UNIVERSITY OF COPENHAGEN

PHARMACOVIGILANCE RESEARCH CENTER

Main supervisor.
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Topic.

Pharmacoepidemiology.

Title of the project.

Comparison of misclassification of exposure among four methods used for computing the duration of pharmacological treatment episodes in secondary data sources

Project description.

A key aspect of pharmacoepidemiological studies aiming at assessing the association between the exposure to pharmacological treatments and the occurrence of an outcome is to define for how long individuals have been exposed to treatments. Analogous considerations apply to studies aiming at evaluating drug utilization, compliance, adherence, persistence, and time to discontinuation of pharmacological treatment. Correctly defining this exposure period is crucial to scenarios when individuals are exposed once or multiple times during the observational window and/or when cumulative exposure is assessed. It may not represent either a methodological challenge when the exact duration of a redeemed prescription along with the indication of use is available, directly (e.g., days of treatments) or indirectly (e.g., posological scheme and administration schedules). However, in secondary data sources, such information is usually not accessible or incomplete, and even then, not all patients may take the drug exactly as prescribed. This leads to a methodological challenge for pharmacoepidemiologists that need to rely on limited available information such as the date of redemption of pharmacological treatment, the number of posological units, and their strength to estimate the length of exposure to a medication. This is typically done by assigning a hypothetical duration to each redeemed prescription in the observational window based on a set of rules and assumptions in a process known as the construction of treatment episodes. This process is typically challenged by the complexity of irregular prescription redemption patterns and overlaps/temporal gaps between consequent redeemed prescriptions. The defined daily dose (DDD) is used for computing the duration of treatment episodes when their exact duration is missing. Other variants include the estimate of the duration of treatment episodes using only the redeemed posological unit and the recommended posological scheme in the summary of product characteristics (SmPC). Both approaches are different variants of a method known as the “user-defined duration” of treatment episodes or rather a method in which researchers arbitrarily assign the duration of each treatment episode. Currently, other methods for assessing the duration of treatment episodes have been developed such as the reverse waiting time distribution (rWTD), the “medicin macro”, and the Sessa empirical estimator (SEE). To date, no studies investigated which method provides the best estimation of the duration of treatment episodes in observational data. In this project, you will simulate refill histories for a single medication over an observation period of 720 days (2 years). This timeframe allows simulating realistic patterns observed for chronic treatments. You will compare four methods to evaluate which one provides the best estimation of the duration of treatment episodes in multiple scenarios with different adherence and persistence pattern.

Acquired skills: statistical programming in R and SAS; data management; Monte Carlo simulation; scientific writing.

References

1) Jahn-Eimermacher A, Ingel K, Ozga AK, Preussler S, Binder H. Simulating recurrent event data with hazard functions defined on a total time scale. BMC Med Res Methodol. 2015;15:16. Published 2015 Mar 8. doi:10.1186/s12874-015-0005-2