantiles respectively.



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Power curves for the two methods with rounded estimated number to reach 80% power threshold (dashed line). The threshold could not be reached for the smallest neuroprotective effect with the available sample size.