Medicine Recommender System

Liam Attard

***Abstract*—**

***Index Terms*—Recommender Systems, Health Care AI, Collaborative Filtering, Electronic Health Records.**

I. Introduction

With over 20,000 FDA approved medications that are prescription-only, doctors may face a challenge when giving out medicine to a specific patient. Unfortunately, the FDA receives more than 100,000 declarations of medication errors each year in the United States alone [1]. As a result, prescribing medicine to patients remains a challenge, and modern solutions are moving from the all-purpose medicine concept to personalised health care [2].

Modern hospitals use Electronic Health Records (EHR) to keep track of everything and control the complexity of data. EHRs are a collection of clinical information gathered from health care patients. The mass adoption of such systems delivers a large amount of data compiled on a patient's visits, such as demographics, diagnosed conditions, medical prescriptions, procedures and any health-related history [3].

This data is being used for machine learning systems to improve and automate clinical care practices, for example, early disease detection and identifying patients at high risk of severe conditions [4], [5].

A system that recommends a list of medicine based on a patient's current state will serve as an essential decision-support tool for medical experts to assist with drug prescriptions and could help prevent prescription errors [6].

Recommender Systems (RS) are techniques that derive patterns and suggest items to a user. Combining RSs with an EHR dataset develops a system that recommends personalised medicine by learning from the prescribed drugs and the patient information. Existing medicine recommender systems make use of user reviews or past diagnosis [2], [7].

However, medicine recommender systems come with both opportunities and challenges. The most difficult challenge is perhaps the lack of available health-related data online. Ibrahim et al. [8] stated that health data poverty stops individuals from implementing data-driven technologies that benefit healthcare. Another data-related challenge is that most health data is anonymised for privacy concerns which is a good thing; however, it presents a challenge for systems to learn. Unlike data from an e-commerce website, medical data in an EHR is implicit, meaning there is no rating about each user-item interaction.

II. Aim and Objectives

The new era of precision medicine brings forward systems that can work hand in hand with clinicians by personalising the patient's results and preventing medication errors. This project aims to build a health RS that uses a person's current state and past medical history (demographics, diagnosis, and physiologic data) to recommend a set of personalised medications from an EHR. We will try to answer the following research question:

Can personalised recommendations suggest medicine for patients?

We form the following objectives to achieve our aim:

- Address cold start issues when introducing new patients.
- Find the best model suited for all possible scenarios.
- Make sure that any pair of recommended medicine does not cause any adverse side effects with each other.
- Determine important features in the EHR that hold the most value when predicting medicine to patients.

III. Related Work

This section briefly explains the medicine RS research area, lists similar systems, and explains what technologies their researchers used to build them. When available, we also try to look into their solutions for the objectives listed in section II. We will split the research into two categories, described in the following subsections.

A. Ontology and Rule-Based Systems

These systems typically rely on a set of rules, referred to as a knowledge base, that mimic the logic of a medical expert [9].

GalenOWL [10] recommends drugs to patients based on the user's diseases, allergies and drug interactions. The system stores the rules in a Resource Description Framework graph and uses SPARQL to query the knowledge space. The results were reviewed and evaluated by a medical expert, and it was stated in future work that there should be an expansion of semantic rules.

Doulaverakis et al. created the Panacea [11] system based on GalenOwl's approach. They use SKOS vocabulary for the rules. Results show better query performance over GalenOwl and accommodate a far greater knowledge base.

Lakkaraju et al. [12] model their RS using a decision list as a Markov Decision Process (MDP) and Upper Confidence Bound Trees to prune the search space efficiently. Their system maps between demographics and treatments and try to maximise outcomes, minimise treatment costs and expresses this into an interpretable tree-based model. They evaluated their system by using criminal justice and health care domains.

Not all medical RS focus on recommending medicine to all types of patients; some decide to focus on a specific group of people. For example, IRS-T2D [13] is a system built to personalise medicine for patients with type 2 diabetes. The solution uses Semantic Web Rule Language from HbA1c tests, anti-diabetics, and dose selection restrictions. To evaluate their system, they used a dataset made up of 30 patients and achieved a very high precision rate.

Hamed et al. [14] make a different approach. They analyse a set of 500,00 tweets to recommend medication. They start by checking the condition of a person, send them a questionnaire to get more info and apply a C4.5 decision tree algorithm to predict the condition of the user. Based on the result, the algorithm can derive the correct medical product.

While rule-based approaches offer reasonable solutions, they also have advantages and disadvantages. Since everything is based on rules, they are more prone to cold start issues [15]. However, They are not easy to scale, and it is challenging to add rules to an ample domain space without introducing conflict [2].

B. *Machine learning-based Approaches*

There are two main ways of approaches to building Machine-Learning based RS. The first method is using Collaborative Filtering (CF). Using this approach, an RS recommends items to a user based on the choices of similar users. The algorithm measures user similarity from features like demographics, diagnosis or prescriptions. Another approach is using content-based filtering (CF), which uses item similarity instead. For example, if a user was given medicine A with similar features to medicine B, that is recommended.

CF is used by CADRE [16], trained on the Walgreens dataset, which unfortunately has been removed. CADRE is a cloud-based RS that performs top-N recommendations in three steps. The data pre-processing part is for clustering and cleaning the data, and after CF, tensor decomposition addresses the sparsity problem of CF. Unfortunately, this system achieved low results; however, not many features were used to train the model, and the dataset contains only around 6000 users. They

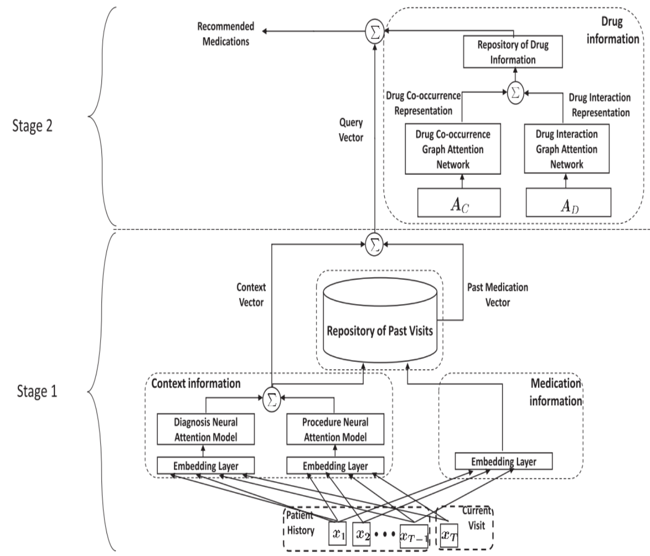

Fig. 1. PREMIER's two Stage Recommender System.

state that future work could use user demographics to increase F1, accuracy and recall scores.

The Mimic dataset is a publicly available EHR dataset that will be described in detail later in section X. Several RS use such datasets like LEAP, PREMIER and Wang et al.'s system.

Zhang et al. [17] created LEAP , an end-to-end learning algorithm that uses a recurrent decoder and content-based attention for treatment recommendation from disease-drug mapping. Leap used reinforcement learning to fine-tune the model and achieved a 10% increase performance overall baselines. Bhoi et al. [2] categorised this approach as an instance-based system that only recommends medicine based on current visits and does not consider past visits.

Recurrent Neural Networks were popular architectural choices for mimic-based RS mainly because of their memory ability which is vital for training on user visits [18]. PREMIER [2] is a two-stage attention-based RS. Figure 1 shows the architecture with information about each stage. In the first stage, the system uses past diagnoses and procedures and embeds this information into the RNN. In the second stage, they combine the second dataset of drug interactions to ensure that each recommendation is safe for the user. The system also justifies the recommendations by splitting them into two parts; one for the diagnosis and one for the procedures, and uses a weight feature to calculate the importance. As a result, PREMIER outperforms state-of-the-art medication recommendation systems while achieving the best tradeoff between accuracy and drug-drug interaction.

Finally, Wang et al. [18] proposed a solution that uses Supervised Reinforcement Learning with RNNs on the Mimic Dataset. They contain an off-policy actor-critic architecture to discover unique optimal personalised treatments and evaluated that their system can decrease the estimated mortality in hospitals by up to 4.4%.

IV. Proposed Idea

Health RS plays an essential role in food, diet, and physical activity recommendation, and RS research is growing fast, especially in the e-commerce sector [19]. However, the RNN prediction solutions like Wang et al. [18] and PREMIER [2] only incorporate past diagnoses and past procedures. Our proposed solution for this study is to use the vast amount of data in EHR like MIMIC in the RS. The following describes our proposed ways of tackling the objectives.

1) Cold start issues: : The more features the system contains, the more it can handle cold start issues for new patients with little data. For example, if the system is trained on the age, diagnoses and procedures and a new user only has the first two, the system should be capable of recommending the right medicine.

2) Finding the best Model : After splitting the dataset into a training set and a testing set, we would like to find the best model that achieves the highest scores.

3) Adverse side effect prevention : We can aggregate the EHR dataset with a drug interactions dataset containing information about a specific medication and its effects and conflicts with other drugs. This combination ensures that any recommended medicine does not cause harm or damaging side effects to any patients.

4) Important Feature selection : Choosing the best features from the EHR dataset helps us build an efficient model. Our goal is to determine which data hold value for increasing accurate predictions.

A. The Dataset

The MIMIC (Medical Information Mart for Intensive Care) is a publicly available EHR dataset under the registration of the university of MIT containing data from patients admitted to the critical care units of the Beth Israel Deaconess Medical Center [20].

There are four versions of this database, and after applying, we have been given access to MIMIC III and MIMIC IV. The third version contains twenty-six tables, over 40,000 patient records (excluding people under 16), and 53,423 visits between 2001 and 2012. Each patient is de-identified and anonymised and contains medical intake, chart events, ICU date stays, demographics, doctor's notes and more. On average, each patient has around 2.68 visits, and table 2 shows some statistics about the dataset, and figure I shows the age distribution of the patients. People over 90 are grouped. Each patient is identified with a patient ID, used throughout the tables. Diagnosis, Procedures are encoded using international standards such as ICD-9 and ATC classification .

TABLE I
MIMIC III Statistics.

Number of patients	46520
Number of Diagnoses	14567
Number of Procedures	3882
Number of Medicine	4204

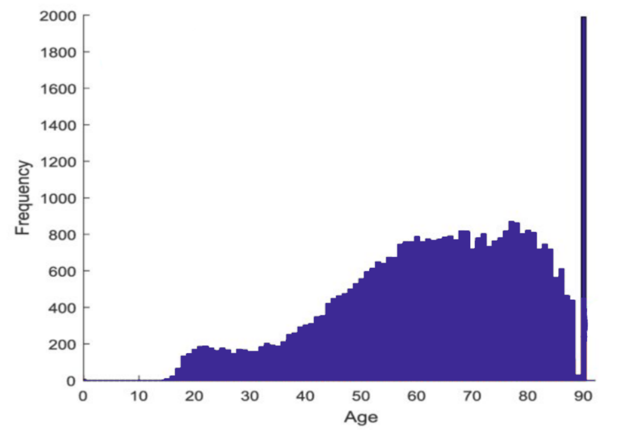

Fig. 2. Age Distribution of MIMIC III

B. Testing and Evaluation

There are three main things to test for evaluating the RS, performance, accuracy scores and drug interactions tests. These three measures will ensure that our system would recommend good medicine as fast as possible whilst also ensuring the patient's safety. We will also compare our system's safety with other RS using standard drug interactions metrics.

We will also split the dataset into training, testing, and validation sets to calculate additional evaluation metrics such as the F1 score, precision,Jaccard, Root-mean-square deviation, and Mean Absolute Errors. Doing so will allow us to compare our system with existing systems that use the MIMIC dataset. We could also package the system in an application and present sample use cases to demonstrate our system.

V. Conclusion

REFERENCES

[1] U. F. . D. A. FDA, "Fact Sheet: FDA at a Glance," nov 2021. [Online]. Available: https://www.fda.gov/about-fda/fda-basics/fact-sheet-fda-glance

[2] S. Bhoi, M. L. Lee, W. Hsu, H. Sen Andrew Fang, N. Chuan Tan, M. Li Lee, and N. Chuan, "Personalizing Medication Recommendation with a Graph-Based Approach," *ACM Transactions on Information Systems (TOIS)*, vol. 40, no. 3, pp. 1–23, nov 2021. [Online]. Available: https://dl.acm.org/doi/abs/10.1145/3488668

[3] E. Kim, S. M. Rubinstein, K. T. Nead, A. P. Wojcieszynski, P. E. Gabriel, and J. L. Warner, "The Evolving Use of Electronic Health Records (EHR) for Research," *Seminars in Radiation Oncology*, vol. 29, no. 4, pp. 354–361, oct 2019.

[4] J. Wu, J. Roy, and W. F. Stewart, "Prediction Modeling Using EHR Data: Challenges, Strategies, and a Comparison of Machine Learning Approaches," *Medical Care*, vol. 48, no. 6, pp. S106—-S113, 2010. [Online]. Available: http://www.jstor.org/stable/20720782

[5] Y. Juhn and H. Liu, "Artificial intelligence approaches using natural language processing to advance EHR-based clinical research," *pubmed.gov*, 2019. [Online]. Available: https://doi.org/10.1016/j.jaci.2019.12.897

[6] S. Jamshidi, A. Torkamani, J. Mellen, M. Jhaveri, P. Pan, J. Chung, and H. Kardes, "A Hybrid Health Journey Recommender System, using Electronic Medical Records," *Semantic Scholar*, vol. 6, 2018.

[7] T. Rao, A. Unnisa, and K. Sreni, "Medicine Recommendation System Based On Patient Reviews," *INTERNATIONAL JOURNAL OF SCIENTIFIC TECHNOLOGY RESEARCH*, 2020.

[8] R. E. Ferner, "Medication errors that have led to manslaughter charges," *BMJ : British Medical Journal*, vol. 321, no. 7270, p. 1212, nov 2000. [Online]. Available: /pmc/articles/PMC1118964/ https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1118964/

[9] B. Stark, C. Knahl, M. Aydin, and K. Elish, "A Literature Review on Medicine Recommender Systems," *IJACSA) International Journal of Advanced Computer Science and Applications*, vol. 10, no. 8, 2019. [Online]. Available: www.ijacsa.thesai.org

[10] C. Doulaverakis, G. Nikolaidis, A. Kleontas, and I. Kompatsiaris, "GalenOWL: Ontology-based drug recommendations discovery," *Journal of Biomedical Semantics*, vol. 3, no. 1, pp. 1–9, dec 2012. [Online]. Available: https://jbiomedsem.biomedcentral.com/articles/10.1186/2041-1480-3-14

[11] ——, "Panacea, a semantic-enabled drug recommendations discovery framework," *Journal of Biomedical Semantics*, vol. 5, no. 1, pp. 1–10, apr 2014. [Online]. Available: https://link.springer.com/articles/10.1186/2041-1480-5-13 https://link.springer.com/article/10.1186/2041-1480-5-13

[12] H. Lakkaraju and C. Rudin, "Learning Cost-Effective and Interpretable Treatment Regimes," in *Proceedings of the 20th International Conference on Artificial Intelligence and Statistics*, ser. Proceedings of Machine Learning Research, A. Singh and J. Zhu, Eds., vol. 54. PMLR, 2017, pp. 166–175. [Online]. Available: https://proceedings.mlr.press/v54/lakkaraju17a.html

[13] N. Mahmoud and H. Elbeh, "IRS-T2D: Individualize Recommendation System for Type2 Diabetes Medication Based on Ontology and SWRL," *Proceedings of the 10th International Conference on Informatics and Systems - INFOS '16*, 2016. [Online]. Available: http://dx.doi.org/10.1145/2908446.2908495

[14] A. A. Hamed, R. Roose, M. Branicki, and A. Rubin, "T-Recs: Time-aware twitter-based drug recommender system," *Proceedings of the 2012 IEEE/ACM International Conference on Advances in Social Networks Analysis and Mining, ASONAM 2012*, pp. 1027–1031, 2012.

[15] Pradeep Kumar Singh, Pijush Kanti Dutta Pramanik, Avick Kumar Dey, and Prasenjit Choudhury, "Recommender Systems: An Overview, Research Trends, and Future Directions," *Int. J. Business and Systems Research*, jan 2021. [Online]. Available: https://www.inderscienceonline.com/doi/abs/10.1504/IJBSR.2021.111753

[16] Y. Zhang, D. Zhang, M. M. Hassan, A. Alamri, and L. Peng, "CADRE: Cloud-Assisted Drug REcommendation Service for Online Pharmacies," *Mobile Networks and Applications*, vol. 20, no. 3, pp. 348–355, dec 2015.

[17] Y. Zhang, R. Chen, J. Tang, W. F. Stewart, and J. Sun, "LEAP: Learning to Prescribe Effective and Safe Treatment Combinations for Multimorbidity," in *Proceedings of the 23rd ACM SIGKDD International Conference on Knowledge Discovery and Data Mining*, ser. KDD '17. New York, NY, USA: Association for Computing Machinery, 2017, pp. 1315–1324. [Online]. Available: https://doi.org/10.1145/3097983.3098109

[18] L. Wang, W. Zhang, X. He, G. Tech, and H. Zha, "Supervised Reinforcement Learning with Recurrent Neural Network for Dynamic Treatment Recommendation Hongyuan Zha ACM Reference Format:-vised Reinforcement Learning with Recurrent Neural Network for Dynamic Treatment Recommendation," *KDD*, vol. 18, 2018. [Online]. Available: https://doi.org/10.1145/3219819.3219961

[19] T. N. T. Tran, A. Felfernig, C. Trattner, and A. Holzinger, "Recommender systems in the healthcare domain: state-of-the-art and research issues," *Journal of Intelligent Information Systems*, vol. 57, no. 1, pp. 171–201, aug 2021.

[20] A. E. Johnson, T. J. Pollard, L. Shen, L. W. H. Lehman, M. Feng, M. Ghassemi, B. Moody, P. Szolovits, L. Anthony Celi, and R. G. Mark, "MIMIC-III, a freely accessible critical care database," *Scientific Data 2016 3:1*, vol. 3, no. 1, pp. 1–9, may 2016. [Online]. Available: https://www.nature.com/articles/sdata201635