

EFFICIENT EXPLAINABLE AND EVIDENCE BASED PRECISION AND PERSONALISATION OF TREATMENT

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Modern advances in computation enable the use of complex machine learning algorithms and artificial intelligence to assist human decision-making. However, the lack of explainability entailing from the black box nature of complex machine learning algorithms, inhibit their adoption in real-world applications especially in fields like healthcare. To address this challenge, we explored using the Odds Ratio (OR)—a clinically well-known measure of evidence—coupled with a sorting algorithm to prototype an explainable clinical decision support system (CDSS). This CDSS intakes relevant patient information such as demographic variables, clinical variables, medical history, and so on, and ranks treatment options personalised for patients, based on OR evidence. We present in this work-in-progress paper how our algorithm performs personalised ranking of therapies, taking Type-2 diabetes as a case study. As future work, we endeavour to codesign this further with clinicians to produce a primary care CDSS and assess long-term clinical outcomes.

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1 Introduction

Computational power has advanced greatly over the recent decades. This has enabled integrating advanced machine learning and deep learning algorithms to assist and augment complex decision-making processes. Along this trajectory, artificial intelligence (AI) has made inroads to assist clinical decision-making as well (Adlung et al., 2021). AI can now assist with various tasks such as pre-clinical data processing, diagnosis, patient stratification, treatment planning, early warning, and more (Adlung et al., 2021). Although AI systems offer such capabilities, many such systems function as “black box models,” providing predictions without adequate reasoning or explanation, thereby limiting the interpretability of system outputs (Ennab & Mcheick, 2024). This lack of explainability undermines the trust healthcare professionals can have on AI systems, as it is essential for clinicians to be able to understand and justify support-system outputs when making crucial clinical decisions (Amann et al., 2020). Black box AI systems have therefore faced significant barriers up to date when it comes to implementation in real-world healthcare settings (Frasca et al., 2024). The repeated emergence of the ‘explainability’ concern emphasises the importance of making AI systems more explainable if they are to be widely adopted in healthcare settings. As an attempt to address this challenge, we attempt to answer the following overarching research question: How might efficient and explainable AI-assisted clinical decision-support systems be developed?

In an attempt to answer the aforesaid research question, we explored making use of the Odds Ratio (OR) (Higgins, Li, & Deeks, 2023)-a clinically well-known and an easily explainable measure of clinical evidence-coupled with a sorting algorithm, to produce an explainable clinical decision support system (CDSS) to assist treatment planning in primary care. This CDSS takes relevant patient information as inputs and provides a personalised ranking of treatment options based on historical clinical evidence. The CDSS intakes variables such as demographic variables, clinical variables, medical history, and so on, and uses OR evidence to rank treatment options personalised for patients.

We present in this work-in-progress paper how personalised ranking of therapies is performed through our algorithm, taking Type-2 diabetes as a case study. Future work will involve codesigning this further with clinicians to produce a CDSS for primary care and assess its usefulness, usability and long-term clinical outcomes.

2 Methodology

2.1 Overarching Methodology

The overarching methodology is based on our previous works on digital twins of patients in healthcare (Wickramasinghe et al., 2025) and is depicted in Figure 1. When a new patient arrives, a digital twin of the patient is constructed using information about the patient. The information considered include the patient’s demographic information (like age, sex, and ethnicity), disease information, medical records, patient history, tests and results, and multi-omics (if available). This digital twin is compared with records of historical patients, and a cohort of historical patients that best matches the present patient is selected based certain pre-defined criteria. Evidence of treatment options and health outcomes within the matching cohort are then evaluated and ranked based on Odds ratio with respect to a target health outcome.

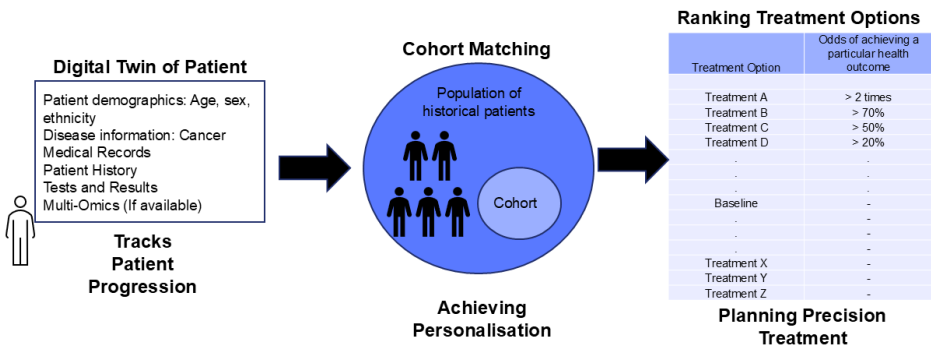


Figure 1: Proposed methodology: Personalised ranking of treatment options based on Odds ratio

Source: Own

2.1 Ranking Treatment Options based on Odds Ratio

The odds ratio (OR) is a commonly used and well-established metric to measure the effectiveness of pharmacological interventions (Higgins, Li, & Deeks, 2023). The way we use OR is depicted in Figure 2. Following the aforementioned approach of cohort matching, we consider the patients within the cohort. We compare all the treatment options against one another and calculate the OR and the Standard Error (SE) as depicted in Figure 1. We then select the statistically significant OR values, i.e., $p\text{-value} \leq 0.05$, and rank the treatment options from highest odds of success to least odds of success, thereby, presenting clinicians an evidence-based ranking of treatment options personalised to a patient.

Odds Ratio (OR) = $\frac{a/b}{c/d}$	Number of patients that achieved the target health outcome	Number of patients that did not achieve the target health outcome	Interpretation: - OR > 1 means historical evidence suggests that patients who received Treatment A have shown higher odds of achieving the target health outcome than those who received Treatment B. - OR < 1 means historical evidence suggests that patients who received Treatment B have shown higher odds of achieving the target health outcome than those who received Treatment A. - Thus, when compared with a baseline Treatment, different treatment options can be ranked based on the OR, from highest odds to least odds of achieving a target health outcome.
Received Treatment A	a	b	
Received Treatment B	c	d	

$$\text{Standard Error (SE)} = \sqrt{\frac{1}{a} + \frac{1}{b} + \frac{1}{c} + \frac{1}{d}}$$

Note: Can calculate a p-value for OR using SE.
 $p < 0.05$ is indicative of a statistically significant OR.

Figure 2: Proposed methodology: Odds ratio-based ranking of treatment options.

Source: Own

2.2 Case Study on Treatment Planning for Type-2 Diabetes

We selected a case of planning Type-2 diabetes therapies using deidentified data from a dedicated Australian diabetes clinic to demonstrate how our approach works. In the diabetes case, when a new patient arrives, historical records of a matching cohort (patient's age ± 10 years and matching sex) is selected. All available therapies from the cohort are compared with the performance of Metformin. Metformin is a commonly used diabetes therapy, and we consider it the baseline therapy against which other therapies are compared against. The odds ratio for each therapy is calculated (with p-value) against Metformin for the target health outcome of post-

therapy $HbA1c \leq 7\%$. We then rank the therapies based on statistically significant (i.e., $p \leq 0.05$) odds ratios within their respective categories of first-, second-, and later-line therapies.

3 Results

The ranked therapies resulting from our approach to two patients are depicted in Figures 3 and 4.

Patient 1 (Sex: Male, Age: 67)			
Matching cohort (Sex: Male; 67±10 years, n = 1,997)			
Personalised Ranking of First-Line Therapies	Personalised Ranking of Second-Line Therapies	Personalised Ranking of Later-Line Therapies	
4 therapies available with statistically significant evidence ($p \leq 0.05$)	8 therapy combinations available with statistically significant evidence ($p \leq 0.05$)	17 therapy combinations available with statistically significant evidence ($p \leq 0.05$)	
Metformin (OR = 1) --- Baseline	GLP1+SGLT (OR = 0.369)	DPP4+Metformin+SGLT+SU (OR = 0.379)	
SGLT (OR = 0.525)	SGLT+SU (OR = 0.305)	DPP4+Metformin+SGLT (OR = 0.371)	
SU (OR = 0.243)	GLP1+Insulin (OR = 0.295)	GLP1+Insulin+SGLT (OR = 0.354)	
Insulin (OR = 0.136)	Insulin+SGLT (OR = 0.221)	GLP1+Metformin+SGLT+SU (OR = 0.354)	
	Insulin+Metformin (OR = 0.193)	GLP1+Metformin+SGLT (OR = 0.284)	
	GLP1+SU (OR = 0.190)	DPP4+SGLT+SU (OR = 0.249)	
	Metformin+SU (OR = 0.177)	GLP1+Metformin+SU (OR = 0.232)	
	Insulin+SU (OR = 0.136)	Insulin+SGLT+SU (OR = 0.221)	
		:	
		Insulin+Metformin+SGLT+SU (OR = 0.0510)	

Figure 3: Ranked type-2 diabetes therapies for a male patient

Source: Own

Patient 2 (Sex: Female, Age 75)			
Matching cohort (Sex: Female; 75±10 years, n = 1,437)			
Personalised Ranking of First-Line Therapies	Personalised Ranking of Second-Line Therapies	Personalised Ranking of Later-Line Therapies	
3 therapies available with statistically significant evidence ($p \leq 0.05$)	6 therapy combinations available with statistically significant evidence ($p \leq 0.05$)	4 therapy combinations available with statistically significant evidence ($p \leq 0.05$)	
Metformin (OR = 1) --- Baseline	DPP4+SU (OR = 3.66)	GLP1+Metformin+SU (OR = 0.349)	
SU (OR = 0.356)	SGLT+SU (OR = 0.418)	DPP4+SGLT+SU (OR = 0.225)	
Insulin (OR = 0.346)	Metformin+SU (OR = 0.382)	Insulin+Metformin+SGLT (OR = 0.0610)	
	Insulin+SGLT (OR = 0.183)	Insulin+Metformin+SU (OR = 0.0505)	
	Insulin+SU (OR = 0.157)		
	DPP4+SGLT (OR = 0.0563)		

Figure 4: Ranked type-2 diabetes therapies for a female patient

Source: Own

4 Discussion and Conclusions

Answering the following research question was attempted: How might efficient and explainable AI-assisted clinical decision-support systems be developed? A CDSS for primary care was prototyped as an attempt to answer the research question by taking treatment planning for Type-2 diabetes as a case study.

The prototype ensured efficiency as the used algorithm was computationally simple. The system also ensured explainability as it is based on Odds ratio—a measure that is commonly known to clinicians. Since the system performs personalised ranking of therapies based on historical evidence, it enables delivering precise and personalised care through providing evidence-based clinical decision support. Internal assessment of this system performed through discussions held with senior clinicians revealed that a system like this could be useful in scenarios like diabetes treatment planning as there is a large list of available treatment options. It was also suggested that further advancements to enable monitoring factors like longitudinal variation of kidney function and body mass index (BMI) are desired.

As a contribution to theory, this work proposed an efficient and explainable system that can be used for evidence-based personalised treatment planning in primary care settings for diverse health conditions. This system not only can provide clinical decision support but can also serve as a passive tracker of clinical evidence.

As a contribution to practice, Type-2 diabetes was considered as a case study, and it was demonstrated how a large list of therapies can be ranked based on evidence personalised to a patient.

The main limitation of this study is the proposed system being developed only to a prototype stage and lacks clinical validation in terms of qualitative feedback from clinicians about the usefulness and usability of the system, and also as to how the use of a system like this might affect long term patient outcomes.

Future work will involve codesigning the proposed system further with clinicians to produce a CDSS for primary care and assess its usefulness, usability and long-term clinical outcomes.

The proposed system is relatively simple and inexpensive to develop and implement, easy to understand, and can be implemented to assist treatment planning for many health conditions subscribing by the value-based healthcare principles.

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