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Supervised signal detection for adverse drug reactions in medication dispensing data

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Abstract

Motivation: Adverse drug reactions (ADRs) are one of the leading causes of morbidity and mortality and thus should be detected early to reduce consequences on health outcomes. Medication dispensing data are comprehensive sources of information about medicine uses that can be utilized for the signal detection of ADRs. Sequence symmetry analysis (SSA) has been employed in previous studies to detect signals of ADRs from medication dispensing data, but it has a moderate sensitivity and tends to miss some ADR signals. With successful applications in various areas, supervised machine learning (SML) methods are promising in detecting ADR signals. Gold standards of known ADRs and non-ADRs from previous studies create opportunities to take into account additional domain knowledge to improve ADR signal detection with SML.

Objective: We assess the utility of SML as a signal detection tool for ADRs in medication dispensing data with the consideration of domain knowledge from DrugBank and MedDRA. We compare the best performing SML method with SSA.

Methods: We model the ADR signal detection problem as a supervised machine learning problem by linking medication dispensing data with domain knowledge bases. Suspected ADR signals are extracted from the Australian Pharmaceutical Benefit Scheme (PBS) medication dispensing data from 2013 to 2016. We construct predictive features for each signal candidate based on its occurrences in medication dispensing data as well as its pharmacological properties. Pharmaceutical knowledge bases including DrugBank and MedDRA are employed to provide pharmacological features for a signal candidate. Given a gold standard of known ADRs and non-ADRs, SML learns to differentiate between known ADRs and non-ADRs based on their combined predictive features from linked sources, and then predicts whether a new case is a potential ADR signal.

Results: We evaluate the performance of six widely used SML methods with two gold standards of known ADRs and non-ADRs from previous studies. On average, gradient boosting classifier achieves the sensitivity of 77%, specificity of 81%, positive predictive value of 76%, negative predictive value of 82%, area under precision-recall curve of 81%, and area under receiver operating characteristic curve of 82%, most of which are higher than in other SML methods. In particular, gradient boosting classifier has 21% higher sensitivity than and comparable specificity with SSA. Furthermore, gradient boosting classifier detects 10% more unknown potential ADR signals than SSA.

Conclusions: Our study demonstrates that gradient boosting classifier is a promising supervised signal detection tool

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