

A Survey: Mining Adverse Drug Reaction

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ABSTRACT

With the early detection of the unknown Adverse Drug Reaction saves the lives of the human. The recognition-primed decision (RPD) Model, Interestingness measure and causal leverage plays an important role in data mining. RPD using fuzzy system is a decision making approach, how human takes decisions while handling complex task. Interestingness measure often used in association rule discovery for mining and ranking patterns. Causal leverage assesses the strength by association of drug symptom. This survey reviews on interestingness measure, recognition prime decision and causal leverage on adverse drug reaction.

Keywords

Data mining, adverse drug reactions, recognition-primed decision, interestingness measure, causal association.

1. INTRODUCTION

Medications have brought better health and longer life to the human race. Every day, hundreds of millions of people from all over the world are affected by the medicines. Adverse drug reactions (ADRs) represent a serious problem worldwide. The term "adverse effect" is preferable to other term such as side effect [1]. They can complicate a patient's medical condition or contribute to increased morbidity, even death. Survey have shown that ADRs contribute to about 5% of all hospital admissions and represent the fifth most common cause of death in hospitals. Signal is the reported information regarding the causal relation between the adverse event and the drug. Postmarketing surveillance deals with the drug safety. Interestingness measure is called potential causal leverage. This causal leverage deals with the causal association between the drug and symptom. The drug symptom pair is evaluated by the computational fuzzy recognition primed decision model [2]. Potential causal leverage measure is performed much better when compared to the risk ratio and leverage measures. RPD model performs decision making process in order to handle the complex problems. The decisions are made based on the experience. Fuzzy interpretations are incorporated by the fuzzy logic. Fuzzy sets are employed by cue values. Cue is the key concept in the RPD model. In the RPD model similarity measure is

needed to assess the degree of likeness between the current situation and the past situation. Fuzzy reasoning is employed to abstract high level cues from elementary data. In Apriori algorithm number of patterns discovered is large. Therefore there is need to rank the discovered patterns according to their degree of interestingness measure.

2. COMPUTATIONAL RPD MODEL

In the computation RPD model some of the cognitive processes that a physician would employ when making decisions under uncertainty regarding suspected adverse drug reactions (ADRs) [3]. For this discussion an ADR will refer to the unanticipated drug-associated adverse incident(s) that follow the administration of a drug when it is used properly and at an appropriate dosage [1]. ADRs represent a significant public health problem. Also, the concept of an adverse reaction following drug administration does not require extensive knowledge and expertise in order to understand the significance for decision making. Computational RPD are limited and do not detect the ADR problem. Fuzzy based Computational RPD provides the effective paradigm to detect the ADR.

Also [8] used intelligent agents with a fuzzy decision model is used to develop a distributed adverse drug reaction. Adverse drug reaction is detected by utilizing distributed electronic patient data. The Recognition-Primed Decision (RPD) model is furnished to a fuzzy RPD model and it uses fuzzy logic technology to represent, compute imprecise, and interpret and subjective cues. They were commonly encountered in ADRs and they retrieve prior experiences that are reported.

3. CUE TYPES

Cue is a key concept in the RPD model for both the situation awareness and action evaluation processes. Cues are usually abstracted from elementary data and their types could be linear, nominal or fuzzy. A linear cue refers to a variable whose values are described by or related to a straight line. For example, the blood pressure of a patient is a linear cue. A nominal cue is represented as discrete cue and their values are not in any linear order. Example, a variable representing the gender of a patient has a value such as male, female, or unknown. A fuzzy cue is inspired by the need of

representing information that is imprecise in nature. The fuzzy set theory provides a breakthrough, relatively new information processing technology for describing such imprecision, uncertainty, and subjectivity which are common issue for more real-world applications, especially those in medicine [4].

Detecting an unknown ADR is a complex process which includes spontaneous ADR reporting, expert clinical reviews and studies related on epidemiology. For example, consider how a physician assesses the evidence for causality between a drug and an adverse event in an individual patient case, which may result in filing a report and trigger further investigation. Cues Temporal association refers to the temporal relationship between taking the occurrence of the adverse reaction and drug. Rechallenge describes the relationship between re-introduction of the drug and recurrence of the adverse event. Dechallenge is defined as the relationship between withdrawal of the drug and reduction of the adverse effect. Cues temporal association, rechallenge and dechallenge are all fuzzy variables and they represent fuzzy sets and they are achieved through fuzzy reasoning.

4. MINING METHOD FOR PHARMACOVIGILANCE

Pharmacovigilance is the science which deals with the detection, assessment and prevention of ADRs. In the pre-marketing stages of a drug, Pharmacovigilance deals with predicting ADRs using preclinical characters of the compounds [7]. For example it consists of chemical structure, drug targets. In the postmarketing stage, Pharmacovigilance has traditionally involved in mining spontaneous reports. The research focus towards the use of data generated from platforms outside the I framework such as biomedical literature, electronic medical records (EMRs), and patient-reported data in online health forums. The emerging of Pharmacovigilance is to link preclinical data with human safety information observed in the postmarketing phase. This provides a general overview of the current computational methods applied for Pharmacovigilance at different stages of drug development and concludes with future directions and challenges.

The Pre-Marketing Surveillance at the stage has been devoted to predict or assess ADRs early in the pipeline drug development. One of the fundamental methods in mining ADRs is the application of preclinical Safety Pharmacology Profiling (SPP) by testing compounds with biochemical and cellular assays. The symptom is that if a compound binds to a certain target, then its effect may translate into possible occurrence of an ADR in humans. However, experimental detection of ADRs remains challenging in terms of cost and efficiency [6]. There has been large amount of research activities devoted to developing computational approaches to predict potential ADRs using preclinical characters of the screening data. Most of the existing research can be categorized into chemical structure and target-based approaches.

5. POTENTIAL CAUSAL-LEVERAGE MEASURE

Early detection of Adverse Drug Reaction protects the life of the patient [11]. It provides the relationship between drug and ICD-9(International Classification of Drug-Ninth Revision) Potential causal leverage assesses the strength of the association of a drug symptom pair [3]. Drug safety depends heavily on the post marketing surveillance. FDA (Food and Drug Administration) currently adopts data mining algorithm called multi item gamma poison shrinker for detecting potential signals from its spontaneous reports. Support measures the statistical significance of a pattern. Minimum support based pruning is good strategy for positively correlated association rules. Confidence measures the strength of the association rule. Measuring the interestingness of discovered patterns is an active and important area of data mining. An association rule is an implication expression in the form of $X \rightarrow Y$, where X and Y are two event sets and they are disjoint (i.e., $X \cap Y = \varnothing$), meaning that they share on common events. An association rule indicates that, if X is present it implies that Y will also present. X and Y temporal constraint is often applied to the association rule. It provides the relationship for temporal association. It is represented as $X T \rightarrow Y$, is called the temporal association rule, where $T \rightarrow$ denotes that Y occurs after X within a time window T in the same event sequence. In the survey, association rule mining is based on two measures that are support and confidence. The association rule for support is represented as $\text{supp}(X \rightarrow Y)$. It is the proportion to the sequences in which both X and Y among all the event sequence occur s at least once. This measure indicates how often a rule is applicable to a given set of event sequences.

The importance of this measure is if a rule has very low support, it may occur simply by chance and thus would be uninteresting. The confidence of an association rule is defined as $\text{conf}(X \rightarrow Y) = \text{supp}(X \rightarrow Y) / \text{supp}(X \rightarrow)$, where $\text{supp}(X \rightarrow)$ is the proportion of sequences that contain X . This measure determines how frequently Y appears in those event sequences that contain X . In the context of ADR signal generation using electronic patient data, a health database often contains many patient records, each of which can be considered as an event sequence where various events such as drug prescription, occurrence of a symptom, and laboratory test occur at different times. The previous two frequency-based measures cannot be used to find the association effectively between a drug and an Adverse Drug Reaction because of the low frequency of ADRs.

6. INTERESTINGNESS MEASURES OF DEPENDENCY FROM DATAMINING

Many of the measures can be adapted to association patterns. It is a well-known fact that the data mining process can generate many hundreds and often thousands of patterns from data [5]. The task for the data miner becomes one of determining the most useful patterns from those that are trivial or are already well known to the organization. It is important to remove

out those patterns through the use of few measures. This survey provides measures devised for evaluating and ranking the discovered patterns produced by the data mining process. The interestingness measures are generally divided into two categories, they are objective measures based on the statistical strengths or properties of the discovered patterns and subjective measures that are derived from the user's beliefs or expectations of their particular problem domain. Existing subjective and semantics-based measures employ various representations of the user's background knowledge, which lead to different measures and procedures for determining interestingness. A general framework for representing knowledge that is related to data mining would be useful for defining a unifying view of subjective and semantics-based measures. Selecting interestingness measures that reflect to real human interest remains an open problem.

6.1 Framework for Finding Unexpected Patterns

Unexpectedness of a pattern is quantified as the impact the pattern has on a prespecified set of prior beliefs (the background knowledge). Beliefs are divided into hard and soft. Hard beliefs cannot change with new evidence. A pattern that violates a hard belief is by definition interesting as it implies incorrect data or incorrect acquisition of patterns. A degree is assigned to each soft belief. In [9], the authors provide five methods for formalizing this degree of belief using tools from Bayesian and Dempster-Schafer theory. The difference between the degrees of the belief system before and after presenting a pattern is used as a measure of pattern's unexpectedness.

6.2. Using a Bayesian Network as Background Knowledge

The use of Bayesian Network (BN) for encoding prior knowledge about the support of itemsets. Interestingness is the difference between the supports of an itemset calculated from the actual data. The construction of the Bayesian Network, however, may be a nontrivial procedure for the user. Furthermore, performing inference in a Bayesian Network can be hard; it depends on the structure of the Bayesian Network. To address this issue, the authors in [10] propose an approximate inference scheme under the same rationale regarding unexpectedness. One approach is to use Meta learning to automatically select or to combine appropriate measures. Another method is to develop an interactive user interface which is interpreting the data by using a selected measure to assist the selection process. Experiments comparing the results of interestingness measures with actual human interest could be used as another approach to analysis. User interactions are indispensable in the determination of rule interestingness, it is important to develop new theories, methods, and tools to facilitate the user's involvement. To reduce the number of mined results, many interestingness measures have been proposed for various kinds of pattern. Based on the form of the patterns produced by the data mining

method, we distinguished measures for association rules, classification rules, and summaries. Survey distinguishes objective, subjective, and semantics-based measures. Objective interestingness measures are based on statistics, probability theory, and information theory. Therefore, they have strict principles and foundations and their properties can be formally analyzed and compared. We surveyed the properties of objective measures, as well as relevant analysis methods and strategies for selecting such measures for applications. However, objective measures take into account neither the context of the domain of application nor the goals and background knowledge of the user. Subjective and semantics-based measures incorporate the user's background knowledge and goals, respectively, and are suitable both for more experienced users and interactive data mining. It is widely accepted that no single measure is superior to all others or suitable for all applications.

7. DISCUSSION

ADR extraction was evaluated using our annotated data set. The training data set was used to mining the adverse drug reactions.

Table 1. Calculating Adverse Drug Reactions

ICD 9 codes	ICD 9 codes description	Exclusive causal leverage	Causal leverage	Leverage	Risk ratio	ADR
784.0	Headache	2	18	267	11/42	Present
585.5	Kidney diseases	4	28	1176	11/73	Not Present
427.32	Atrial flutter	7	37	122	61/8	Present

The drug signal pairs provides the pair generation. Based on the fuzzy RPD the pair is generated. Generated pairs detect the adverse reaction based on the drug consumed by the patient. Adverse effect of the patient is determined using the consumption of the drug and dosage. The focus of this survey is to mine the adverse drug reaction (i.e., finding interesting ADR signal pairs) and mine all possible rare event sets and association rules based on minimal support. In contrast, in this survey work data from a relational (medical) database composed of several related tables. Developing an efficient algorithm is suitable for analyzing its complexity and efficiency in the future. The table 1 shows the details of the ADRs present or not present. By calculating and comparing the ranks of Exclusive causal leverage, leverage, causal leverage the ADR is found out. Based on the drug intake and the dosage the Adverse Reaction can be calculated for the future scope.

8. CONCLUSION

This paper describes various approaches to handle the ADR in data mining. Many significant works has been done in the field of fuzzy based RPD, interestingness measures and causal leverage. Potential causal leverage and experience based fuzzy RPD model have developed a data mining algorithm. Fuzzy rule based approach can be used in post marketing surveillance system to enhance the detection of ADR signal pairs. These approaches discussed the merits and demerits of each technique. Many significant works has been made in the field of mining adverse drug event, yet there is more scope for future research in this field. This survey reviews interestingness measure, recognition prime decision and causal leverage on adverse drug reaction. And this can be made more accurate by using fuzzy RPD and causal leverage measures in the future.

9. REFERENCES

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