Machine learning for individualised antibiotic intravenous to oral switch decision-making

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Why?

- **Antimicrobial resistance** (AMR) and healthcare associated infections (HCAIs) pose a significant **global threat**
- One key prevention strategy is to follow **antimicrobial stewardship** practices, in particular, to **switch from intravenous (IV) to oral** administration as early as possible and reduce the use of indwelling vascular devices
- Despite numerous infection prevention, safety and cost **benefits** as well as evidence, oral efficacy is often non-inferior to IV[1,2], the **uptake of early oral switching remains low**[3]

Aim

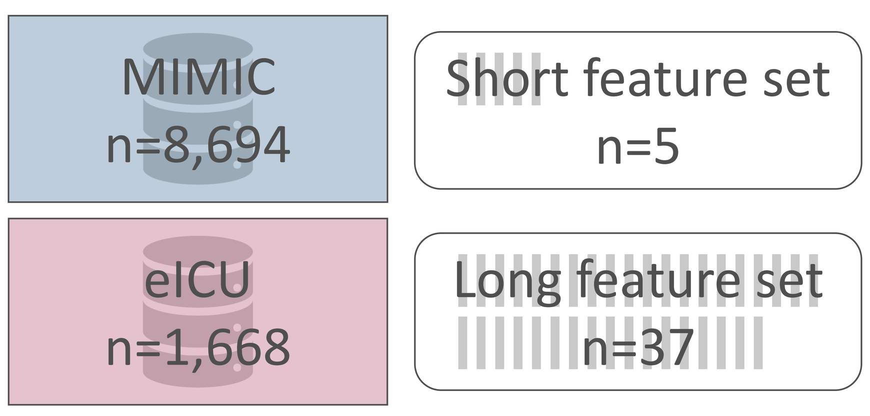
Develop a **real time**, **simple**, **fair and interpretable machine learning** based **clinical decision support system** for predicting when a patient can **safely switch from IV to oral** treatment based on **routinely collected** clinical parameters.

How?

- Extracted features based on the UK Health Security Agency national antimicrobial **IV-to-oral switch guidelines**[4] from two real-world electronic health record datasets[5,6,7]
- Conducted feature selection and examined alternative cutoff thresholds for **traffic light clinical decision support**
- Trained **machine learning models** to predict patients route of administration on each day
- We aimed to **maximise clinical utility** by ensuring fairness[8], interpretability[9] and minimising model complexity

Results

Preprocessing:



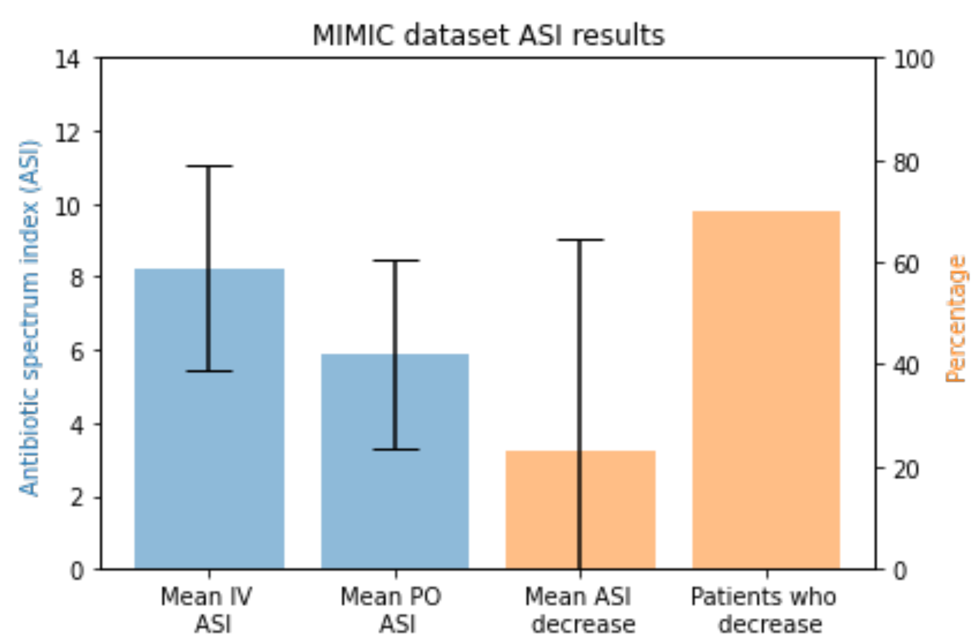


Figure 1: MIMIC antibiotic spectrum index results for the day before switching (IV) and the day after switching (oral).

Table 1: Model evaluation results for the short feature set.

Metric	1st threshold	2nd threshold
AUROC	0.78 (SD 0.02)	0.69 (SD 0.03)
Accuracy	0.76 (SD 0.01)	0.83 (SD 0.01)
TPR	0.80 (SD 0.05)	0.48 (SD 0.06)
FPR	0.25 (SD 0.02)	0.10 (SD 0.02)

Table 2: Fairness results for the model on the short feature set.

Sensitive attribute	Group	Equalised odds demonstrated: Initially	Equalised odds demonstrated: With threshold optimisation
Sex	Female	✓	-
	Male	✓	-
Age	20	✓	✗
	30	✓	✓
	40	✓	✓
	50	✓	✓
	60	✓	✓
	70	✓	✓
	80	✓	✓
	90	✗	✓
Race	Asian	✓	✓
	Black	✓	✓
	Hispanic	✓	✓
	Native	✗	✗
	Other	✓	✓
	Unknown	✓	✓
	White	✓	✓
Insurance	Medicaid	✗	✓
	Medicare	✓	✓
	Other	✓	✓

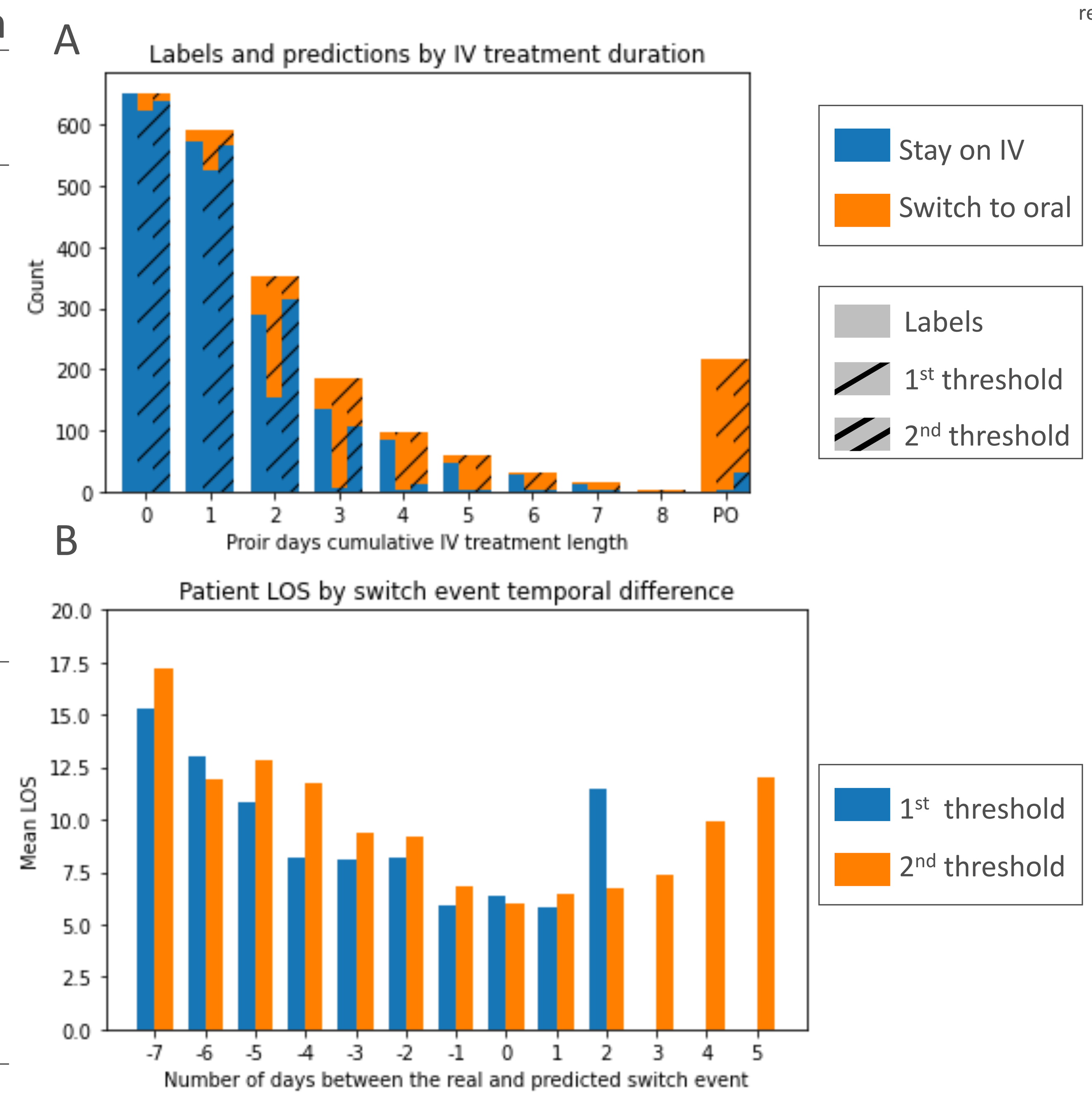


Figure 2: [A] Labels and predictions by IV treatment duration. [B] Mean patient LOS outcomes by days between the real and predicted switch event.

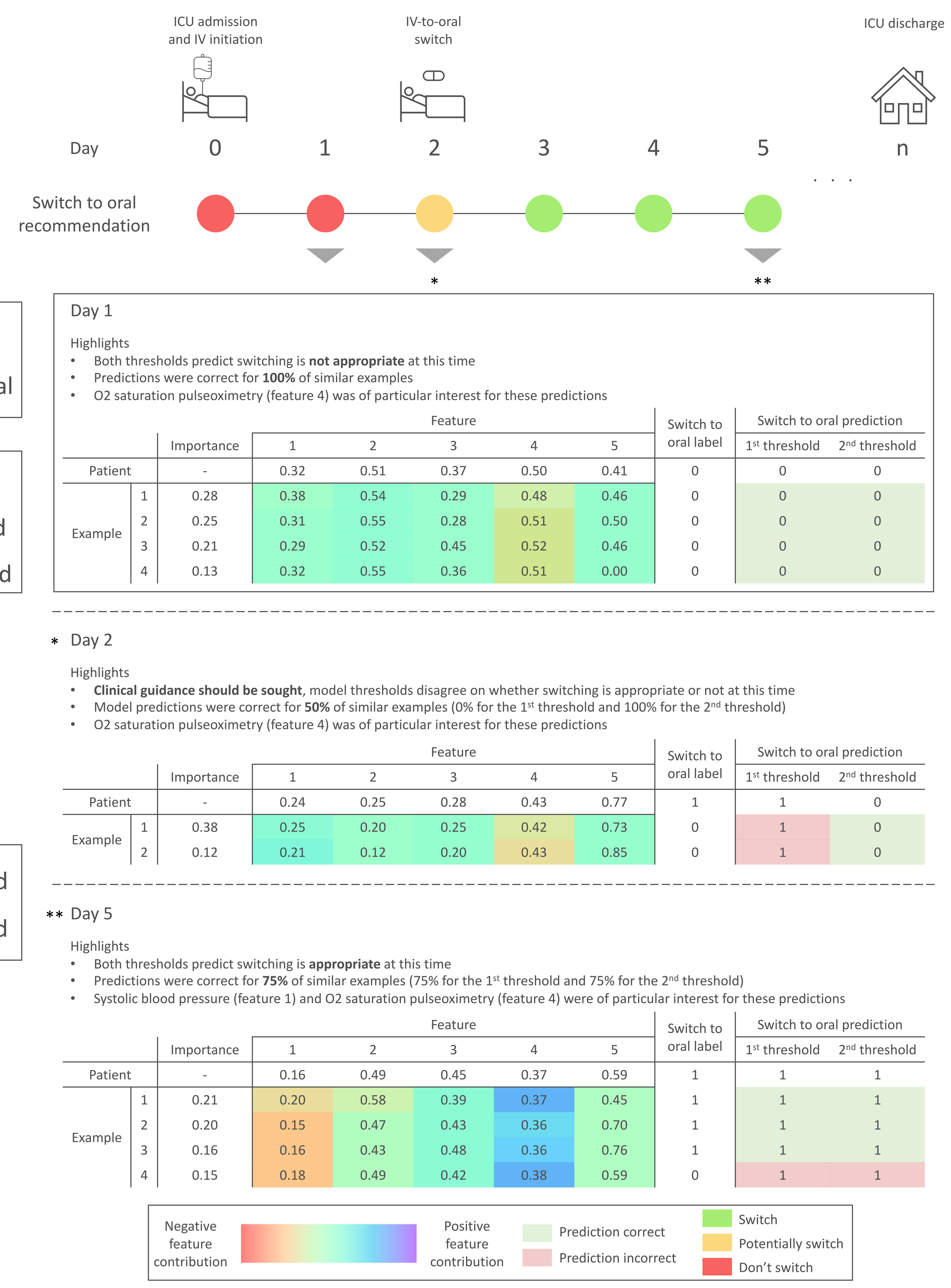


Figure 3: Example visual representation to improve interpretability. 'Traffic light' recommendations are displayed in a temporal manner and if required clinicians can obtain more information on any given day of the patients stay.

Discussion

- Identified **clinically relevant features** to determine when switching is appropriate
- **Fair performance** across sensitive attributes and **consistent results** across subgroups
- Interpretability enables **clinically useful** decision support systems
- Future work includes prospective evaluation and understanding how such a system could influence antimicrobial decision making to **promote early switching when appropriate**

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References

[1] Noah Wald-Dickler et al. "Oral Is the New IV. Challenging Decades of Blood and Bone Infection Dogma: A Systematic Review". English. In: The American Journal of Medicine 135.3 (Mar. 2022). Publisher: Elsevier, 369–379.e1. issn: 0002-9343, 1555-7162. doi: 10.1016/j.amjmed. 2021.10.007. [2] Jan Jelrik Oosterheert et al. "Effectiveness of early switch from intravenous to oral antibiotics in severe community acquired pneumonia: multicentre randomised trial". en. In: BMJ 333.7580 (Dec. 2006). Publisher: British Medical Journal Publishing Group Section: Research, p. 1193. issn: 0959-8138, 1468-5833. doi: 10.1136/bmj.38993.560984.BE. [3] Duane R Hospenthal et al. "Practice Patterns of Infectious Diseases Physicians in Transitioning From Intravenous to Oral Therapy in Patients With Bacteremia". In: Open Forum Infectious Diseases 7.12 (Dec. 2020), ofz386. issn: 2328-8957. doi: 10.1093/ofid/ofz386. [4] UK Health Security Agency. National antimicrobial intravenous-to-oral switch (IVOS) criteria for early switch. en. Nov. 2022. [5] Alistair Johnson et al. MIMIC-IV. 2021. doi: 10.13026/s6n6-xd98. [6] Tom Joseph Pollard et al. The eICU Collaborative Research Database (version 2.0). PhysioNet. Type: dataset. 2019. doi: 10.13026/C2WM1R. [7] Carl H. Lubba et al. "catch22: CAnonical Time-series CHaracteristics". en. In: Data Mining and Knowledge Discovery 33.6 (Nov. 2019), pp. 1821–1852. issn: 1573-756X. doi: 10.1007/s10618- 019-00647-x[8] Moritz Hardt, Eric Price, and Nathan Srebro. "Equality of Opportunity in Supervised Learning". In: arXiv:1610.02413 [cs] (Oct. 2016). arXiv: 1610.02413. [9] Jonathan Crabbe et al. "Explaining Latent Representations with a Corpus of Examples". In: Advances in Neural Information Processing Systems. Ed. by M. Ranzato et al. Vol. 34. Curran Associates, Inc., 2021, pp. 12154–12166.