Imperial College London

AI Health CAMO centre for antimicrobial optimisation

Artificial intelligence based clinical decision support for antibiotic stewardship

William Bolton

Exploring AI's impact on AMR

9th February 2024

Antimicrobial stewardship aims to optimise antibiotic decision making.

STAGES OF ANTIBIOTIC DECISION MAKING

Hospital admission

Antimicrobial stewardship

Hospital discharge

0 — 1 — 2 — 3

0: Does the patient have a bacterial infection or not

Which empiric antibiotic treatment to prescribe

1: De-escalation of therapy

2: Cessation of therapy

Antimicrobial stewardship

A coordinated effort and set of practices aimed at **optimising antimicrobial use** and **prolonging their therapeutic life**, to improve infection patient **outcomes** while minimizing the development of **antimicrobial resistance**

Artificial intelligence can support optimised antibiotic decision making.

STAGES OF ANTIBIOTIC DECISION MAKING

Hospital admission

Antimicrobial stewardship

Hospital discharge

0 — 1 — 2 — 3


BMC Medical Informatics and Decision Making
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Research article | Open access | Published: 08 December 2017
Supervised learning for infection risk inference using pathology data
Bernard Hernandez, Pau Herrero, Timothy Miles Rawson, Luke S. P. Moore, Benjamin Evans, Christofer Toumazou, Alison H. Holmes & Pantelis Georgiou


Journal of Antimicrobial Chemotherapy
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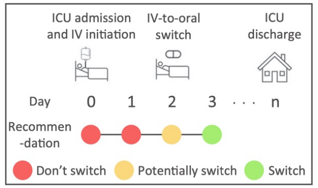
JOURNAL ARTICLE EDITOR'S CHOICE
Supervised machine learning for the prediction of infection on admission to hospital: a prospective observational cohort study
T M Rawson, B Hernandez, L S P Moore, O Blandy, P Herrero, M Gilchrist, A Gordon, C Toumazou, S Sriskandan, P Georgiou ... Show more
Volume 74, Issue 4

IV-to-oral switch



Antibiotic readmission

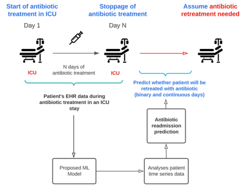


Figure 1.2: Proposed ML-based decision support model

Side effects

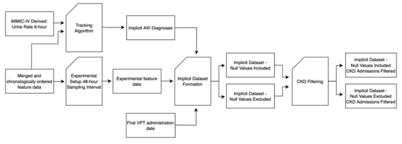
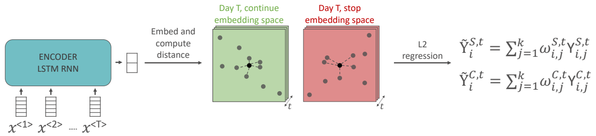


Figure 13: Implicit dataset formation workflow.

Antibiotic cessation



Switching from IV-to-oral antibiotic treatment is complex and under-researched.

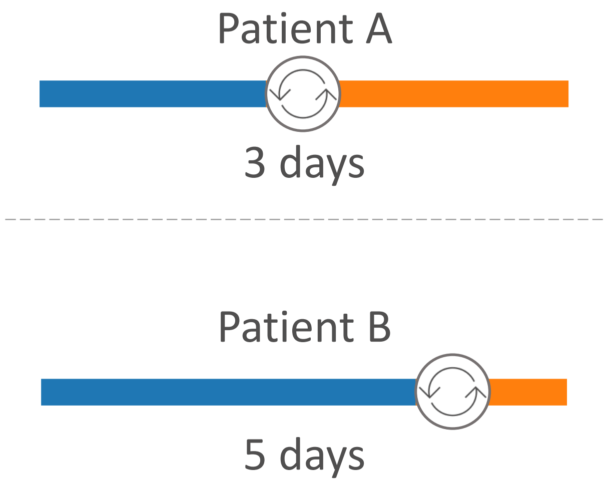
One key challenge of stewardship is **determining when to switch** antibiotics from **IV-to-oral administration**

Clinical Infection in Practice
Volume 16, November 2022, 100202
ELSEVIER
Clinical Audits/Service improvements
Oral step-down for bacteraemia: An op stewardship?
Stephen Platts [a], Brendan A.I. Payne [b c], Ulrich Schwab [c]

Review
March 30, 2020
Evaluation of a Paradigm Shift From Intravenous Anti Therapy for the T Endocarditis
A Narrative Revie
Brad Spellberg, MD[1]; Henry F. Chambers,

The American Journal of Medicine
Volume 135, Issue 3, March 2022, Pages 369-379.e1
ELSEVIER
Clinical Research Study
Oral Is the New IV. Challenging Decades of Blood and Bone Infection Dogma: A Systematic Review
Noah Wald-Dickler MD [a b c], Paul D. Holtom MD [a b], Matthew C. Phillips MD [a], Robert M. Centor MD [d e], Rachael. A. Lee MD [d e], Rachel Baden MD [a], Brad Spellberg MD [a]

Numerous studies have shown that **oral therapy can be non-inferior to IV**



There is a **poor understanding** of the factors that facilitate or inhibit an individual from receiving oral therapy

Aim

Utilise a **machine learning** and **routinely collected clinical parameters** to predict whether a patient could be **suitable for switching** from IV-to-oral antibiotics on **any given day**

Routinely collected electronic health record data were used, with clinical guided features.

DATASET

MIMIC dataset
n=8,694

eICU dataset
n=1,668

FEATURES

UK Health Security Agency

Antimicrobial Intravenous-to-Oral Switch (IVOS) Decision Aid

Based on the National Antimicrobial IVOS Criteria

Co-produced through a UK-wide multidisciplinary consensus process involving 279 participants

Open Access | Published: 09 August 2019

catch22: CAnonical Time-series CHaracteristics

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Carl H. Lubba, Sarab S. Sethi, Philip Knaute, Simon R. Schultz, Ben D. Fulcher & Nick S. Jones

Data Mining and Knowledge Discovery **33**, 1821–1852 (2019) | Cite this article

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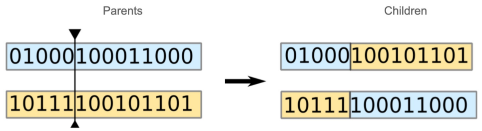
FEATURE SELECTION

1 SHAP Values

SHAP

2 Genetic algorithm

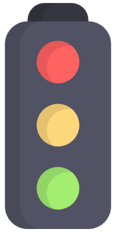


MODEL SELECTION

1 Hyperparameter optimization

OPTUNA

2 Cutoff point



The model achieves generalisable performance across a range of datasets and patient populations.

MIMIC

Metric	1ST threshold results	2nd threshold results	IVOS criteria baseline
AUROC	**0.78 (SD 0.02)**	0.69 (SD 0.03)	0.66
FPR	0.25 (SD 0.02)	**0.10 (SD 0.02)**	0.43

eICU

Metric	1st threshold results	2nd threshold results	IVOS criteria baseline
AUROC	**0.72 (SD 0.02)**	0.65 (SD 0.05)	0.55
FPR	0.24 (SD 0.04)	**0.05 (SD 0.02)**	0.28

NHS Imperial College Healthcare NHS Trust

Metric	Results	Prospective data
AUROC	0.78 (SD 0.01)	0.77
FPR	0.23 (SD 0.02)	0.46

SUBGROUPS

Bio-availability

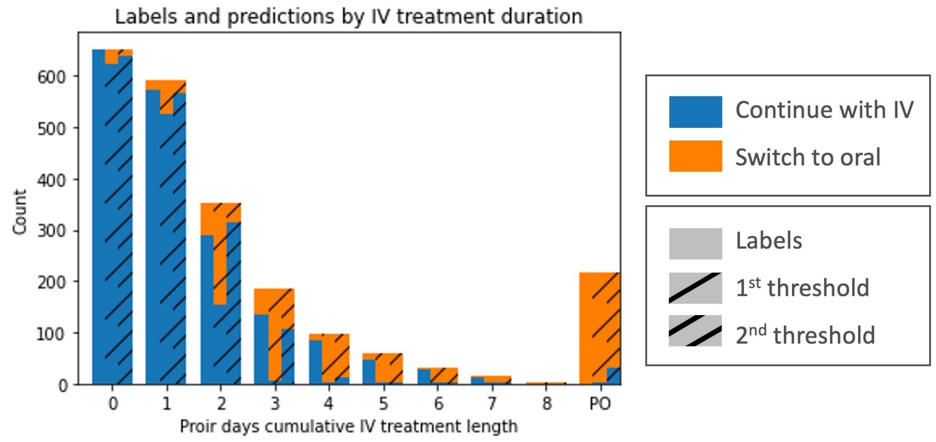
Mal-absorption

Sepsis

Pneumonia

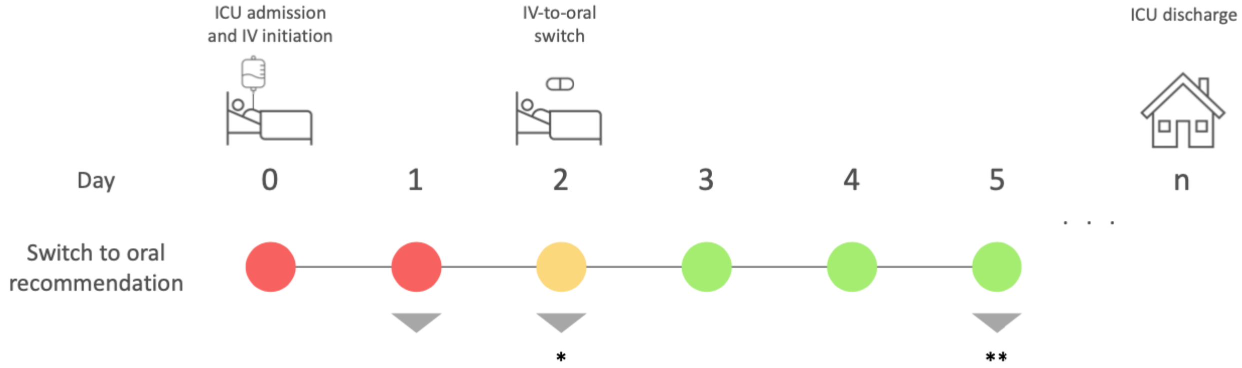
UTI

ANALYSIS



Models predict some patients could be **suitable for switching to oral administration earlier**

Traffic light recommendations and informative visual representations improve model interpretability.



Day 1

Highlights
- Both thresholds predict switching is likely **not appropriate** at this time
- Predictions were correct for **100%** of similar examples
- O2 saturation pulseoximetry (feature 4) was of particular interest for these predictions

		Importance	Feature 1	Feature 2	Feature 3	Feature 4	Feature 5	Switch to oral label	Switch to oral prediction: 1st threshold	Switch to oral prediction: 2nd threshold
Patient		-	0.32	0.51	0.37	0.50	0.41	0	0	0
Example	1	0.28	0.38	0.54	0.29	0.48	0.46	0	0	0
	2	0.25	0.31	0.55	0.28	0.51	0.50	0	0	0
	3	0.21	0.29	0.52	0.45	0.52	0.46	0	0	0
	4	0.13	0.32	0.55	0.36	0.51	0.00	0	0	0

Day 2

*

Highlights
- **Clinical guidance should be sought**, model thresholds disagree on whether switching could be appropriate or not at this time
- Predictions were correct for **50%** of similar examples (0% for the 1st threshold and 100% for the 2nd threshold)
- O2 saturation pulseoximetry (feature 4) was of particular interest for these predictions

		Importance	Feature 1	Feature 2	Feature 3	Feature 4	Feature 5	Switch to oral label	Switch to oral prediction: 1st threshold	Switch to oral prediction: 2nd threshold
Patient		-	0.24	0.25	0.28	0.43	0.77	1	1	0
Example	1	0.38	0.25	0.20	0.25	0.42	0.73	0	1	0
	2	0.12	0.21	0.12	0.20	0.43	0.85	0	1	0

** Day 5

Highlights
- Both thresholds predict switching could be **appropriate** at this time
- Predictions were correct for **75%** of similar examples (75% for the 1st threshold and 75% for the 2nd threshold)
- Systolic blood pressure (feature 1) and O2 saturation pulseoximetry (feature 4) were of particular interest for these predictions

		Importance	Feature 1	Feature 2	Feature 3	Feature 4	Feature 5	Switch to oral label	Switch to oral prediction: 1st threshold	Switch to oral prediction: 2nd threshold
Patient		-	0.16	0.49	0.45	0.37	0.59	1	1	1
Example	1	0.21	0.20	0.58	0.39	0.37	0.45	1	1	1
	2	0.20	0.15	0.47	0.43	0.36	0.70	1	1	1
	3	0.16	0.16	0.43	0.48	0.36	0.76	1	1	1
	4	0.15	0.18	0.49	0.42	0.38	0.59	0	1	1

Note this system does not cover all aspects of the switch decision making process and should only be used as decision support to highlight when a patient may be suitable for switch assessment

Negative feature contribution | Positive feature contribution | Prediction correct | Prediction incorrect | Switch | Potentially switch | Don't switch

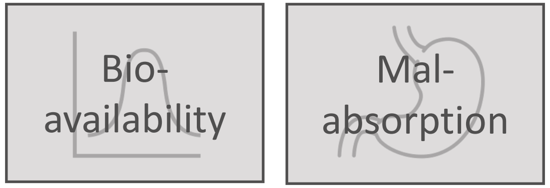
Models demonstrate reasonably fair performance and threshold optimisation can improve results.

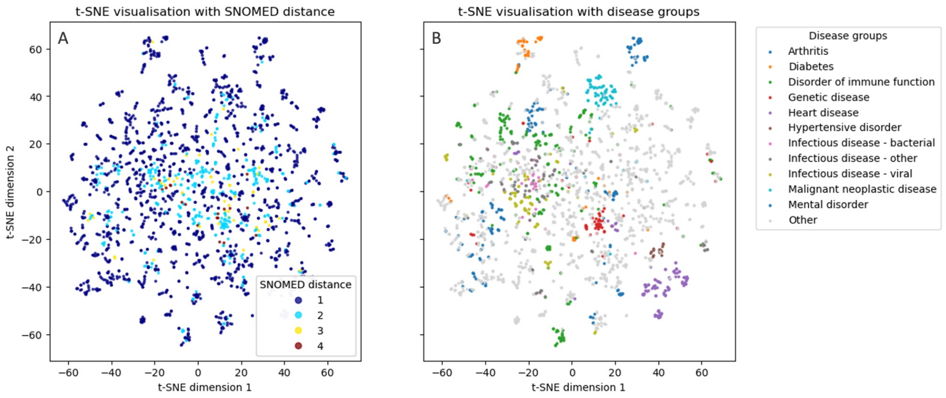
Sensitive attribute	Group	Equalised odds demonstrated	
		Initially	With threshold optimisation
Sex	Female	✓	-
	Male	✓	-
Age	20	✓	✗
	30	✓	✓
	40	✓	✓
	50	✓	✓
	60	✓	✓
	70	✓	✓
	80	✓	✓
	90	✗	✓
Race	Asian	✓	✓
	Black	✓	✓
	Hispanic	✓	✓
	Native	✗	✗
	Other	✓	✓
	Unknown	✓	✓
	White	✓	✓
Insurance	Medicaid	✗	✓
	Medicare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

Data often poses a challenge for AI systems in healthcare, particularly those focusing on AMR.

DATA QUALITY AND MISSINGNESS

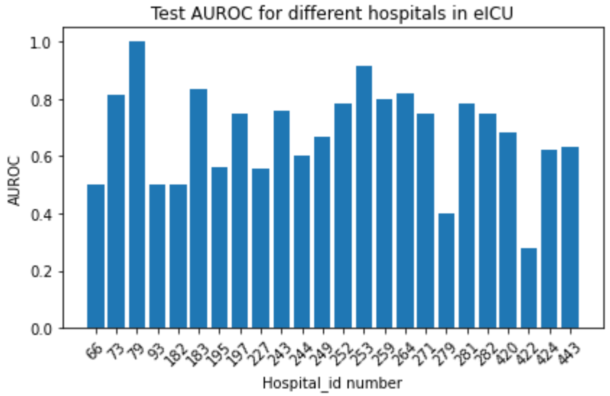
- **Lack of reliable data** on important factors such as absorption
- Appling some important parameters such as **co-morbidities** to AI systems is **combinatorially complex**



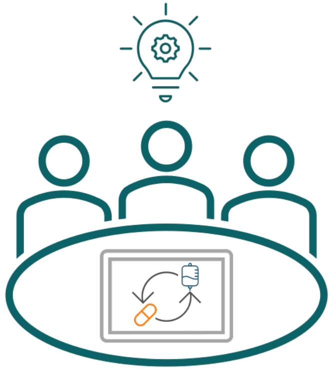


HUMAN BEHAVIOUR IS HETEROGENEOUS

- Antimicrobial stewardship is driven by **human actions** which can be **difficult to model and predict**

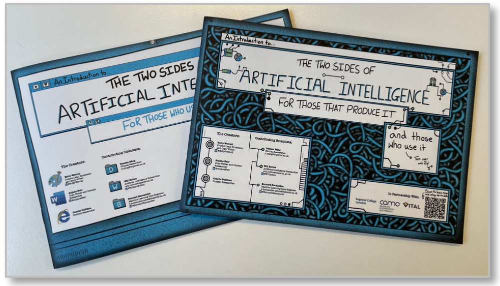


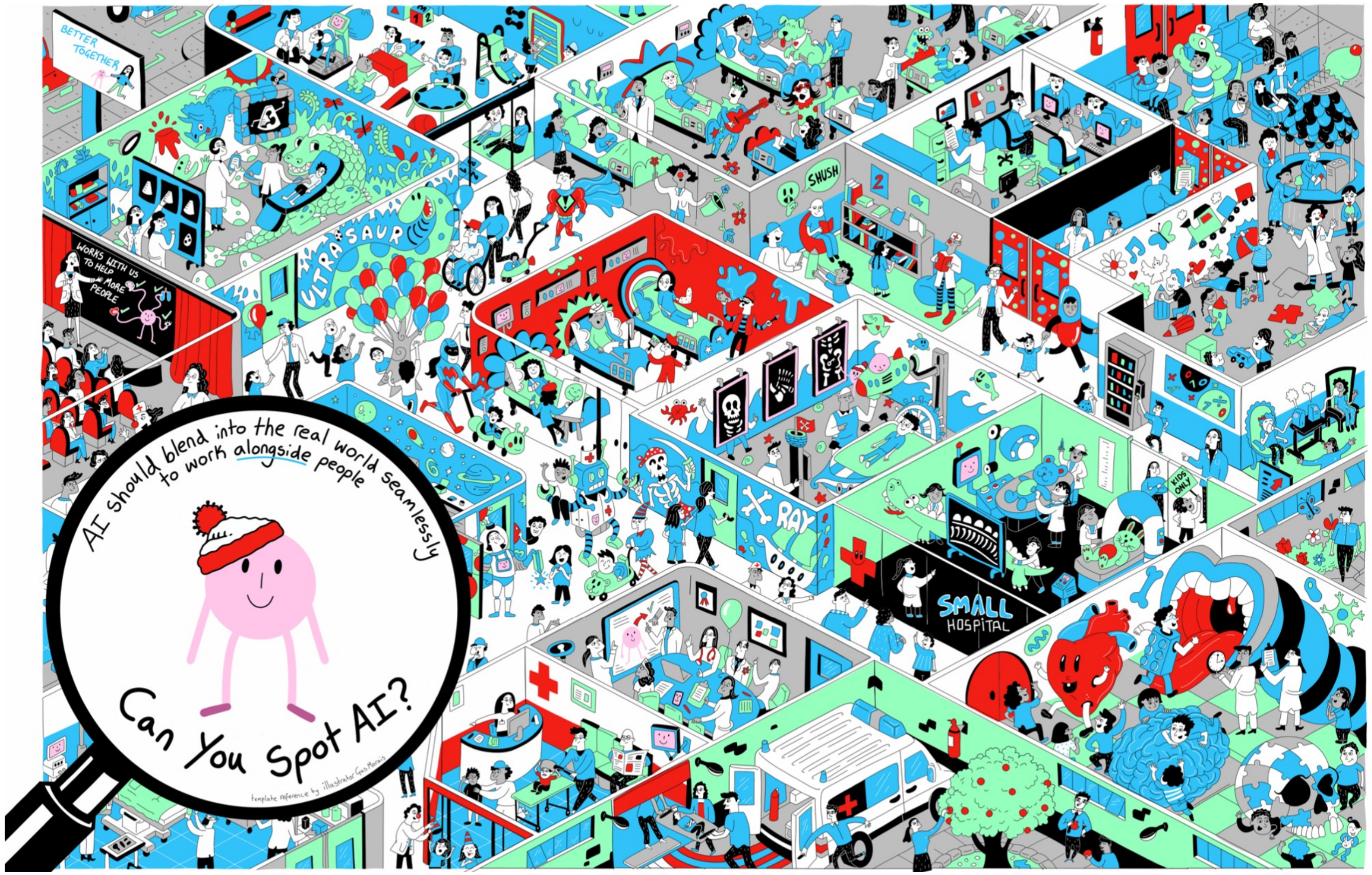
Prospective evaluation and education are essential for technological adoption, implementation and impact.



We are currently in the process of obtaining **ethics** to conduct **end user assessment** and **prospective testing** with clinicians in **real-world clinical settings**

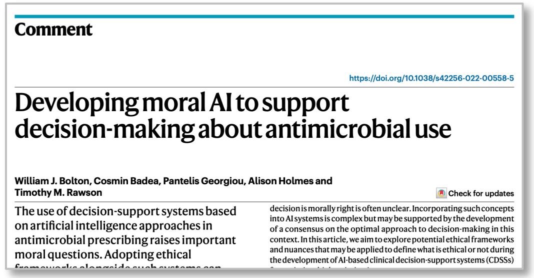
PRIMARY RESEARCH AND EDUCATION





Using AI to optimize antimicrobial prescribing raises important ethical questions.

ETHICAL VIEWPOINT


Comment

https://doi.org/10.1038/s42256-022-00558-5

Developing moral AI to support decision-making about antimicrobial use

William J. Bolton, Cosmin Badea, Pantelis Georgiou, Alison Holmes and Timothy M. Rawson

Check for updates

The use of decision-support systems based on artificial intelligence approaches in antimicrobial prescribing raises important moral questions. Adopting ethical

decision is morally right is often unclear. Incorporating such concepts into AI systems is complex but may be supported by the development of a consensus on the optimal approach to decision-making in this context. In this article, we aim to explore potential ethical frameworks and nuances that may be applied to define what is ethical or not during the development of AI-based clinical decision-support systems (CDSSs)

nature machine intelligence

Variables	Description	Exemplar of starting antimicrobial treatment	Corresponding ad-hoc utility value
Intensity	How strong is the pleasure?	Treating a relevant infection with antimicrobials has the potential to save that person's life	Highly positive utility
Duration	How long will the pleasure last?	Any extension of life is immeasurable while it is reasonable AMR will continue in the near-term future	Positive utility
Certainty or uncertainty	How likely or unlikely is it that the pleasure will occur?	Limited information often means treatment may or may not be helpful and there is always an inherent risk of developing AMR	Neutral utility, without more information
Propinquity	How soon will the pleasure occur?	Treatment can be effective immediately however the same is true for the evolution of AMR	Neutral utility, without more information
Fecundity	The likelihood of further sensations of the same kind	-	Unable to assign
Purity	The likelihood of not being followed by opposite sensations	-	Unable to assign
Extent	How many people will be affected?	Prescribing antimicrobials effects the patient and those close to them, while the development of AMR is a certainty and may affect everyone, causing significant suffering and mortality	Immense negative utility

Artificial intelligence based clinical decision support for antibiotic stewardship.

Conclusion

- Artificial intelligence can support antibiotic stewardship through **optimising antibiotic decision making**
- We developed **simple, fair, interpretable, and generalisable models** to estimate when a patient could **switch from IV-to-oral antibiotic treatment**.
- This system could potentially provide **clinically useful antimicrobial stewardship decision support**, but how it could influence antimicrobial decision making needs to be understood
- For healthcare focused artificial intelligence projects, considering ethical implications, data quality and **prospective** evaluation is essential

Imperial College London

I would like to acknowledge the contribution of the following individuals.

Dr Tim Rawson

Professor Pantelis Georgiou

Professor Alison Holmes

Dr Bernard Hernandez Perez

Mr Richard Wilson

Dr David Antcliffe

Dr Mark Gilchrist

Imperial College London

AI Health
camo
centre for antimicrobial optimisation

Thank you!

William Bolton

Exploring AI's impact on AMR

9th February 2024

william.bolton@imperial.ac.uk

nature communications

LinkedIn

Imperial College London

GitHub

Imperial College London

Routinely collected electronic health record data were used, with clinical guided features.

DATASET

MIMIC dataset

Received IV and oral antibiotic treatment in the ICU

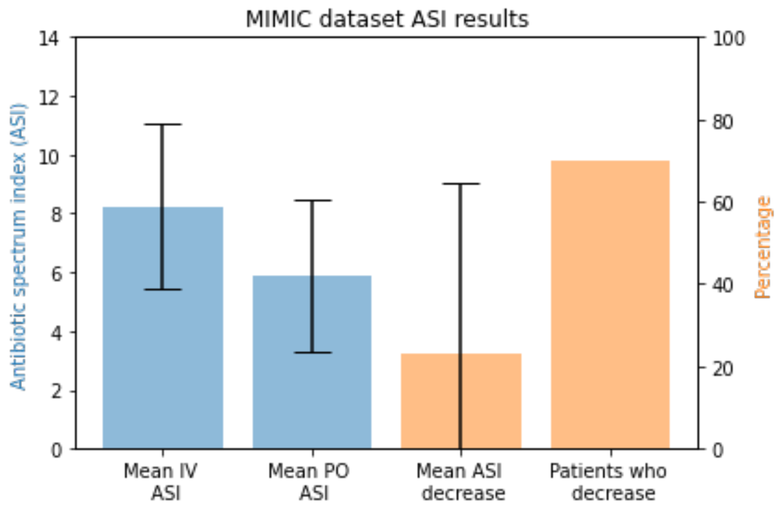
eICU dataset

Received IV and oral antibiotic treatment in the ICU

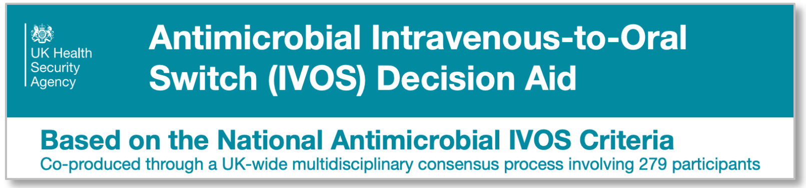
Preprocessing subset n=4,347

Hold-out subset n=4,347

Hold-out subset n=1,668



FEATURES


UK Health Security Agency

Antimicrobial Intravenous-to-Oral Switch (IVOS) Decision Aid

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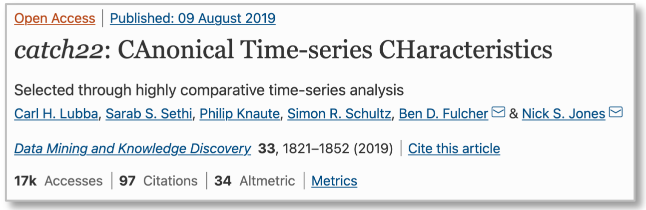
Open Access | Published: 09 August 2019

catch22: CAnonical Time-series CHaracteristics

Selected through highly comparative time-series analysis

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Data Mining and Knowledge Discovery **33**, 1821–1852 (2019) | Cite this article

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UKHSA **IVOS** criteria

10 clinical parameters extracted, catch24 applied to each day, each stay and difference calculated

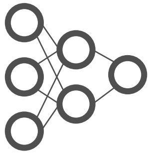
960 unique features

The preprocessing subset was used for unbiased feature and model selection.

FEATURE SELECTION

1 SHAP Values

960



- AUROC 0.76 for predicting if a patient switch's or not on a given day
- SHAP importance value for each feature

2 Genetic algorithm

Features clinical parameter	Shap value
blood pressure systolic	2.27
heart rate	2.05
blood pressure mean	1.62
o2 saturation pulseoxymetry	1.38
gcs - motor response	1.37

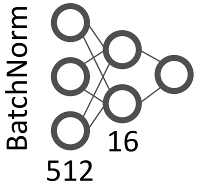
AUROC 0.80

MODEL SELECTION

1 Hyperparameter optimization

OPTUNA

5

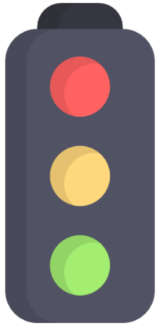


- AUROC 0.80

2 Cutoff point

Youden's index: 0.54

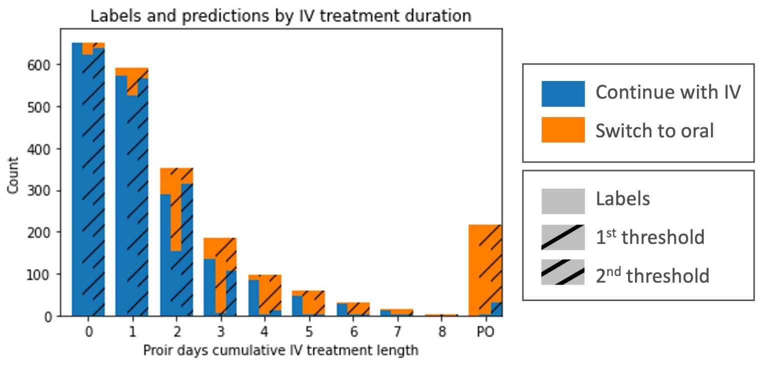
Precision-Recall-F1score: 0.74

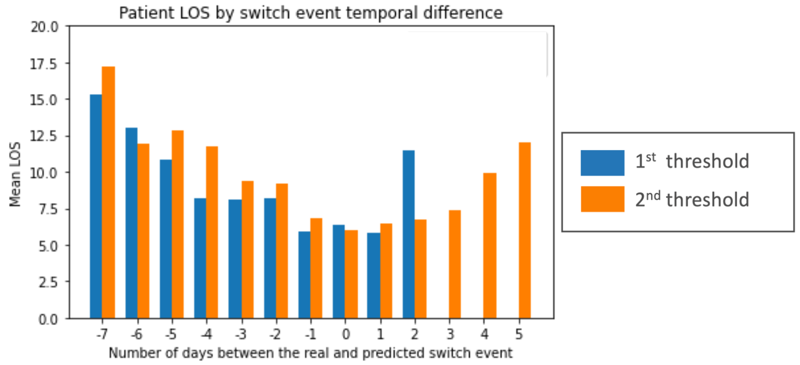


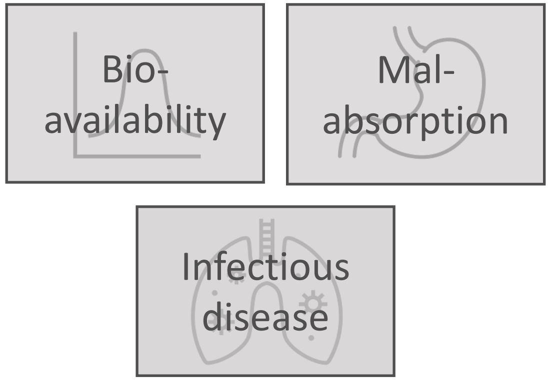
AUROC 0.80, FPR 0.26

AUROC 0.70, FPR 0.11

Such technology could provide appropriate decision support and promote switching when appropriate.







Models predict some patients could be **suitable for switching to oral administration earlier** from a clinical parameter, health status perspective

When the difference between the real and predicted switch event was minimal, mean patient **LOS outcomes were lower**

Models only analyse a **snapshot of the patient** and **not all factors** that are clinically used to assess a patient’s suitability for switching

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Developing Moral AI to Support Antimicrobial Decision Making.

Health CAMO centre for antimicrobial optimisation

Regarding antimicrobial decision making, we believe a **utilitarian approach** is most suitable for developing AI-based CDSSs, and that technology should focus on the **likelihood of drug effectiveness and that of resistance** in order to have the biggest impact on supporting moral antimicrobial prescribing (Table. 1). Furthermore, for antimicrobials, **spatial and temporal considerations are critical** to optimise treatment outcomes and minimise the development of side effects or AMR. Decision making in antimicrobial prescribing is frequent, pressing, and both morally and technically complex. But by applying ethical theories to specific scenarios and incorporating moral paradigms, we can **ensure that AI-based CDSSs tackle global problems, such as the emerging AMR crisis, in a moral way.**

Variables	Description	Exemplar of starting antimicrobial treatment	Corresponding ad-hoc utility value
Intensity	How strong is the pleasure?	Treating a relevant infection with antimicrobials has the potential to save that person’s life	Highly positive utility
Duration	How long will the pleasure last?	Any extension of life is immeasurable while it is reasonable AMR will continue in the near-term future	Positive utility
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Purity	The likelihood of not being followed by opposite sensations	-	Unable to assign
Extent	How many people will be affected?	Prescribing antimicrobials effects the patient and those close to them, while the development of AMR is a certainty and may affect everyone, causing significant suffering and mortality	Immense negative utility

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Co-morbid obesity leads to significantly worse infection outcomes.

MEAN	BODY MASS INDEX (BMI)	LENGTH OF ICU STAY	ANTIBIOTIC TREATMENT LENGTH
HEALTHY (HE)	22.40	5.86	5.18
OVERWEIGHT (OW)	27.38	7.98	5.86
OBESE (OB)	33.34	7.14	5.60
MORBIDLY OBESE (MB)	46.28	8.14	6.39