Constant effect assumption versus individualized medicine

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Background: There is a rising body of new literature warning about outcome variability among patients after interventions, which is usually interpreted as a treatment-patient interaction [1]. On the other hand, the evidence paradigm for developing practical clinical guides based on trial results relies on the homoscedasticity assumption —which is a consequence of a constant intervention effect. If this does not hold, treatments for new patients should be based on specific n=1 trials. But, as those can only be performed in stable (neither curative nor fatal) clinical situations, the future role of statistical evidence may be compromised.

Objective: To empirically study homoscedasticity.

Methodology: We performed a literature search of parallel clinical trials published in the years 2004, 2007, 2010 and 2013, which provided baseline and final outcome variability for both treatment groups.

Both homoscedasticity assumptions (over-time and between-treatment arms) were explored by the ratio of their respective standard deviation estimates. For the former, all studies reporting baseline and final variance were selected and, for the latter, only studies with a passive control group were selected (either placebo or non-active treatment).

Results: Over-time: of the 85 papers that met the criteria in years 2004 and 2007, the Lin coefficient of concordance between the baseline and the outcome standard deviations was 0.98, with $_{95\%}$CI from 0.97 to 0.99. Between-arms: variability of treated and control groups were retrieved from 32 papers and the Lin coefficient was 0.97, with $_{95\%}$CI from 0.94 to 0.99. We observed large extreme values for both the initial/final outcome SD ratio (0.2 and 2.9) and the SD ratio between the treated and the control group (0.2 and 4.2).

Discussion: Both Lin coefficients agree with over-time and between-groups homoscedasticity. Nevertheless, the observed extreme values advise researchers to assess these premises in their specific situations.

The research suggests that the constant effect assumption behind population-based evidence medicine holds. As patient outcome variability can be explained by only patient variability, we provide empirical evidence for the rationale to write clinical guides (protocols) for new patients based on previous trial results.

Keywords: population based medicine; individualised medicine; homoscedasticity.

1. Sacristán, JA. Patient-centered medicine and patient-oriented-research: improving health outcomes for individual patients. BMC Med Inform Decis Mak, 13 (2013), p. 6