Aufgabe 1:
Rule-based decision support: Drug-drug Interaction (DDI) check tool

Hagar Ahmad - 01529618,
Asim Oguz - 11911461,
Moritz Alois Berne - 11911278,
Rei Ymeraj - 01503823

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1 Introduction

The rapid increase of technology has also had its impact in medicine. Throughout the years, different technologies are being implemented into medicine various fields in medicine, with the aim to prevent medical errors and improve the quality of service. One tool, which has had enormous impact to error prevention, when it comes to drug prescription is the DDI (Drug Drug Interaction) tool.In this assignment, we will take a closer look to the DDI tools and their definition, and also introduce prototype, which has been designed and implemented by our team.

2 DDI tools

DDI Tool checks for possible interactions between two or more drugs. In case a patient is prescribed two or more drugs, it could be that the drug combination is harmful for the patient. The DDI Tool alerts and informs for avoidable drug combinations, and also explains the reason why these drugs shouldn't be interacting with one another.

2.1 The ideal DDI tool

When it comes to the ideal DDI tool, there a lot of things that need to be improved.

Firstly, as shown in [1], the tool should always be operating in a dataset, which provides as much accuracy as possible. The authors of the article performed an evaluation of the publicly available DDI dataset sources. The evaluation was performed based on confidence value, description, clinical effect, citation of evidence, management options, mechanism, modality, participant/object distinction, related drugs and severity concept. Each of the publicly available DDI datasets performed differently with regards to these criterias. The authors also managed to create an improved dataset, where they merged the datasets which performed the best into an improved one.

Secondly, when it comes to a DDI tool implemented for the clinicians, it should generate as few alerts as possible, in order to prevent alert fatigue.

Lastlty, in cases where drugs prescribed has a harmful effect on the patient, an extension of the DDI tool could be to give recommendations, on possible exchange with similar drugs, which do not cause the same interactions as the prescribed ones do.

2.2 Alert fatigue and how to prevent it

Alert fatigue is a commonly used term in medicine, which refers to the multiple alerts sent from the hospital information system to the clinicians, which eventually ends up in mental exhaustion and ignoring the alerts from the clinicians, and could potentially lead to burnouts.

According to the article in [2], in a study in 2014, took the alerts from a 66 bed ICU, which generated roughly 2 million alerts per months, meaning approximately 187 warnings per patient a day. But what strategy could be used to minimize alert fatigue?

1. Improve alert specificity, by filtering the unnecessary alerts.
2. Tier alerts according to severity.
3. Distinguish high-level alerts by making them interruptive.
4. Apply human factors principles when designing alerts (e.g., format, content, legibility, and color of alerts).
5. Acceptable number of drugs from different therapeutic categories to treat a specific condition factored into duplicate therapy screening.
6. Users should also be encouraged to report irrelevant and overused/misused alerts to avoid noisy clutter. [2][3]

2.3 DDI tool target group

DDI tools can be used by different target groups such as:

1. Medical staff (clinicians, nurses, etc)
2. Researchers from different fields of studies, interested in drug interaction.
3. Concerned patients, who would like to have a better overview on the prescribed medications.

2.4 Motivating target group to use DDI tools

DDI tools are publicly available for usage, but also available for the medical system. The challange which is faced is how to motivate the users to use the DDI tools efficiently.
As described in section 2.2, alert fatigue is a factor which prevents clinicians into using the tools as productive as possible. Avoiding such alerts with the methods introduced in the section, would definitely increase the motivation of the DDI tool usage within that group.
For the rest of the target group, it could be that they are unaware that such tool actually exists and is publicly available online. Maybe informing them about the existence of the tools and giving reference to the publicly available DDI tool webpages would be a solution to this.

2.5 Recommendations of the DDI tools

Currently, the recommendations that the publicly available DDI tools give, is whether the drugs should be combined together or not, and an evaluation based on weighted grading system starting from:

1. **Do not use together**: Drugs should not be taken as prescribed.
2. **Serious**: Drugs have serious interaction with one another. Could potentially still used together.
3. **Monitor closely**: Drugs have an interaction with one another, but patient should be under observation, while taking them.
4. **Monitor**: Could potentially be an interaction between the drugs.
5. **No interaction**: Drugs combination is safe, and there is no interaction between them.

This form of evaluation is pretty much the same across all the online DDI tools, maybe with different grading schemes.
What potentially could be an extenson, and recommendation from this tool, would be as mentioned in section 2.1, the extension of recommending possible drug alternation in the cases "Do not use together" and "Serious".
Another extension that could be implemented for the DDI tools used by clinicians, would be the reminder to recommend dosage alternation to the clinician after a certain period of time, that the prescription has been issued.

2.6 Currently available DDI tools

As of today, there are several DDI tools available online, which can be used by researchers and patients. The list below shows some of these webpages:

- **Drugs**: drugs.com (No registration required)
- **Epocrates**: epocrates.com (Registration required)
- **DrugBank**: go.drugbank.com (No registration required)

Whereas in the medicine, the DDI tools are implemented inside the EHR. However, there are some companies, which provide DDI softwares for clinics. An example would be Lexicomp , which offers this kind of service.

3 Developing an DDI tool

3.1 Design-Mockup

3.1.1 Idea

We have chosen to implement the app as a web using Python and html programming languages to stay away from complexity for us and the user.
We have thought of a simple and flexible implementation as follows: With the search box you can add a drug via the button "Add Drug". This allows all added drugs to be counted and also marked for the user. If several drugs have been added successfully, you can also see the communication between them with "Add Result" button.

3.1.2 Usability Aspects

With this we have covered several usability aspects:

- Flexible and efficient: Add a drug or get a result with just one click
- Visual Clarity: All added drugs are transparent to the user so you don't forget what was added
- Expected and error prevention: Only the drugs can be added and if anything else is added it will not be accepted
- Consistency: strict intellectual connection in logic

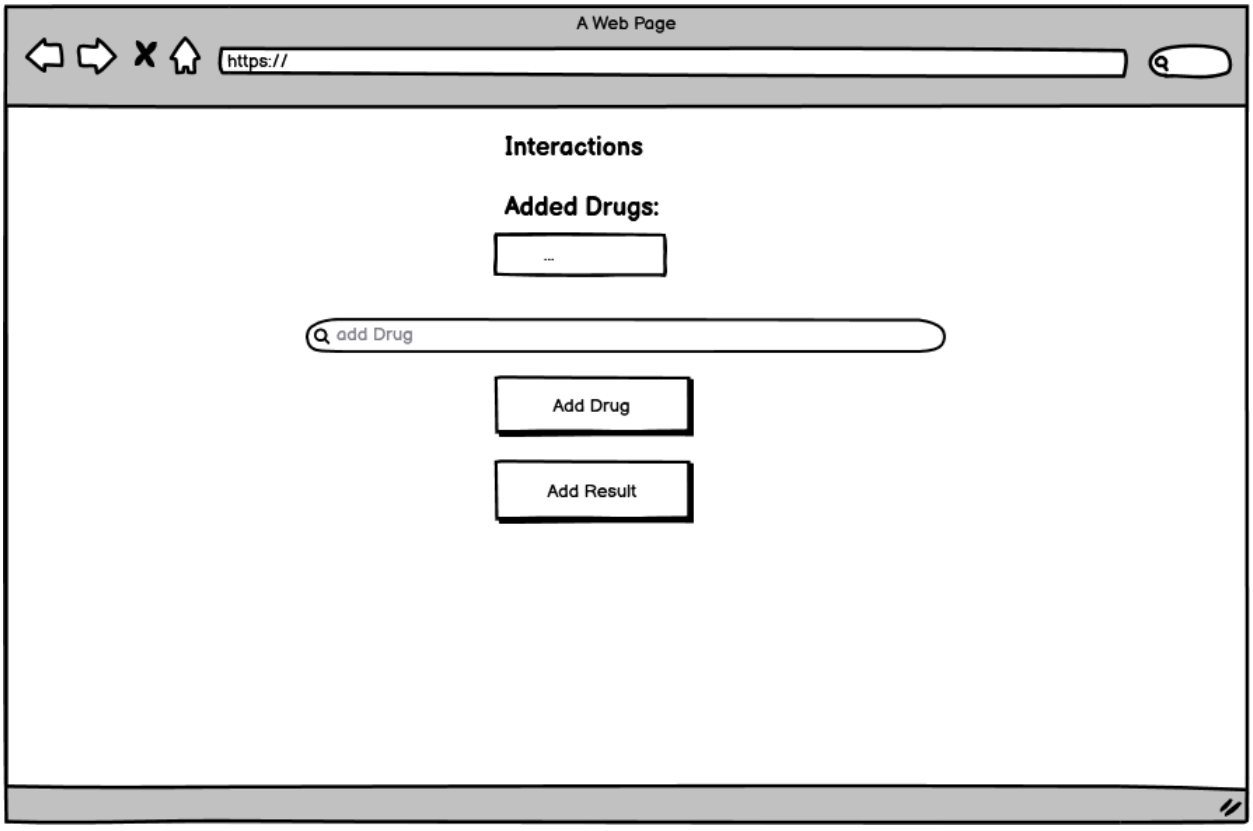

Figure 1: Mockup: DDI Tool user interface

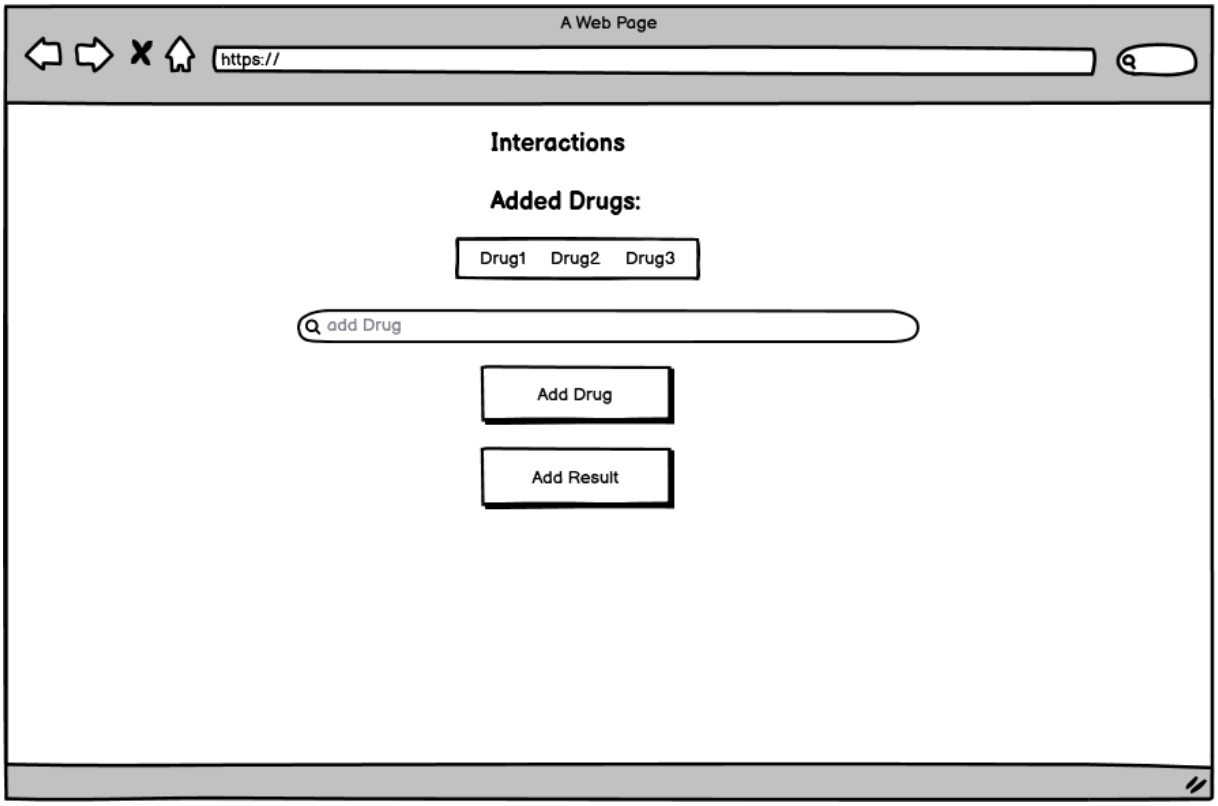

Figure 2: Mockup: Add some Drugs

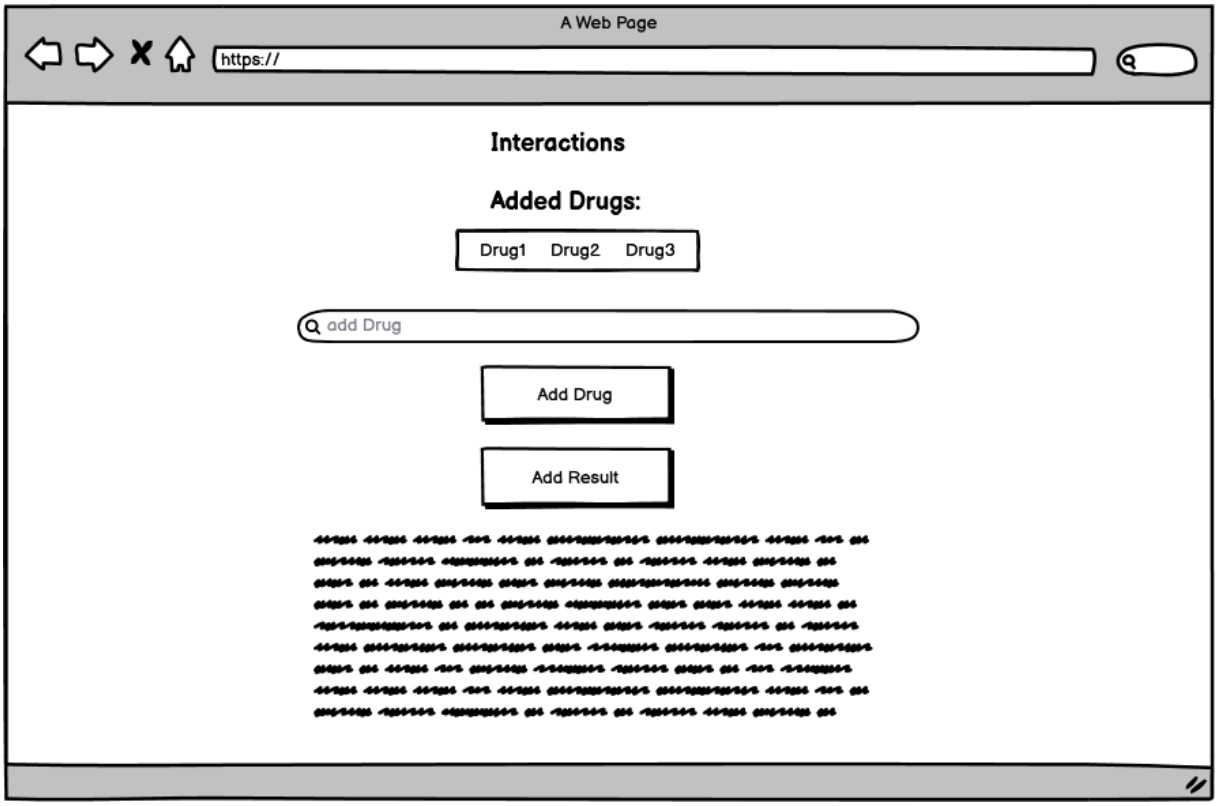

Figure 3: Mockup: Show Result

3.2 Prototypes

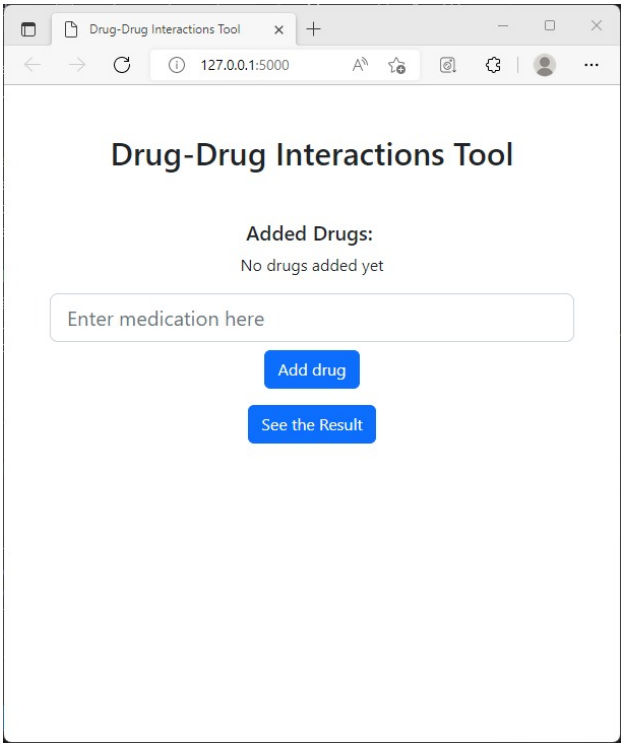

Figure 4: Prototype: DDI tool user interface

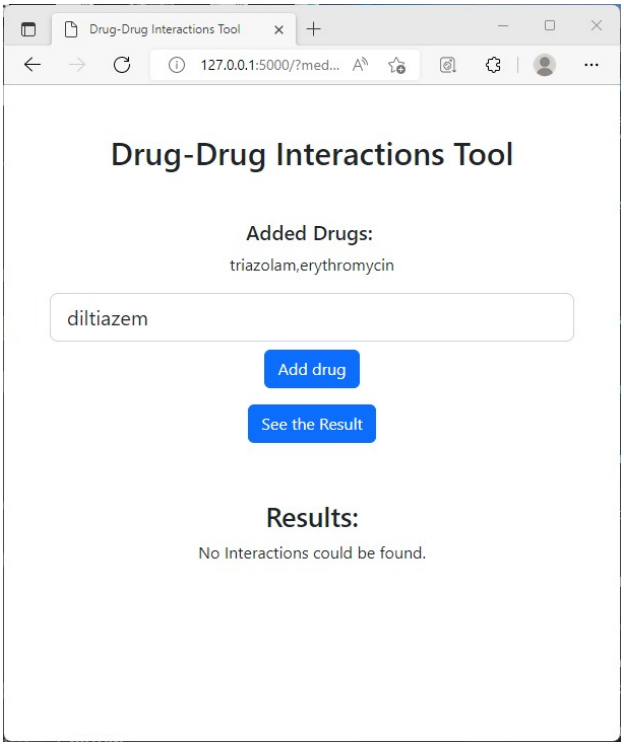

Figure 5: Prototype: Add some Drugs

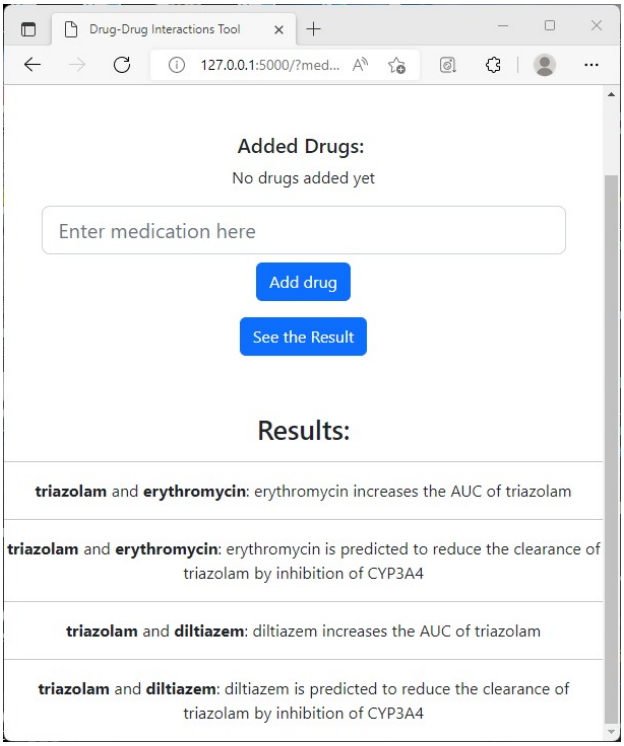

Figure 6: Prototype: Show result

Figure 4 shows the user interface for the prototype of the DDI Tool created by our team. Our implementation follows similar structure as the publicly available online DDI tools (See section 2.6). The dataset that we used for drug comparison, is a subset of the dataset created by the authours of [1]. Figure 5 present a use case, where the user enters 3 different drugs, and the results of the interaction these three drugs have with each other are shown in figure 6.

Link to GitHub repository: https://github.com/AsimO03/Drug-Drug-Interaction.git

4 Work distribution

The workload for this assignment was distributed as follows:

- Hagar and Rei: Dokumentation and Mockup
- Moritz and Asim: Functional Prototype

5 References

1. **Ayvaz S., Horn J., Hassanzadeh O., Zhu Q., Stan J., Patonetti N., Vilar S., Brochhausen M., Samwald M., Rastegar-Mojard M., Dumontier M., Boyce R.** "Towards a complete dataset of drug-drug interaction information from publicly available sources." Journal of Biomedical Informatics, Volume 55, June 2015, p.206-2017
DOI: doi.org/10.1016/j.jbi.2015.04.006

2. https://psnet.ahrq.gov/primer/alert-fatigue

3. Alert Fatigue and Patient Risk: An Effective Drug Decision Support System Could Eliminate Both