VAE-Insight: A Vaccine Adverse Event Prediction System

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1 INTRODUCTION

During the past two years of the pandemic, people have seen voluminous hype about the vaccine's effectiveness and, at the same time, heaps of misinformed allegations about the vaccine's side effects. The non-transparency of the potential danger of vaccines makes it challenging to build utter trust in them. As recipients, people often oscillate between the hazards of the virus and the vaccine's potential side effects and often feel fear and anxiety. Therefore, our team is interested in making some difference in helping every person who may not understand those obscure biomedical sciences figure out the effects of the vaccine, especially its harmful effects, considering that its positivity has been well reported and publicized.

2 PROBLEM DEFINITION

Our group proposes a system that integrates data and text mining in numerous records, side effects prediction for the user, and provides alerts and recommendations based on the predicted results. The proposed system first employs YAKE to extract keywords from all the recorded symptoms. Then, it includes a classification model using the recipients' information as input and output for the potential adverse reactions. The final product will be a UI that allows users to enter their health conditions and vaccine type of interest and obtain appropriate information interactively. More specifically, the website presents the potential risk to users based on their health conditions and the vaccine type. Accordingly, some relevant medical records are provided to the users. These records are believed to be the most accurate, honest, and convincing evidence to help users estimate whether they will experience adverse effects and how severe they will be. At the same time, the system will give some reasonable vaccination recommendations and side effect prevention suggestions for any particular vaccine.

There are certain groups of people that could be related to our work. First, vaccine recipients. Vaccine recipients are the ultimate beneficiaries of the vaccine development process. They receive the vaccine in order to protect themselves from infectious diseases. They also play a role in reporting any adverse reactions they experience after receiving a vaccine, which can help identify and manage any possible side effects. Secondly, vaccine developers. Vaccine developers are responsible for creating new vaccines and determining the most effective way to stimulate the immune system to provide protection against specific diseases. In doing so, they must carefully consider the potential side effects of each vaccine and work to minimize any risks associated with vaccination. Secondly, Last but not least, regulatory agencies. Regulatory agencies such as the US Food and Drug Administration (FDA) are responsible for evaluating the safety and efficacy of new vaccines before they can be approved for use so they can gain insights from our work.

It is common for individuals to be insufficiently informed by the time they receive their vaccinations. If our project achieves success, we will furnish our users with a comprehensive safety briefing, which comprises details concerning the different types of vaccines available and their respective manufacturers, along with information pertaining to vaccine-related adverse events. Furthermore, studies indicate that individuals exhibit greater trust in CDC and demonstrate a higher likelihood of accepting vaccines when they receive information about VAERS and summary data in addition to the standard Vaccine Information Statement (VIS) (Scherer, Shaffer et al. 2016). If our project attains its goal, vaccine hesitancy will be reduced, and the public will likely exhibit increased confidence in the efficacy and safety of vaccination. To assess the effectiveness of our project, a user study could be conducted via surveys or questionnaires, including questions pertaining to: 1) the user's decision to take the vaccine, 2) the user's level of preparedness after using our application, and 3) whether or not the user experienced any of the adverse events suggested by our application.

Several risks of machine learning in healthcare have been asserted in the literature. The delivery of modern-day healthcare can carry inherent, elusive biases that might affect algorithms. Char (2015) presents racial differences, individual case differences, and other factors. Similarly, VAERS data might contain implicit biases. We will carefully inspect the VAERS data through its user guide and add features that direct patients to recognize our output as a reference that assists in bridging a more compatible patient-medic relationship. Previous research (Kata, n.d.; Poland, n.d.) has shown that a crucial cause of said issues is the misinformation through various media that has made credible information unconvincing. Upon the rightful conduct of our study, we expect to create a compelling tool for patients to prompt correct information and a subsequently informed vaccination choice, which will debunk misinformation and enhance trust towards healthcare professionals.

3 LITERATURE SURVEY

There have been numerous studies to investigate the influence of distinct factors on adverse effects. Woo et al. (2003) analyzed several cases to figure out what could possibly lead to ELS symptoms after receiving vaccines. The importance of various measures associated with adverse effects after COVID-19 vaccination has also been explored in a prior study by Betty et al. (2021). In addition, Nguyen et al. (2021) emphasized that the most important factors of the adverse event of AZD1222 are gender, age, and vaccine doses. Cai et al. (2021) offer a comprehensive review of the use of mRNA vaccines for infectious diseases. However, we argue that previous literature suffers from certain weaknesses: the types of vaccines they focused on were too narrow, which prevented them from reaching a general conclusion about the relationship between various side effects and factors. The lack of power of the models they used is another reason why they were unable to make such an analysis. Both points will be improved in our project.

Besides, some authors (Clements et al., 2023; Smith et al., 2017) have recognized that people's expectations and acceptance of the vaccine's side effects are significantly influenced by extra features other than the vaccine itself. The authors are well aware of these influences. However, they have not attempted to use them to help recipients better understand and face the adverse effects of vaccines by affording them reasonable recommendations and warnings. Our proposed system will cover this part.

Moreover, in the field of text-mining, YAKE (Campos et al., 2020) is an unsupervised algorithm that does not rely on dictionaries, external corpora, text size, language, and domain but only executes statistical text feature extraction from the limited text provided. This algorithm outperforms other state-of-the-art approaches in 20 testing datasets. In our project, it is employed to extract clear-cut and transparent features from the symptom descriptions for the subsequent prediction, interaction, and recommendations. Despite the booming development and extensive research in the NLP area, these techniques have not yet been widely adapted and applied in the healthcare domain, and some examples of attempts have apparent limitations. Komenda et al. (2016) and Shan et al. (2022) use text-mining techniques to understand traditional Chinese medicine records and medicine curricula, respectively. However, their study is conservative since they do not try to utilize the obtained results to help people go more profound, like uncovering hidden connections between knowledge or driving certain decisions.

In addition, previous studies (Shimabukuro et al., 2015; Varricchio et al., 2004) have been identified on gaining a better understanding of the Vaccine Adverse Event Reporting System (VAERS), which provide us with valuable insights into its objectives and limitations. A notable drawback of the system is its passive reporting nature, where individuals are responsible for voluntarily submitting their adverse event experiences to the CDC and FDA.

4 METHODOLOGY

4.1 Data Pre-processing

We incorporated data from 2017-2017 about vaccination adverse effects from the VAERS dataset. Each year has three documents respectively, including 'VAERSDATA' that contains data on each incident, 'VAXDATA' that contains data on each vaccine, and 'SYMPTOMS' that contains data on the reported symptoms. To facilitate the use of the data in the subsequent modeling section, we use various non-trivial methods to transform the input data containing various patient information into a one-dimensional numeric array and the output data representing the patient's side effects into a binary vector. More specifically, the concrete data cleaning process contains the following steps:

- Conform data types: Transforming data to either int64 or float64 formats as needed.

- Dropping unusable data points: First, we dropped several features based on domain knowledge. Then we implemented several machine learning algorithms to help us complement missing values. In order to maintain validity, we chose to only insert values to rows that have one missing value. This prevents the need for a large number of models(the current method would already require n models for n features) and ensures enough dimensions are used for each column. After this process, the column 'ALLERGY' became an empty column and was subsequently dropped.
- Attempt to complement missing values with intuition, mean value, and non-trivial ML methods: Out of the 21 features, we complement the missing values respectively with their enlisted methods if needed; some complete features are left untouched. The detailed methods are organized in Table. 1.
- Extract symptoms from 'VAERS' and 'SYMPTOMS' for output vectors using categorization and NLP: We concatenated all the symptom text into one big corpus and implemented the proposed 'YAKE' module to extract keywords from it. Unfortunately, without a proper corpus to preprocess the input, we were unable to extract defining keywords from the data. Hence we turned to count the most frequent symptoms, which is similar to term-frequency, to pinpoint our symptoms. We eventually selected the 24 most common symptoms with one additional 'Others' column for those that are not included.
- Encode non-numerical categorical values for output: we used one-hot encoding to turn the column 'SYMPTOM_TEXT' into vectors as our output data.
- Join 'VAX' and 'VAERS' datasets for input vectors: We inner joined cleaned VAX dataset and VAERS dataset to get our final input dataset.

4.2 Model & Evaluation

4.2.1 Model. We choose to use multi-layer perceptron (MLP) as our backbone to train the model due to its versatility, simplicity, and ability to model non-linear relationships between input and output variables. Our model has four fully connected layers. The detailed structure is shown below:

Feature	Method
VAX_TYEP	KNN
VAX_MANU	KNN
VAX_DOSE_SERIES	XGBoost
VAX_ROUTE	KNN
VAX_SITE	XGBoost
V_FUNDBY	None
V_ADMINBY	None
ER_VISIT	Intuition
HOSPITAL	Intuition
DISABLE	Intuition
RECOVD	Intuition
HOSPDAYS	Intuition
SEX	None
FORM_VERS	None
LAB_DAT	Count Encode
OTHER_MEDS	Count Encode
CUR_ILL	Count Encode
HISTORY	Count Encode
PRIOR_VAX	Count Encode
NUMDAYS	Mean
AGE_YRS	Mean

Table 1: Methods used to complete the missing values.

```
MultiLabelModel(
  (fc1): Linear(in_features=21, out_features=128, bias=True)
  (fc2): Linear(in_features=128, out_features=64, bias=True)
  (fc3): Linear(in_features=64, out_features=32, bias=True)
  (fc4): Linear(in_features=32, out_features=25, bias=True)
)
```

Figure 1: The detailed structure of the proposed model.

The input of our model is the 21 personal information, which are AGE_YRS, SEX, ER_VISIT, HOSPITAL, HOSPDAYS, DISABLE, RECOVD, NUMDAYS, V_ADMINBY, V_FUNDBY, FORM_VERS CUR_ILL_num, HISTORY_num, PRIOR_VAX_num, LAB_num, MEDS_num, VAX_TYPE, VAX_MANU, VAX_DOSE_SERIES, VAX_ROUTE VAX_SITE, and the output are the 25 kinds of common symptoms. In our project, we extracted 12 kinds of the most important and most popular symptoms as the final results, which are Pain in extremities, Fatigue, Headache, Myalgia, Malaise, Pyrexia, Injection site pain, Erythema, Pain, Chills, Injection site swelling, Nausea. In this way, our model becomes a muti-label binary classification problem. Every dimension of our output is in the range of 0 to 1. That's why we choose sigmoid as the activation function on the last layer.

We must notice that there are related state-of-the-art prediction methods for vaccine side effects. For example, Vaccine Safety Datalink (VSD) is a collaborative project between the CDC (Centers for Disease Control and Prevention) and several healthcare organizations that collects and analyzes data on vaccine safety. This is more like an open dataset for people to view. Brighton Collaboration, a global network of vaccine safety experts, develops standardized definitions and guidelines for assessing adverse events following immunization. This community is committed to improving health by promoting and enhancing vaccine safety through rigorous science and global collaboration. Nevertheless, there is no exact competing product with our approach. The existing methods are either indirect data collection or rely heavily on human expertise. There isn't an application that utilizes machine learning methods to make a prediction. Compared with those state of art methods, we have a more direct prediction application with a complete user interface. Our approach has several advantages over the current state of the art. The first advantage is that we provide users with a more direct and visible prediction result. The second advantage is the ease to use. Since we have an application for it, the user needs to type in their conditions, and the prediction of side effects will pop out. Last but not least, our approach is valid. Although the results are primarily for reference only, the results are provided through machine learning algorithms and thus mathematically reliable and reproducible.

4.2.2 Evaluation. Except for our own MLP model, we try some vanilla models like LSTM or CNN models, which act as the first network that people think up when doing the classification task, for predicting results. We train them on 18481 data points and then test them on 4621 data points. The evaluation is based on Mean Absolute Error (MAE) between predicted outputs and actual labels and on all exact matches, which requires all 25 categories' results to be the same. The results are shown in Table. 2.

Model	MAE	Exact Match Accuracy
LSTM	79.48%	18.57%
CNN	81.56%	17.53%
Proposed Method	94.39%	26.75%

Table 2: Evaluation: Prediction Results of Different Model.

4.3 User Interface

We have built an integrated website to provide users with complete information on vaccines and side effects as well as visualization of models and their results, including information on:

- The website is built by the flask framework, which uses js to achieve a beautiful UI design.
- The website uses SQL to connect to the database and supports users to register, login, organize and record their health and vaccine-related information. It is important to note that the site makes a lot of effort to protect user's private data. Their personal information is encrypted, and non-logged-in users are only allowed to browse the site in restricted mode.
- The presentation of the prediction's output was achieved through the utilization of HTML, Fig. 2. The predictive algorithm generates forecasts pertaining to 12 prevalent adverse events that may arise following vaccine administration, specifically: sore arm, tiredness, headache, muscle aches/pain, feeling unwell, fever, injection site pain, redness in the arm, joint pain, chills, swollen arm, and nausea. In addition, the predictive model assigns a corresponding level of confidence, denoting the likelihood of an individual experiencing the aforementioned adverse events based on the information inputted into the system.
- We used Dash to build two powerful interactive visualizations to help users explore the in-depth relationships between various features and side effects. First, the user can select the features and side effects they want to know about. As shown in Fig. 3, the heatmap plainly visualizes the correlation between the selected variables using a set of color gradients. In addition, the Sankey diagram is a good choice when the user wants to get a clearer picture of the statistics, such as the percentage of side effects caused by each feature. As shown in Fig. 4, the user can select the features and side effects he is concerned about in the dropdown list. The Sankey diagram will show the

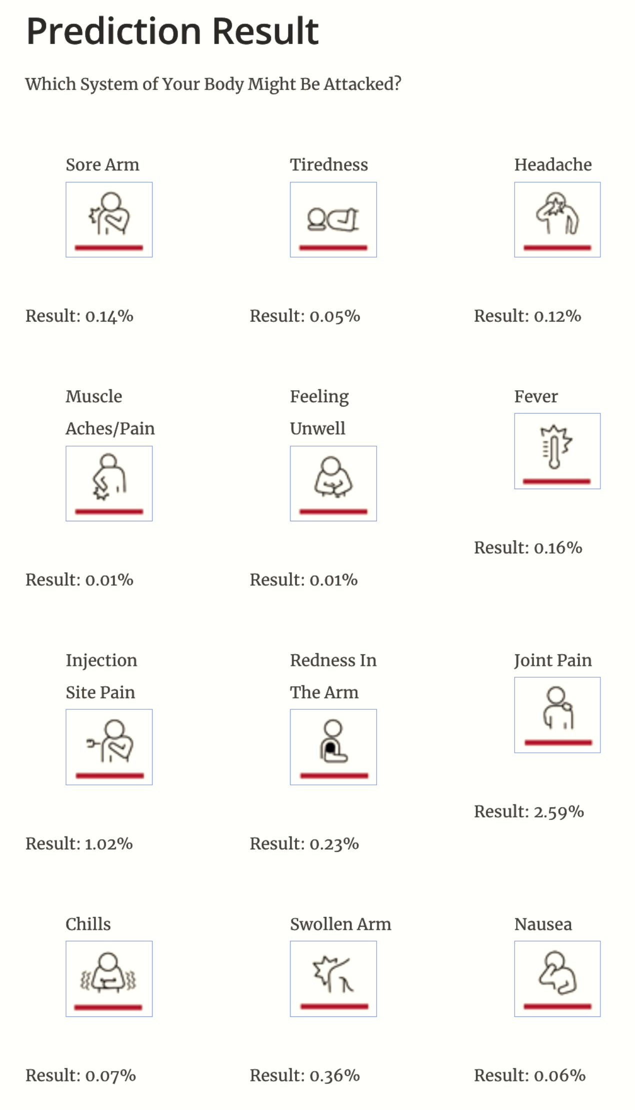

Figure 2: Prediction Result (Demo).

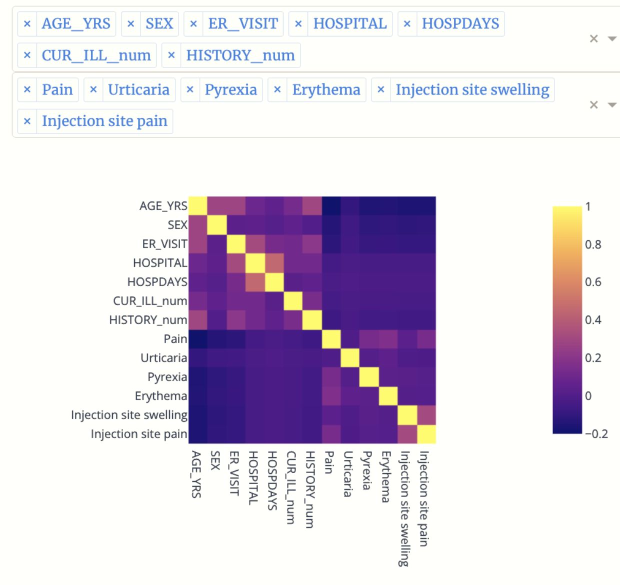

Figure 3: Heatmap (by Dash).

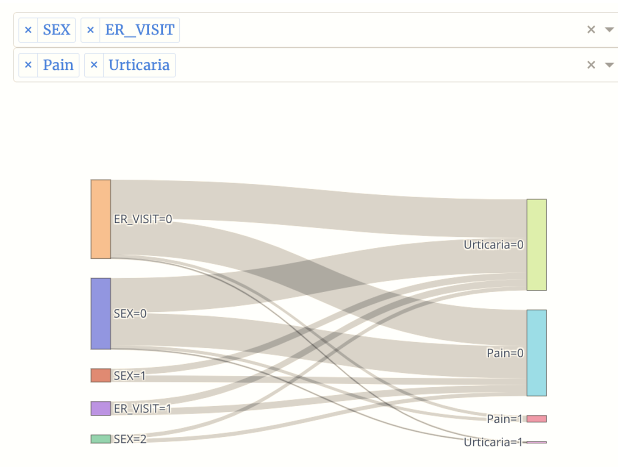

Figure 4: Sankey Diagram (by Dash).

correlation (causality) between them in the form of flows, and the width of the flows will intuitively reflect the size of the different links. Through the presentation of the Sankey diagram, the user can well assess his own situation regarding the risk of side effects, which is one of the main goals of our project.

5 CONCLUSION

The widespread and intense debate about vaccine effectiveness and side effects during the new coronavirus epidemic was impressive. Among them, we are able to see not only the decisive role of public opinion in promoting vaccination but also the heaps of misinformed allegations about the vaccine's side effects that deceive people. We are also perceptive that the non-transparency of the avail and potential danger of vaccines leaves the public without any ability to make rational judgments when faced with various vaccines and is forced to become a puppet under the coercion and manipulation of external factors. Motived by this situation, our project aims to help every potential recipient, every ordinary person who struggles with those obscure biomedical sciences, figure out the effects of vaccines, especially their harmful effects, with the limited context they are capable of providing about target vaccine and themselves, and with the powerful prediction models we've worked so hard to build.

Comprehensive investigation and many attempts with assorted models were made before determining the final prediction model. The results of the evaluation proved that our efforts were well-spent. The proposed model outperforms under a variety of criteria. More specifically, given a set of patient backgrounds and vaccine information, the model was able to offer a precise probability of various side effects appearing in that patient. Moreover, a user-friendly and integrated website is constructed based on the prediction model. By registering an account on this website, users can record their own health conditions and vaccine information, which is ensured to be invisible to anyone else. Based on the provided data, the website will plainly visualize the explanation of various side effects and their probability obtained from the prediction. In addition, the website offers handy visualization tools additionally to help users freely explore the connection between different factors of the vaccine and the side effects.

The dataset in our project is untargeted, coarse-grained, and has many missing values. While we work hard to complement missing values with intuition, mean-value, and non-trivial ML methods and try to diminish the impact of these on the prediction model, it is clear that much effort still needs to be made in the future. We recommend first using a more complete dataset in subsequent studies, or actions should be taken to construct a robust prediction model to handle the missing entries. In addition, a continued effort is needed to collect targeted data on every vaccine. This is definitely difficult, as the security of personal privacy is an unavoidable issue when trying to collect information about patients, and it is even more arduous to collect data for vaccines that only have a small number of recipients. However, we believe it is worth the effort and will significantly improve the model's performance.

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