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Combining Propensity Score and Random Coefficient Modelling as an Approach to Analyse Complex Longitudinal Data

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Objectives

We looked for an approach to analyze/visualize a set of repeated measures of renal laboratory data (eGFR [estimated Glomerular Filtration Rate] from an observational population-based data set) as safety parameters in a longitudinal design and calculate annual changes in different sub-cohorts.

Previous meta-analyses had struggled to address this problem (due to poor data quality and strong heterogeneity in underlying historical studies) and previous large population-based observational studies had only looked into binary outcomes.

Particular challenges lay (1) in the complexity of the data set with irregularly spaced observation points, (2) in the observational character of the data with associated bias and confounding by indication and co-medication and (3) in the change of lab method during the observation period.

Results

Out of a population base of 400.000 we analysed linked longitudinal data of more than 1000 eligible patients with over 1000.000 prescription records of index drug or co-prescription drugs. Data were provided by the Dundee University Health Informatics Centre (HIC).

We addressed the differences in covariates (which typically can lead to biased estimates of treatment effects in observational studies) via individual propensity scores (to reduce this bias by balancing the covariates in the two groups) and a hierarchical modelling approach.

A Random Coefficient Model (via proc mixed in SAS 9.3) proved a much more powerful statistical tool than analysis of covariance of the summary measure during follow-up, particularly as the latter approach is less efficient when applied to longitudinal data with missing data points and irregularly spaced repeated measures.

Visualization was achieved with the SAS 9.3 GPLOT procedure combined with a spline function. The historical change in lab method was addressed via a conversion of lab results to an internationally recognized standard (IDMS aligned method).

We were able to achieve plausible and more precise estimates of the annual decline in eGFR in the patient group of interest than previous attempts from other research publications. This led to a publication in a high profile journal.

Conclusion

Our approach of combining a Propensity Score and Random Coefficient Modelling was successful to answer a question in drug safety using repeated measurement data from a longitudinal observational population based data set. This approach may be useful for other research questions in Drug Safety or in Comparative Clinical Effectiveness Research for continuous outcome measures.

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