Imperial College London

AI Health
CAMO
centre for antimicrobial optimisation

Artificial intelligence based clinical decision support for antibiotic stewardship

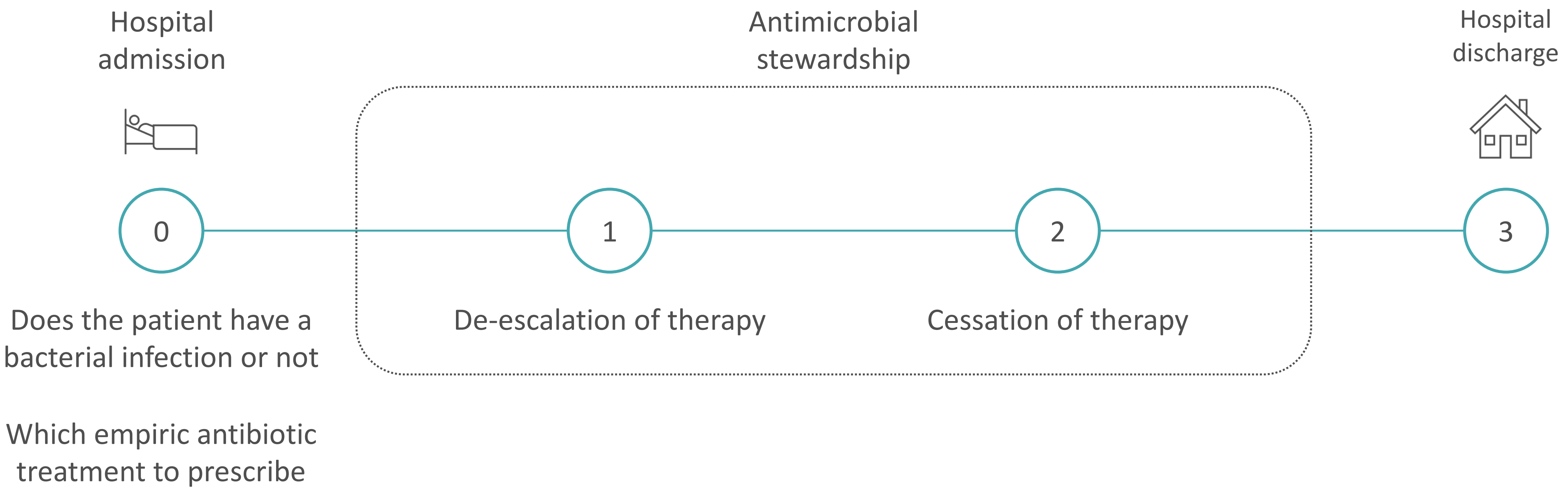
William Bolton

ADTCA

20th June 2024

Antimicrobial stewardship aims to optimise antibiotic decision making.

STAGES OF ANTIBIOTIC DECISION MAKING



Antimicrobial stewardship aims to **optimising antimicrobial use** and **prolonging their therapeutic life** to improve infection patient **outcomes** while minimizing the development of **antimicrobial resistance**

We research antimicrobial stewardship from a **data driven perspective** and use **artificial intelligence** to build **clinical decision support systems**

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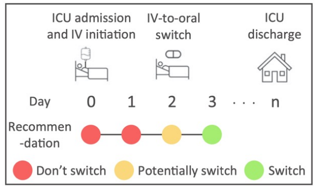
JOURNAL ARTICLE EDITOR'S CHOICE
Supervised machine learning for the prediction of infection on admission to hospital: a prospective observational cohort study
T M Rawson, B Hernandez, L S P Moore, O Blandy, P Herrero, M Gilchrist, A Gordon, C Toumazou, S Sriskandan, P Georgiou ... Show more
Volume 74,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

IV-to-oral switch



Antibiotic readmission

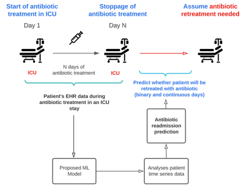


Figure 1.2: Proposed ML-based decision support model

Side effects

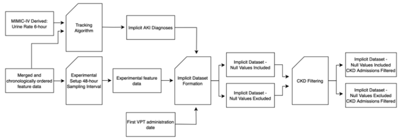
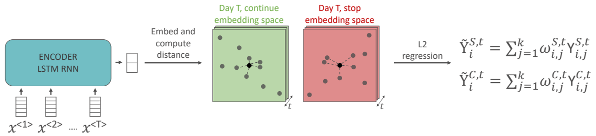


Figure 13: Implicit dataset formation workflow.

Antibiotic cessation

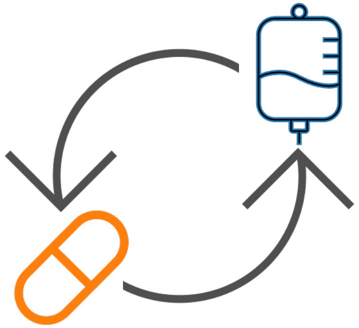


nature communications

frontiers in Digital Health

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

make the switch
FROM IV TO ORAL ANTIBIOTICS



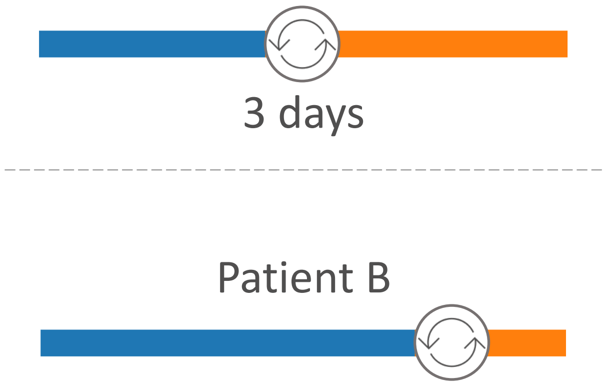
One key challenge of stewardship is **determining when to switch** antibiotics from **IV-to-oral administration**


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

Review
March 30, 2020
Evaluation of a Paradigm Shift From Intravenous Anti… Therapy for the T… Endocarditis
A Narrative Revie…
Brad Spellberg, MD; 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, Paul D. Holtom MD, Matthew C. Phillips MD, Robert M. Centor MD, Rachael. A. Lee MD, Rachel Baden MD, Brad Spellberg MD

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

eICU dataset

NHS Imperial College Healthcare NHS Trust

FEATURES

UK Health Security Agency

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

Based on the National Antimicrobial IVOS Criteria

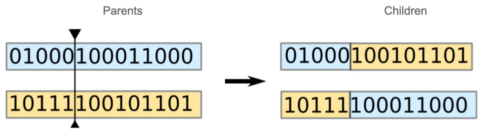
Co-produced through a UK-wide multidisciplinary consensus process involving 279 participants

FEATURE SELECTION

1 SHAP Values

SHAP

2 Genetic algorithm

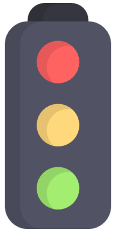


MODEL SELECTION

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

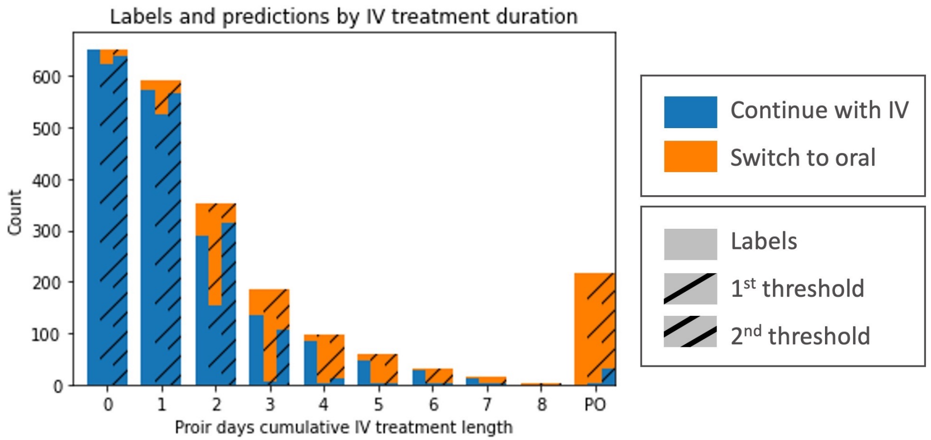
Mal-absorption

Sepsis

Pneumonia

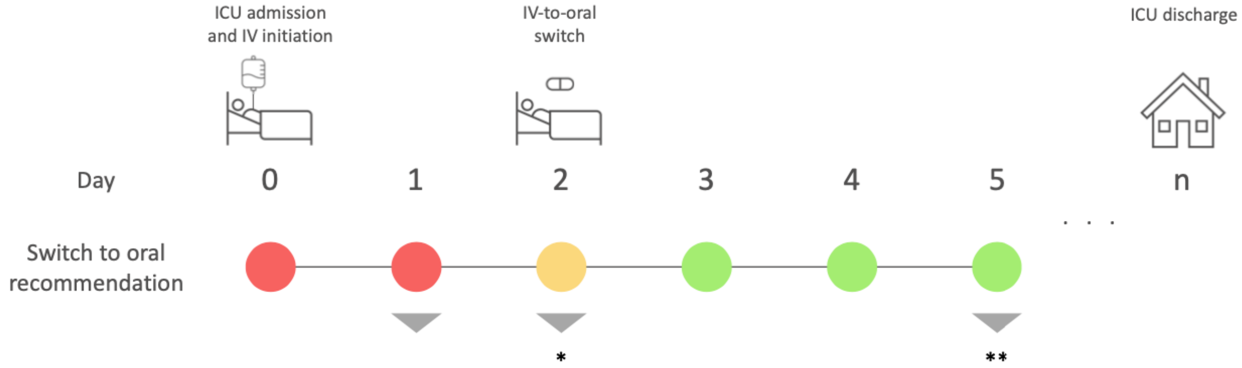
UTI

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

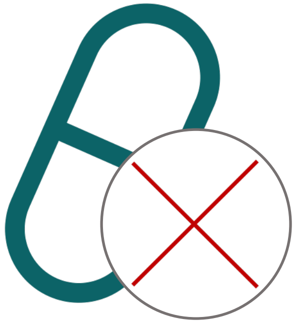
Potentially switch

Don't switch

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

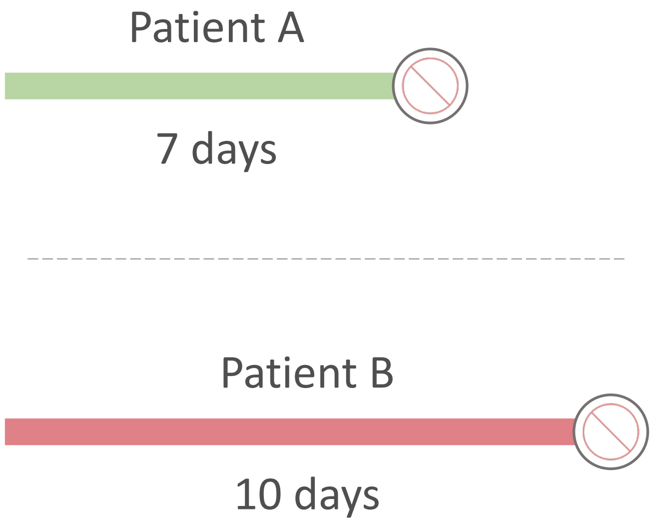
Sensitive attribute	Group	Equalised odds demonstrated	
		Initially	With threshold optimisation
Sex	Female	✓	-
	Male	✓	-
Age	20	✓	✗
	30	✓	✓
	40	✓	✓
	50	✓	✓
	60	✓	✓
	70	✓	✓
	80	✓	✓
	90	✗	✓
Race	Asian	✓	✓
	Black	✓	✓
	Hispanic	✓	✓
	Native	✗	✗
	Other	✓	✓
	Unknown	✓	✓
	White	✓	✓
Insurance	Medicaid	✗	✓
	Medicare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

Understanding when is the optimum time to stop antimicrobial treatment is not trivial.



One major question within antimicrobial prescribing is when is it most appropriate to **stop treatment**

Numerous studies have shown that on a population level, **shorter treatment durations** are often **non-inferior** to longer ones



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

Aim

Estimate patients' **length of stay** (LOS) and **mortality** outcomes for **any given day**, if they were to **stop vs continue** antibiotic treatment

Machine learning and synthetic outcome estimation for individualised antimicrobial cessation.

1 DATASET

Filter relevant patient stays from MIMIC-IV, **extract and aggregate features** including lab test results, clinical parameters, ventilation settings and demographics to create a **regular temporal dataset** for estimation of their **length of stay and mortality outcomes**.

MIMIC-IV
>40,000 ICU patients
ICU intravenous antibiotic treatment (1<days<21)
OUR DATASET
18,988 ICU patients 22,845 unique stays

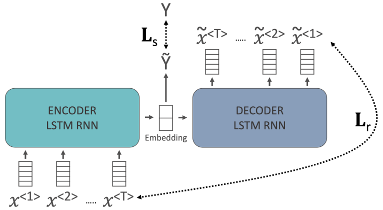
43 FEATURES

MORTALITY

LENGTH OF STAY (LOS)

2 AUTO ENCODER

Train autoencoders to create an **embedding that is representative** of the patients' temporal features and a **linear predictor** of their outcomes.

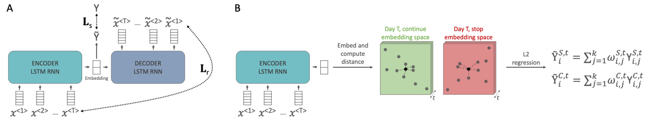


Train n=15,991

Validation n=3,427

3 SYNTHETIC OUTCOME ESTIMATION

Apply the **adapted synthetic control methodology** to **estimate patient outcomes** if they were to **stop vs continue treatment** on each antibiotic day within their ICU stay.



Test n=3,427

4 EVALUATION AND VALIDATION

Evaluate stop and continue estimations through **'impact' and 'control' days**. Validate the model through numerous tests and application to **pneumonia and UTI datasets**.

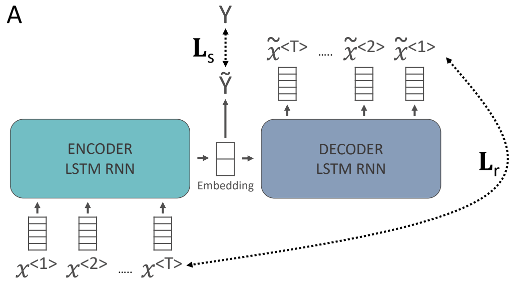
STOP IMPACT	STOP CONTROL
CONTINUE CONTROL	CONTINUE IMPACT

Metrics:
- Mean delta
- Wilcoxon rank-sum test
- RMSE
- AUROC

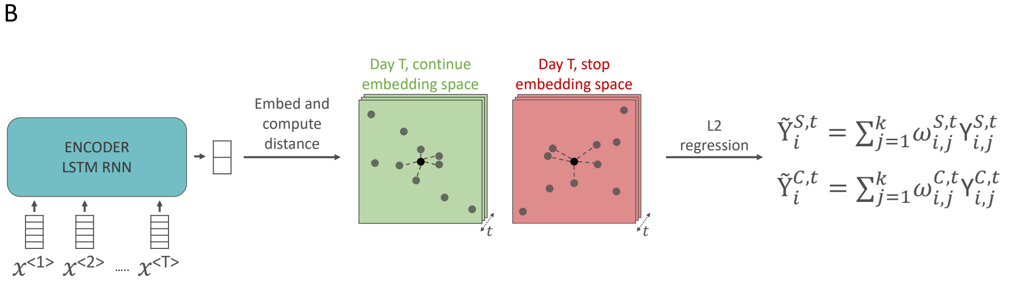
Pneumonia n=2,473

UTI n=923

AUTOENCODER TRAINING



SYNTHETIC OUTCOME ESTIMATION

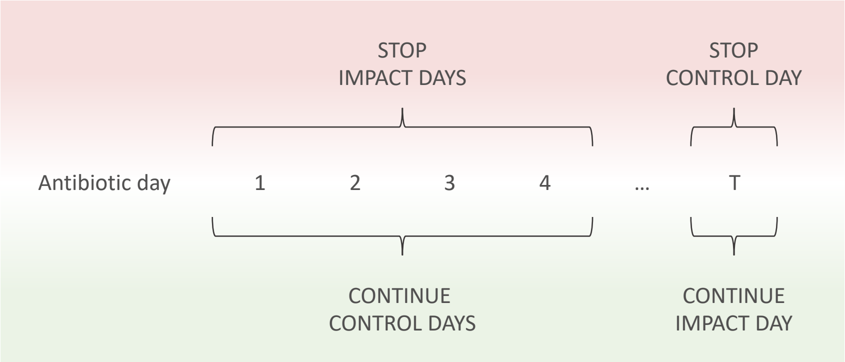


Synthetic outcome estimation can make us one stop ahead of antimicrobial resistance.

AUTOENCODER PREDICTIONS

	Metric	Result
Mortality Classification	AUROC	0.77 (95% CI 0.73–0.80)
	Accuracy	0.73 (95% CI 0.71–0.75)
	Precision	0.44 (95% CI 0.36–0.46)
	Recall	0.67 (95% CI 0.61–0.72)
	F1 Score	0.75 (95% CI 0.72–0.78)
	AUPRC	0.55 (95% CI 0.42–0.56)
LOS Regression	RMSE	3.88 (95% CI 3.84–3.92)

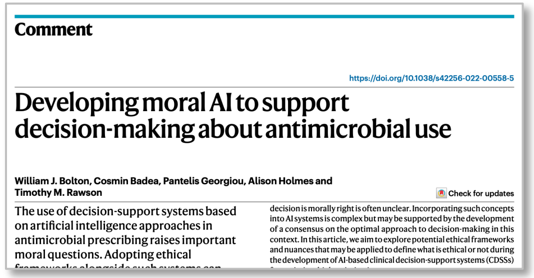
SYNTHETIC OUTCOME ESTIMATION



SCENARIO	DAY(S)	LOS				Mortality		
		Mean delta (days, p-value)	MAPE	MAE	RMSE	Mean delta	MAE	AUROC
STOP	IMPACT	2.71*, <0.01	0.36	3.30	4.80	0.06	0.25	0.66
	CONTROL	0.24, 0.60	0.26	1.32	1.93	0.05	0.15	0.72
CONTINUE	IMPACT	-2.09*, <0.01	0.77	2.85	3.16	0.05	0.18	0.67
	CONTROL	0.42*, 0.01	0.48	2.72	3.76	0.07	0.24	0.64

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

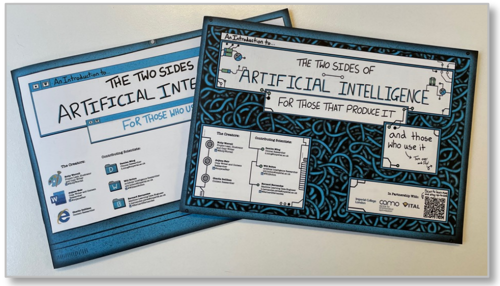
decision is morally right is often unclear. Incorporating such concepts into AI systems is complex but may be supported by the development of a consensus on the optimal approach to decision-making in this context. In this article, we aim to explore potential ethical frameworks and nuances that may be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

nature machine intelligence

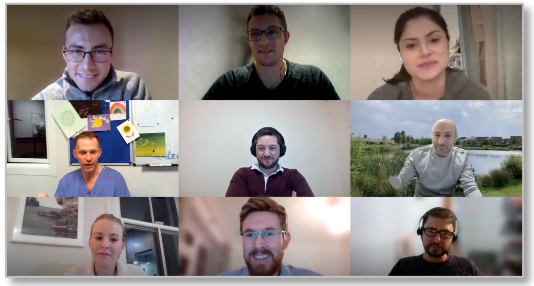
Variables	Description	Exemplar of starting antimicrobial treatment	Corresponding ad-hoc utility value
Intensity	How strong is the pleasure?	Treating a relevant infection with antimicrobials has the potential to save that person's life	Highly positive utility
Duration	How long will the pleasure last?	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

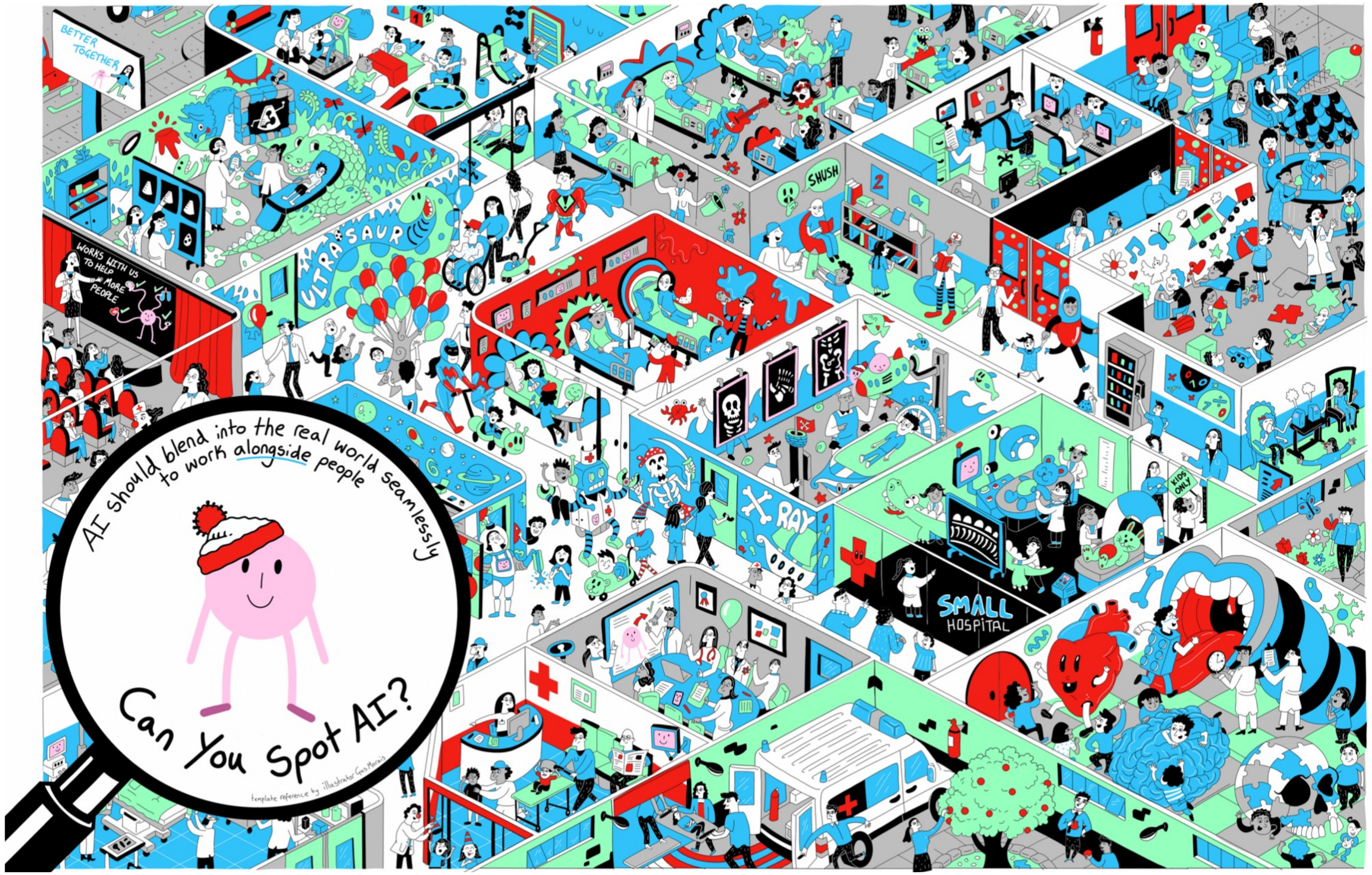
Patient and clinician views have been considered, with the public and stakeholder educated.

EDUCATION



PRIMARY RESEARCH





Prospective evaluation is necessary to ensure safety and technological adoption.

PARTICIPATE IN OUR STUDY!

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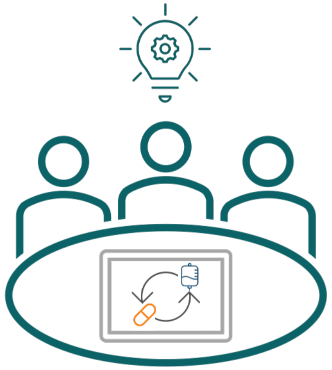
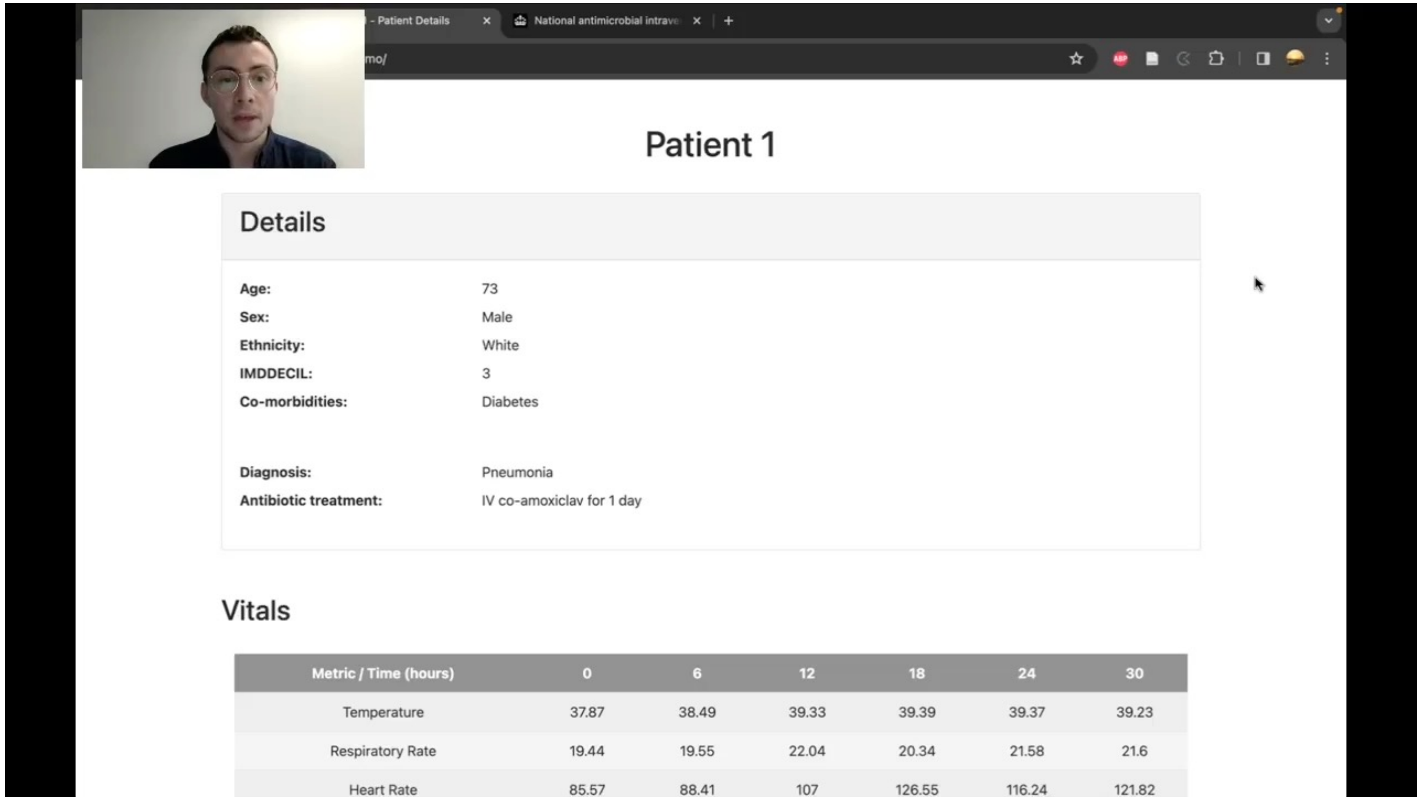


We are currently in the process of conducting **end user assessment** and **prospective testing** with clinicians in **simulated and real-world clinical settings**



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** and a novel approach to estimate the **potential impact of stopping treatment**
- Such systems could provide **clinically useful antimicrobial stewardship decision support**, but prospective validation is required

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

Dr Tim Rawson

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Mr Richard Wilson

Dr David Antcliffe

Dr Mark Gilchrist

Imperial College London

Health CAMO centre for antimicrobial optimisation

Thank you!

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