Title of the System: superDUR
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I. Motivation

In clinical settings, adverse reactions from Drug-Drug Interactions (DDIs) have contributed to a significant increase in hospitalisation rates (Bucsa et. al., 2014; Dechanont et.al., 2014). Though physicians are generally seen as the party responsible for checking a patient's medical history, there are instances where information conveyed is inaccurate, such as when patients receive treatments from different healthcare practitioners, resulting in inaccurate or incomplete medication histories (Yeh et.al., 2014). As such, prescriptions entered in the in-house drug utilisation review (DUR) system to check for DDIs only flag for medications that have been dispensed by the specific healthcare practitioner and those declared by the patient, increasing the likelihood that an adverse reaction results from mixing certain medications (Van De Sijpe et.al., 2022, Yeh et.al., 2014).

Current systems for DUR exist to expand the information network among healthcare providers and give the public access to run their own DURs, such as the nation-wide DUR in Korea known as Health Insurance and Review Assessment (HIRA), and open-access DUR sites such as DDInter (*Development of DUR Criteria*, n.d.; Xiong et.al., 2022). However, these databases are not without limitations: DDRs can only be assessed between two drugs, and do not factor in patient allergies and comorbidities (Van De Sijpe et.al., 2022; Xiong et.al., 2022). High numbers of false positive alerts arising from the lack of checking parameters can result in a false positive rate of up to 88.2%, and in the hospital setting requires a manual override, causing a trade-off for healthcare professionals between patient care and time spent on DUR (Van De Sijpe et.al., 2022). Lapses in physician judgement also affects patient outcomes, increases unnecessary institutional healthcare utilisation and damages the credibility of the healthcare institution.

Adverse reactions from DDIs also arise in cases of self-medication (SM). This management of minor illnesses through self-medication is prevalent worldwide (Vacher et.al., 2020), and is an easily accessible alternative that saves time and money for patients and reduces unnecessary institutional healthcare utilisation. Self-medication has been associated with a higher risk of clinical adverse events due to the potential pharmacokinetic or pharmacodynamic interactions with other drugs that may lead to deleterious health effects, microbial resistance, treatment failure, or delayed diagnosis and treatment (Vacher et.al., 2020). Data collected in Basel, Switzerland indicated that 26.7% of respondents that purchased Over-The-Counter (OTC) drugs for self-medication were exposed to potential DDIs with their prescribed medications (Indermitte et.al., 2007). Less than half of respondents were aware of potential DDIs between their prescriptions and OTC drugs (Indermitte et.al., 2007). With the democratisation of healthcare brought about by easier access to drugs, data and technology (I. Hernandez-Neuta et al., 2018), SM is likely to increase in prevalence and it is vital for consumers to have safeguards against adverse reactions due to DDIs.

Given the current gaps in existing DUR systems and SM scenarios, our group has identified an opportunity to use propositional logic databases to create a novel, comprehensive system available for both healthcare institutions and general consumers.

II. System Function Descriptions

We propose to build a diagnostic AI tool that helps consumers/doctors prevent prescribing/consuming potentially harmful drugs.

Initially, the AI is given a list of all the drugs that the patient is currently taking as well as any medical conditions and allergies the patient might be suffering from. The existing drugs and allergies are then passed into the AI to populate its knowledge base (KB).

When a new drug is to be prescribed, the AI will first create a query to extract all known DDIs of this drug from a DDI database as well as create a secondary query from another database to extract all known drugs that cannot be prescribed given the patient's current medical condition. All this additional information is then fed into the AI's KB. All the logical statements in the KB are then simplified to determine whether there would be an adverse reaction. Should there be an adverse reaction, the AI would output "adverse" together with the relevant adverse condition. If there is no such reaction, the AI would output "clear".

The approach of keeping an external database for interactions information and only extracting those relevant to the drug in question helps in decreasing the time and space complexity of the algorithm, thus providing greater efficiency.

III. CI/AI Techniques Applied on the Systems

This system uses propositional logic to represent the different truth statements. The presence of a drug can be represented using its representative boolean symbol while allergies and conditions that prevent drug prescriptions can be represented as the negation of the drug's symbol. Logical connectives such as "and" and "or" will be utilised to build the logical statements. As for drug-drug interactions, the relationship can be translated to its logical equivalence of the implication between antecedent and consequent. The same can be said for drugs that must be taken together whose relationship can be established as a biconditional.

These logical statements are then populated into a knowledge base (KB) representative of the patient. To determine if a drug can be prescribed or not, we represent these logical statements in conjunctive normal form represented by α. We then apply a resolution algorithm where we determine if KB entails the negation of α. The algorithm then resolves the KB via proof by contradiction.

We first assume the scenario where the patient takes the drug in question. A database query of an external database is then made to extract all known DDI of the drug. Each DDI is then translated to the negation of its corresponding logical statement which is then passed into the checking algorithms one by one. The order of passing the statements will be determined by the number of matches between the logical statement and all existing symbols in the KB with interactions of a higher match being passed in first.

This KB is then passed into an Inference Engine operating the Modus Ponens inference rules. It will be forward chaining by nature, starting from the current knowledge base and terminating when either an empty clause or the conjunctive normal form is reached. More specifically, it will first use Modus Ponens rules to convert the existing propositions into the conjunctive normal form followed by factoring to remove any duplicate symbols. If conjunctive normal form is reached with no contradictions, the loop will be run again for the next statement. Should there be no contradictions for all DDIs, the drug can then be safely prescribed. However, if there is at least one instance where an empty clause is formed, the clauses' value will become false by definition. As such, the entire KB will become false due to the universal bound laws. With the KB being false, we would arrive at a contradiction and can conclude that this drug should not be taken else it will cause an adverse effect on the patient.

IV. System Target Users and Environments

The system aims to act as a diagnostic tool to prevent users from being prescribed or consuming potentially harmful drugs. The large variety and quantity of drugs out there make it difficult to ensure that suitable drugs are used in the treatment of any given ailment. Hence, we designed the system to work in settings where large quantities of drugs are available to people who may not have a comprehensive medical record. These settings include primary and secondary healthcare settings and our target audience will be the healthcare professionals that work in these settings, and consumers that intend to take responsibility for their own healthcare needs.

Our first target audience will be healthcare professionals. Professionals such as doctors, pharmacists, specialists etc. will find our system helpful in aiding their workflows. They will be able to run suitability analyses on drugs with respect to patients' medical background. Such analyses will be based on the rules established in our system and will work to ease the cognitive workload of such professionals. One example of this will be in the emergency departments of hospitals. Doctors and other medical personnel will have to make critical time-sensitive decisions (Li Chen et al., 2019); our system can act as a quick reference that allows such personnel to quickly make educated decisions on the suitability of drugs in emergency situations.

Apart from healthcare professionals, we also intend for our system to be applicable to consumer self-medication as a safeguard. With the democratisation of healthcare, consumers are increasingly empowered to take charge of their own health. This democratisation is brought about by easier access to drugs, data and technology (I. Hernandez-Neuta et al., 2018) and we intend for our system to contribute to this trend. Our system will enable patients with a multitude of chronic illnesses to better manage their medications that may be dispensed from different medical institutions. They will be able to cross-check the suitability of their prescriptions with reference to their personal medical history, adding a second layer of insurance against potentially harmful drug prescriptions. Consumers who intend to purchase OTC drugs for self-medication can also use our system to check if these drugs are compatible with their current medical status, as our system will take into account their current prescriptions, allergies etc. and advise them on the appropriate action forward.

V. System Operation Scenario

There are two main scenarios where this system would be utilised.

Scenario 1: Formal Healthcare Settings. Designed as an aid for healthcare professionals when prescribing drugs, this system would be a module embedded within the primary and secondary healthcare sectors' Computerised Physician Order Entry system. When a doctor wants to prescribe a drug, the system will already have the patients' drug allergies, existing drugs that he/she is taking, as well as pre-existing conditions. When the doctor

inputs the newly prescribed drug into the system for the patient, our AI would check the drug in the background and alert the doctor if there are any potential DDI or if the drug is a drug that the patient cannot take. If there is a problem, the AI will return the DDI that is problematic or the allergy that it will trigger. If there are no potential problems, the AI will take note of this new drug that the patient is taking for future reference. As such, this diagnostic aid will mostly be working in the background unless there is a contradiction. A possible edge case would be the system giving a false negative should a drug not exist in the knowledge base. However, with timely updates, this problem will be mitigated.

Scenario 2: Consumer Usage. After the AI has been trained, it can also be used in the consumer setting through an app. When the consumer first installs and opens the app, they will be prompted to authorise retrieval of their healthcare records stored on public healthcare information systems. The app will have a search bar where patients or caregivers can key in the drug they were prescribed or want to purchase. When they key in the drug, there will be a list of suggested drugs already in the system in order to prevent spelling errors. With the user input, the algorithm checks for potential complications or adverse DDIs. If there is a problem, the app will return the DDI that is problematic, the allergy that it will trigger or the pre-existing condition that causes a problem. If there are no potential problems, the AI will take note of this new drug that the patient is taking for future reference. The edge cases here would be similar to in the professional healthcare setting and can be mitigated similarly.

VI. Conclusions

Our system resolves a preventable gap in the wider healthcare system. While there have been existing solutions dealing with adverse DDIs, our system contributes through considering multiple databases of different parameters. This widens the scope of our system while also ensuring a more efficient algorithm as compared to existing solutions. A potential area for consideration would be the inclusion of DDI-specific screening intervals. Existing DDI solutions are hampered by a lack of consideration of the time factor in DDI evaluations, which adds to false positives and risks of alert fatigue (Van De Sijpe et.al., 2022). Future development of our system could use a neural network to consider the sequence and time in which the drugs are administered, which can lead to timelier and more accurate DDI alerts. As our solution relies on accurate patient information, it could also be limited should there be no existing centralised healthcare IT infrastructure where our AI can retrieve patient data from. However, there will need to be a shared effort from the government and healthcare providers to provide the necessary legislations and protections for such a system. As such, our solution might only be applicable to countries with high IT integration in their health infrastructure.

For future scalability, we could create a web or mobile application linked to a centralised cloud processing facility that stores the AI engine. Such an engine could be granted temporary access to existing healthcare databases on the specific patient to determine whether there would be an adverse drug reaction. This solution could potentially face the same challenge of data accuracy plaguing existing governmental databases as well as an increased cybersecurity risk in passing sensitive data to the cloud. As such, enhanced cybersecurity practices may be required to ensure the data stays confidential. This would allow for wider acceptance of our system in our proposed environments of healthcare and general use.

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