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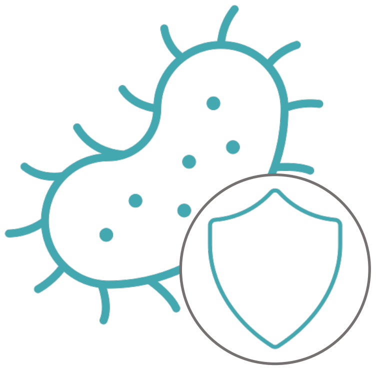
Personalising intravenous to oral antibiotic switch decision making through fair interpretable machine learning

William Bolton

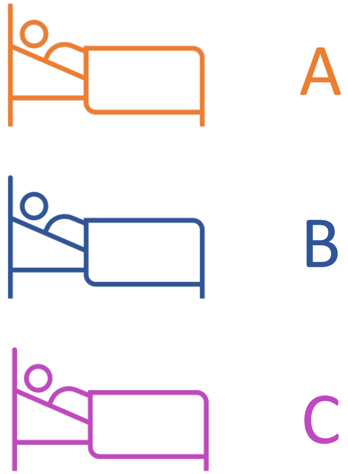
ACDS 2023

7th September 2023

Machine learning can support optimised antibiotic decision making.



Antimicrobial resistance (AMR) is a global threat and one key strategy to tackle this is to optimise antimicrobial use



Clinical decision support systems (CDSSs) utilising machine learning (ML) have been developed to assist with managing infections

STAGES OF ANTIBIOTIC DECISION MAKING

1 Infection or not

2 Empiric treatment

3 Narrow therapy — IV to oral switch

4 Duration — Cessation, Side effects

Antibiotic stewardship decision making is complex and under-researched.

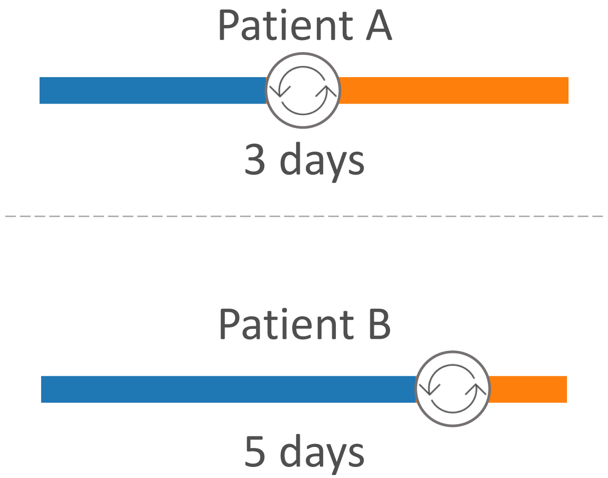
One key challenge is determining when to switch antibiotics from IV-to-oral administration


Clinical Infection in Practice
Volume 16, November 2022, 100202
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
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 based on clinical guidelines were used.

DATASET

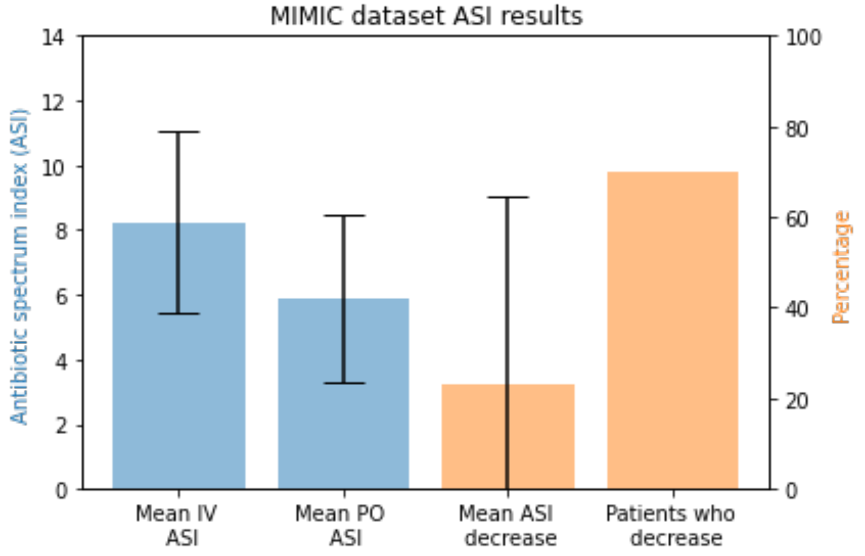
MIMIC dataset

Received IV and oral antibiotic treatment in the ICU

eICU dataset

Received IV and oral antibiotic treatment in the ICU

Preprocessing subset	Hold-out subset	Hold-out subset
n=4,347	n=4,347	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

Selected through highly comparative time-series analysis

Carl H. Lubba, Sarah 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

17k Accesses | **97** Citations | **34** Altmetric | Metrics

UKHSA **IVOS** criteria

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

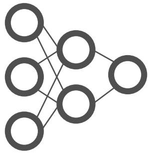
960 unique features

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

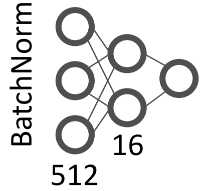
AUROC 0.80

MODEL SELECTION

1 Hyperparameter optimization

OPTUNA

5

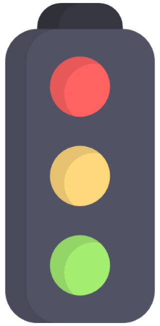


- AUROC 0.80

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

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

MIMIC-IV Hold-out

METRIC	1ST THRESHOLD RESULTS	2nd THRESHOLD RESULTS
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)

Bio-availability
Mal-absorption
Pneu-monia
Sepsis
UTI

OTHER DATASETS

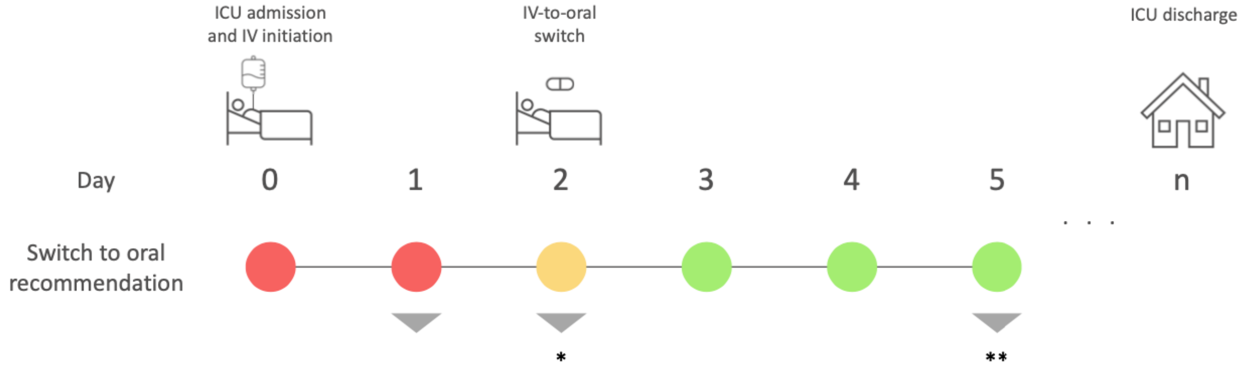
eICU

METRIC	1ST THRESHOLD RESULTS	2nd THRESHOLD RESULTS
AUROC	0.72 (SD 0.02)	0.65 (SD 0.05)
ACCURACY	0.75 (SD 0.03)	0.85 (SD 0.02)
TPR	0.68 (SD 0.06)	0.34 (SD 0.10)
FPR	0.24 (SD 0.04)	0.05 (SD 0.02)

ICHT

METRIC	RESULTS	PROSPECTIVE DATA
AUROC	0.78 (SD 0.01)	0.77
ACCURACY	0.71 (SD 0.01)	0.68
TPR	0.66 (SD 0.03)	0.80
FPR	0.23 (SD 0.02)	0.46

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

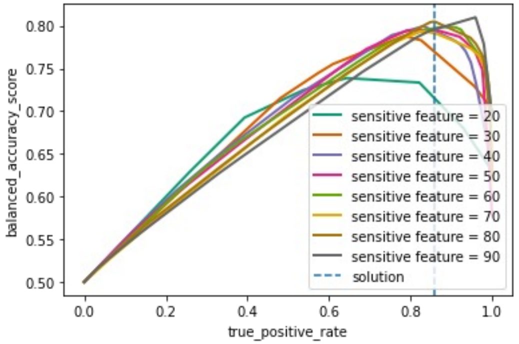
Potentially switch

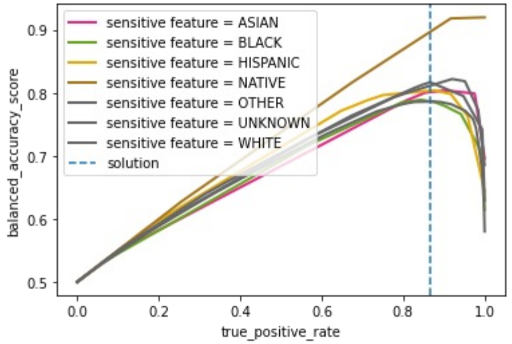
Don't switch

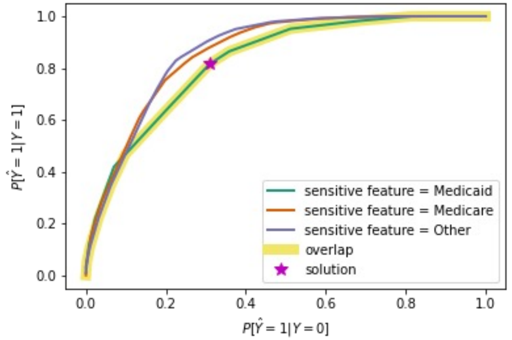
Models demonstrate reasonably fair performance and threshold optimisation can improve results.

Sensitive attribute	Group	Original results AUROC	TPR	FPR	EO	Threshold optimisation results AUROC	TPR	FPR	EO
Age	20	0.73	0.74	0.27	✓	0.63	0.86	0.61	✗
	30	0.80	0.86	0.26	✓	0.72	0.73	0.28	✓
	40	0.78	0.81	0.25	✓	0.76	0.82	0.31	✓
	50	0.76	0.78	0.25	✓	0.81	0.86	0.25	✓
	60	0.79	0.82	0.23	✓	0.79	0.87	0.29	✓
	70	0.73	0.69	0.23	✓	0.78	0.87	0.31	✓
	80	0.77	0.81	0.26	✓	0.80	0.87	0.26	✓
	90	0.78	0.79	0.23	✗	0.78	0.86	0.3	✓
Race	Asian	0.79	0.83	0.24	✓	0.71	0.81	0.38	✓
	Black	0.78	0.83	0.27	✓	0.79	0.86	0.28	✓
	Hispanic	0.80	0.85	0.25	✓	0.76	0.84	0.31	✓
	Native	0.78	0.97	0.43	✗	0.75	0.93	0.43	✗
	Other	0.76	0.72	0.19	✓	0.78	0.84	0.29	✓
	Unknown	0.79	0.83	0.25	✓	0.81	0.86	0.23	✓
	White	0.77	0.79	0.24	✓	0.78	0.87	0.31	✓
Insurance	Medicaid	0.72	0.69	0.26	✗	0.74	0.82	0.34	✓
	Medicare	0.78	0.81	0.25	✓	0.77	0.88	0.33	✓
	Other	0.78	0.80	0.24	✓	0.79	0.9	0.33	✓

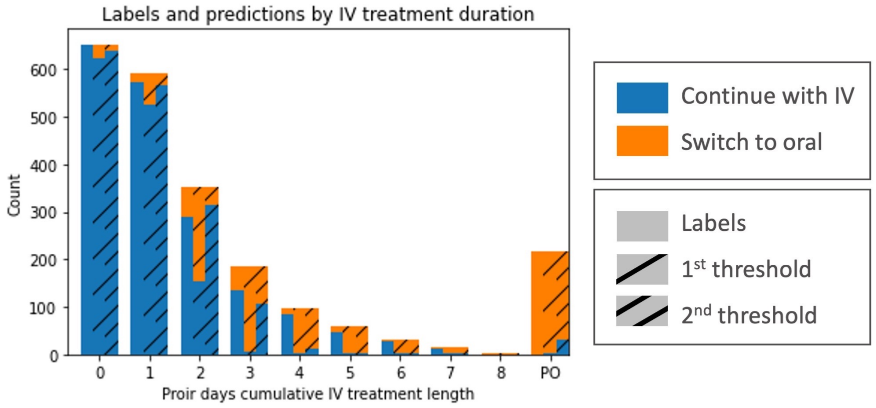
AUROC;Area under the receiver operating characteristic, TPR;True positive rate, FPR;False positive rate, EO;Equalised odds

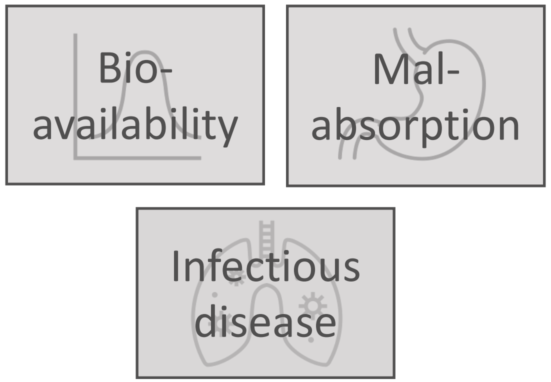


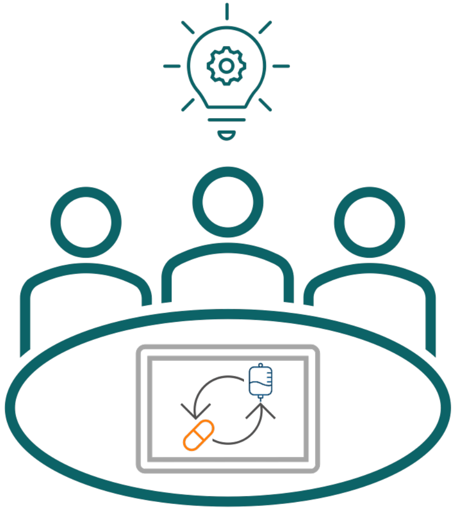




Prospective evaluation is needed to understand how such a system can influence antimicrobial decision making.







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

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

Incorporating logic-based rules and prospective testing in real-world clinical settings are avenues for future work

Personalising intravenous to oral antibiotic switch decision making through fair interpretable machine learning.

Conclusion

- Identified clinically relevant features from routinely collected clinical parameters
- Developed simple, fair, interpretable, and generalisable models to estimate when a patient could switch from IV-to-oral antibiotic treatment.
- Such a system holds great promise to provide clinically useful antimicrobial stewardship decision support

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

Dr Tim Rawson

Professor Pantelis Georgiou

Professor Alison Holmes

Mr Richard Wilson

Dr David Antcliffe

Dr Bernard Hernandez Perez

Dr Esmita Charani

Thank you!

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ACDS 2023

7th September 2023

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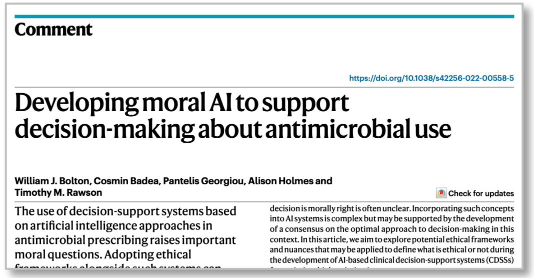
Patient, public and stakeholder views as well as ethical theories have been considered to ensure solutions are fair.

AI Health CAMO centre for antimicrobial optimisation

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

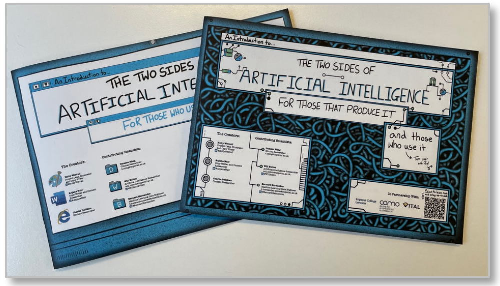
Check for updates

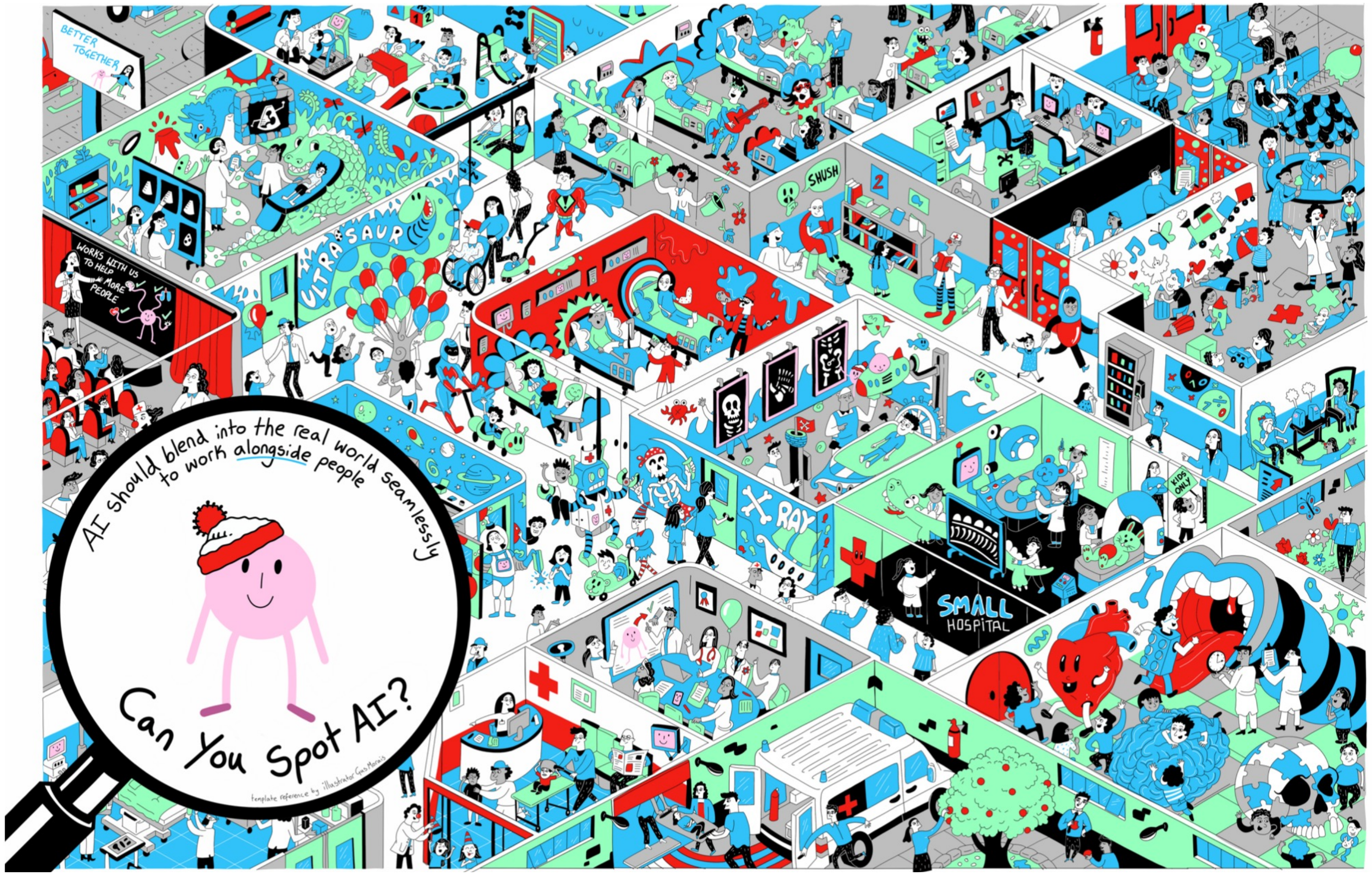
The use of decision-support systems based on artificial intelligence approaches in antimicrobial prescribing raises important moral questions. Adopting ethical

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

PRIMARY RESEARCH





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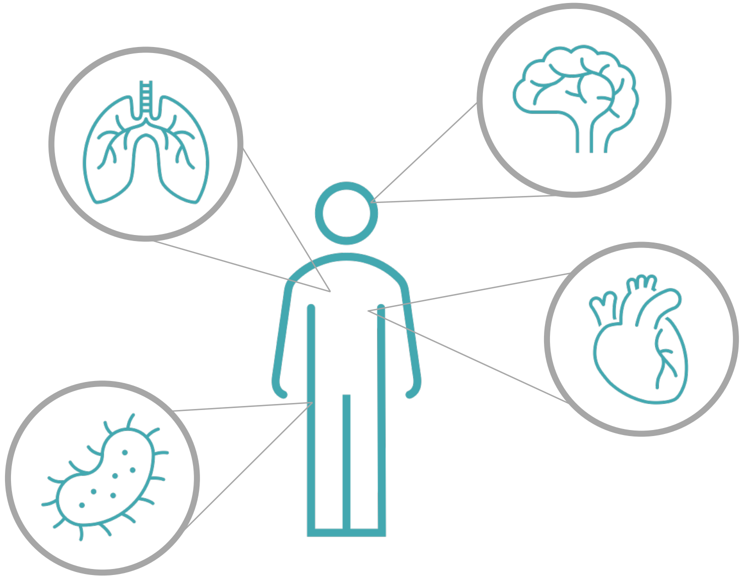
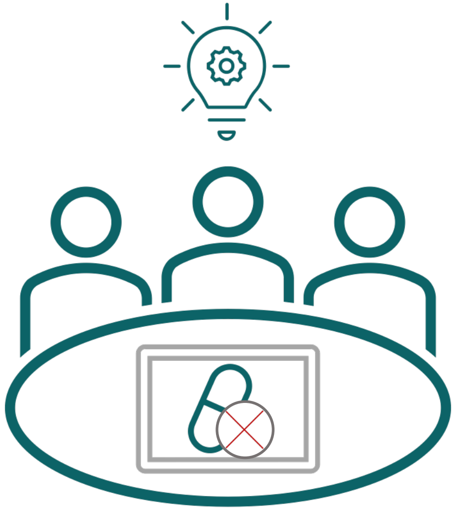
Future research includes modeling patients' co-morbidities and addressing AI biases.



Model infection patients’ co-morbidities through graphical methods



Investigate other aspects of antibiotic optimization and explore testing algorithms in real-world clinical settings

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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
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

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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