An extension of the individual causal association for continuous non-normal endpoints in a causal inference framework

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Surrogate endpoints are used to provide earlier informative results on the effectiveness of drug development and new treatment studies in clinical trials. Replacing the true endpoint with a surrogate endpoint is a well-known strategy due to its advantages in reducing the follow-up time and the cost. The evaluation of surrogate variables is complex, and one of the factors that contribute to this complexity is the fact that the true and the surrogate endpoints can be of different natures. Therefore, for each combination of them, complex models and their corresponding surrogate metrics must be developed. The individual causal association (ICA) proposed by Alonso *et al.* (2015) is known to work properly for the normal causal model. In this work, surrogacy is assessed using ICA when both endpoints are continuous and non-normally distributed, and a new approach is suggested to estimate the distribution of the endpoints using non-parametric techniques. The performance of the new approach is analyzed under different scenarios through a simulation study.

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