Imperial College London

NIHR | Imperial Biomedical Research Centre

ASSURING AUTONOMY INTERNATIONAL PROGRAMME

Evolution des Métiers de la Réanimation: Apport de l'Intelligence Artificielle

Matthieu Komorowski MD PhD

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Consultant, ICU, Charing Cross Hospital, London

Visiting scientist, Laboratory of Computational Physiology, MIT

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AER ACTUALITÉS EN RÉANIMATION

Lyon, 18 Nov 2022

Conflicts of interest

- Speaking honoraria from GE Healthcare
- Consulting fees from Philips Healthcare

The views expressed are my own.

Personalised Medicine in the ICU with AI

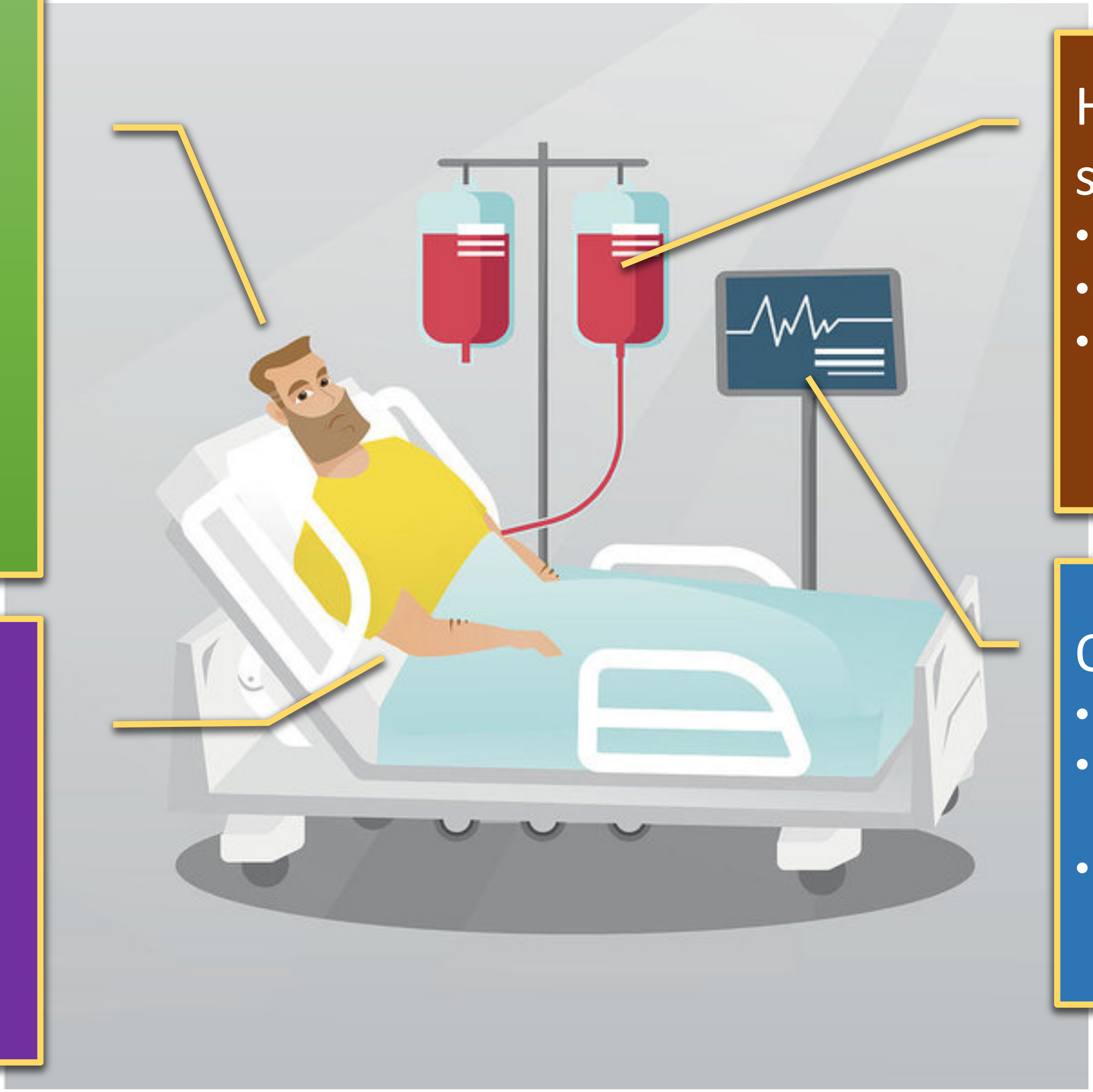
The hype → The reality → The path to clinical impact

The hype

Imagine if AI could help us…

- Predict admission
- Predict outcomes
- Identify phenotypes for clinical trial enrolment

In sepsis:
- Predict sepsis
- Predict antibiotic resistance
- Discover novel antibiotics



Haemodynamic support:
- Predict shock
- Predict hypotension
- Suggest fluids and/or vasopressor dosing

Organ support:
- Predict organ failure
- Sedation / ventilation strategy
- Optimise drug dosing

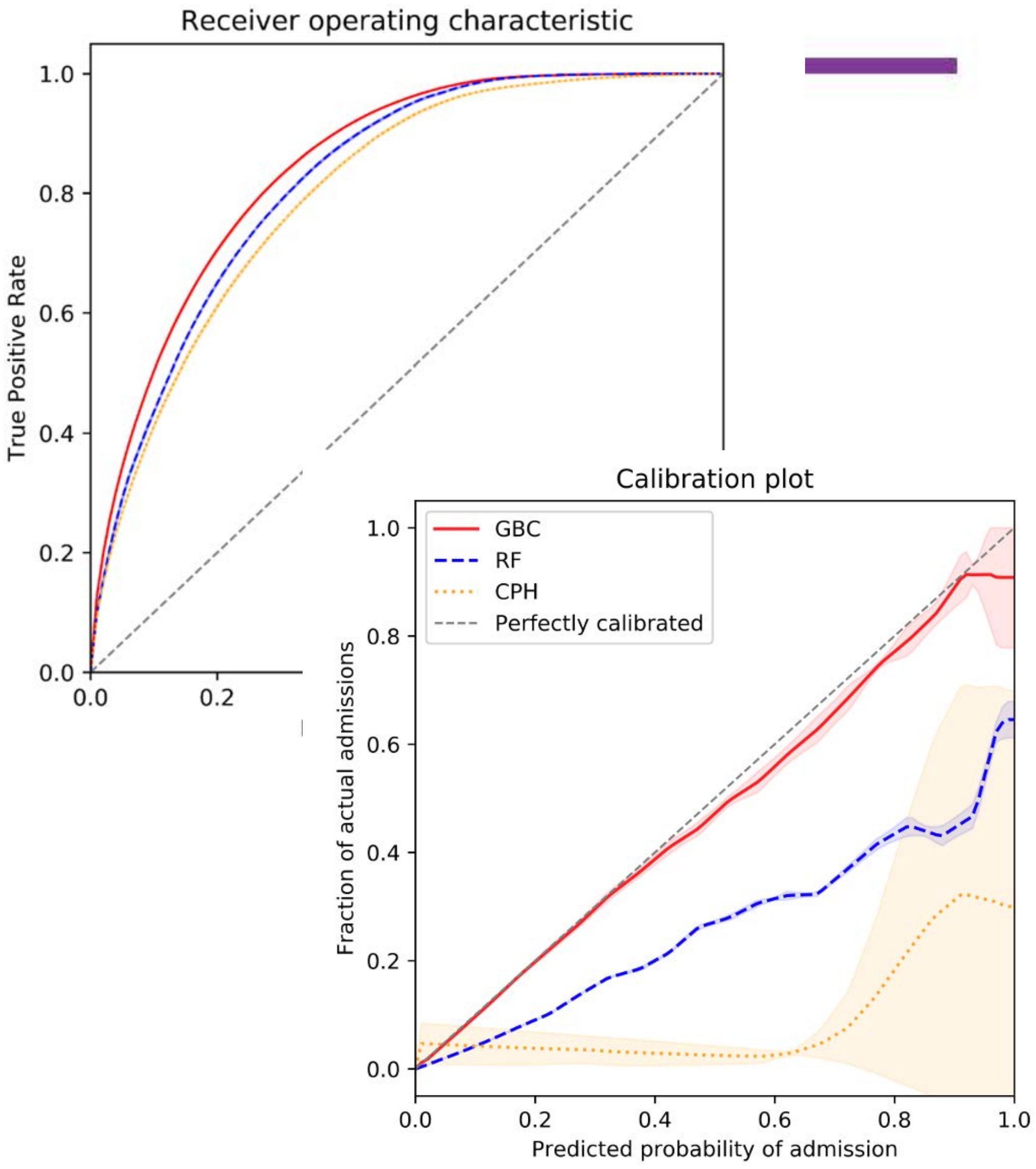
Machine learning = « learning from data»

Supervised learning	Unsupervised learning	Reinforcement learning
• Learn the function y=f(x) 1. Regression 2. Classification	• Learn data structure 1. Clustering 2. Dimensionality reduction	• Learn an optimal strategy

PLOS | MEDICINE

Predicting A&E admission

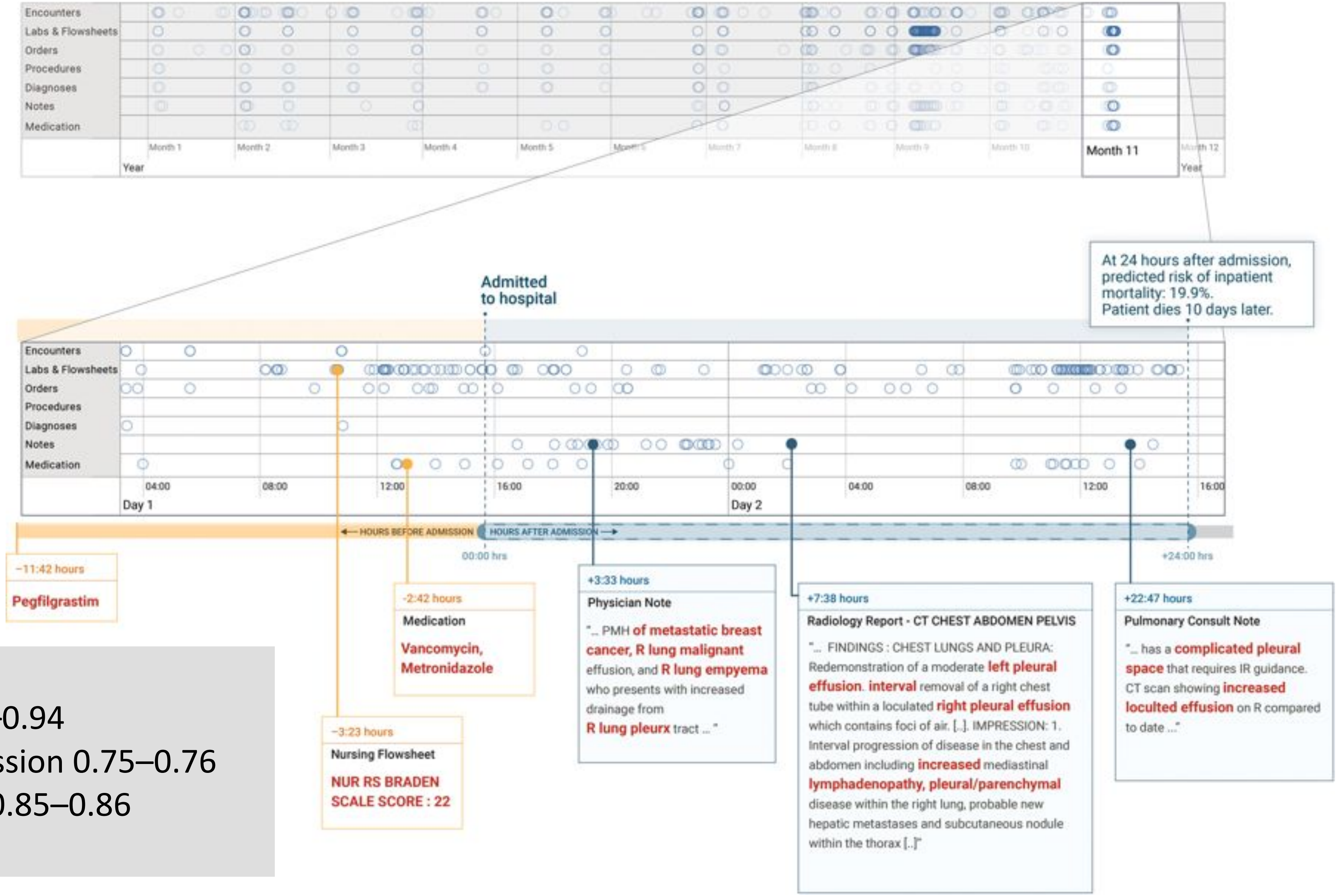
- 4.6 M patients from 389 GP practices from UK Clinical Practice Research Datalink
- **Covariates:** demographics, lifestyle factors, vital signs, laboratory tests, medications, comorbidities, previous emergency admissions
- AUC 0.848 for emergency admission within 24 months



[Rahimian, PLOS Med 2018]

[Rajkomar npj Digital Med 2018]

Predicting Outcomes



AUROC for:

- In-hospital mortality 0.93–0.94
- 30-day unplanned readmission 0.75–0.76
- Prolonged length of stay: 0.85–0.86
- Discharge diagnoses 0.90

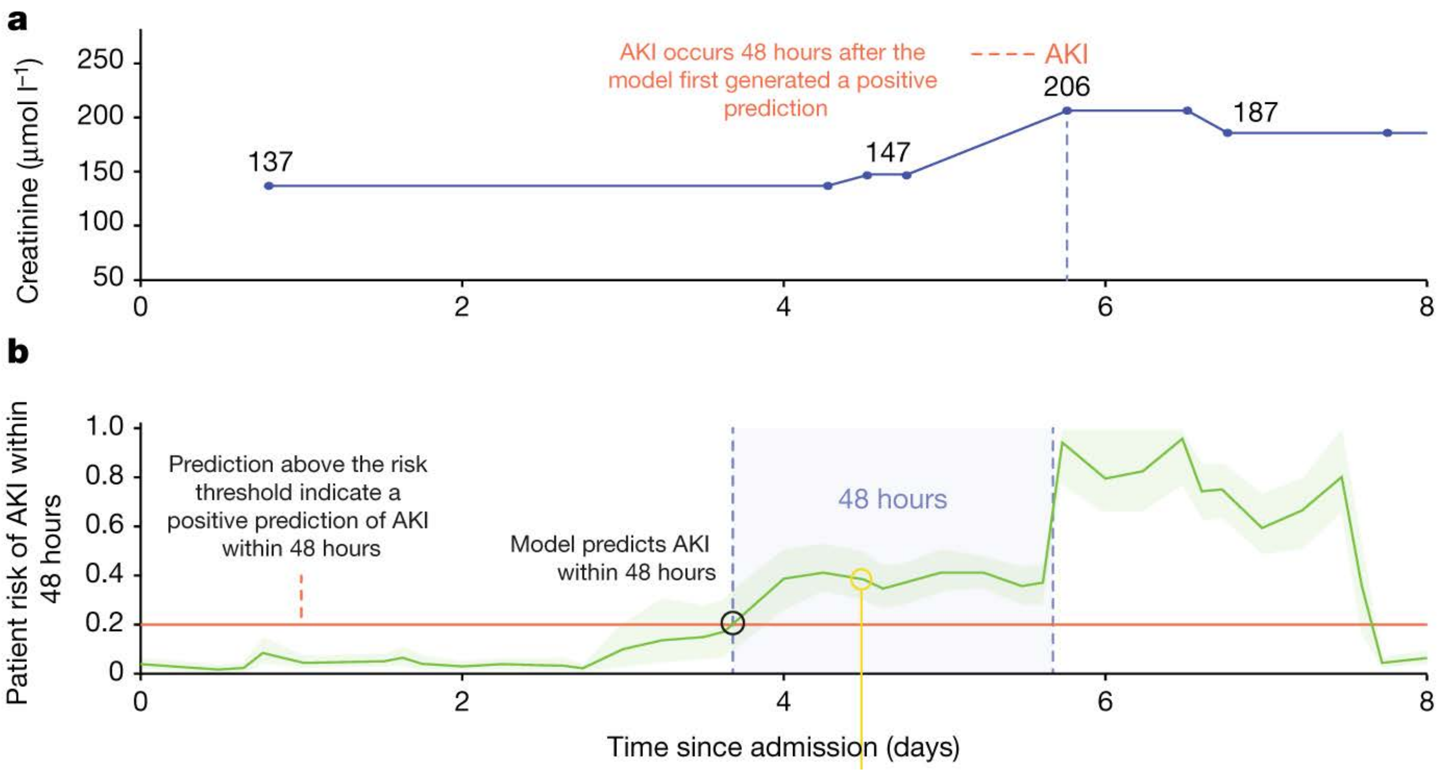
LETTER

https://doi.org/10.1038/s41586-019-1390-1

nature

A clinically applicable approach to continuous prediction of future acute kidney injury

Nenad Tomašev[1]*, Xavier Glorot[1], Jack W. Rae[1,2], Michal Zielinski[1], Harry Askham[1], Andre Saraiva[1], Anne Mottram[1], Clemens Meyer[1], Suman Ravuri[1], Ivan Protsyuk[1], Alistair Connell[1], Cían O. Hughes[1], Alan Karthikesalingam[1], Julien Cornebise[1,12], Hugh Montgomery[3], Geraint Rees[4], Chris Laing[5], Clifton R. Baker[6], Kelly Peterson[7,8], Ruth Reeves[9], Demis Hassabis[1], Dominic King[1], Mustafa Suleyman[1], Trevor Back[1,13], Christopher Nielson[10,11,13], Joseph R. Ledsam[1,13]* & Shakir Mohamed[1,13]



- N=703,782
- 1000+ sites
- 13.4% KDIGO AKI+

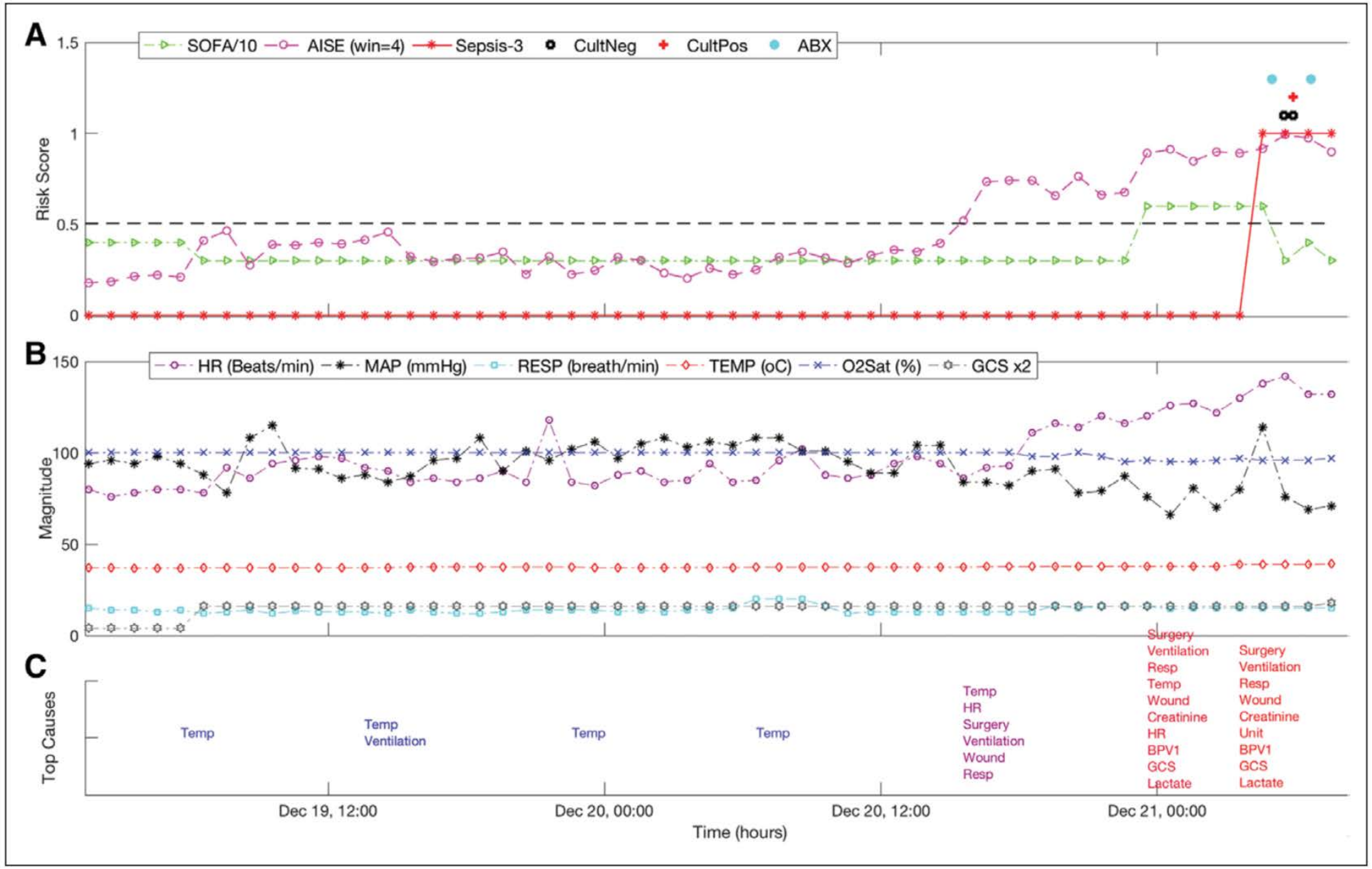
- AUC = 0.92
- 55.8% of AKI detected
- FP rate 2:1

(2019)

[Crit Care Med 2018]

An Interpretable Machine Learning Model for Accurate Prediction of Sepsis in the ICU

Shamim Nemati, PhD[1]; Andre Holder, MD, MSc[2]; Fereshteh Razmi, MS[1]; Matthew D. Stanley, MD[3]; Gari D. Clifford, PhD[1,4]; Timothy G. Buchman, PhD, MD[3,5]



[Oct 2021]

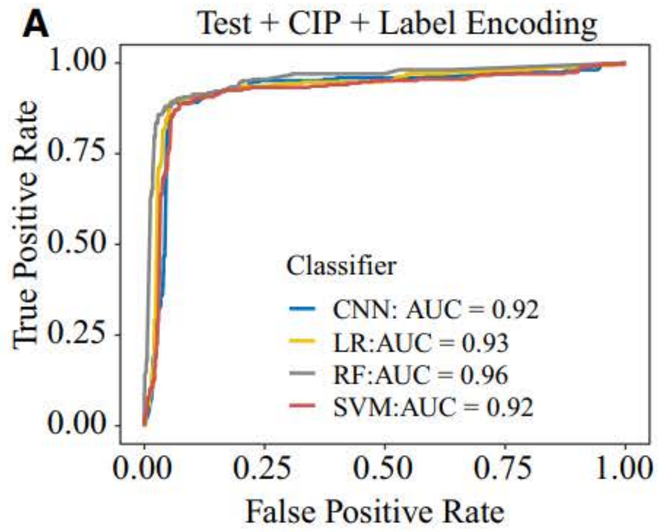
Bioinformatics, 38(2), 2022, 325–334
doi: 10.1093/bioinformatics/btab681
Advance Access Publication Date: 6 October 2021
Original Paper

OXFORD

Genome analysis

Prediction of antimicrobial resistance based on whole-genome sequencing and machine learning

Yunxiao Ren[1], Trinad Chakraborty[2,3], Swapnil Doijad[2,3], Linda Falgenhauer[3,4,5], Jane Falgenhauer[2,3], Alexander Goesmann[3,6], Anne-Christin Hauschild[1], Oliver Schwengers[3,6] and Dominik Heider[1,*]

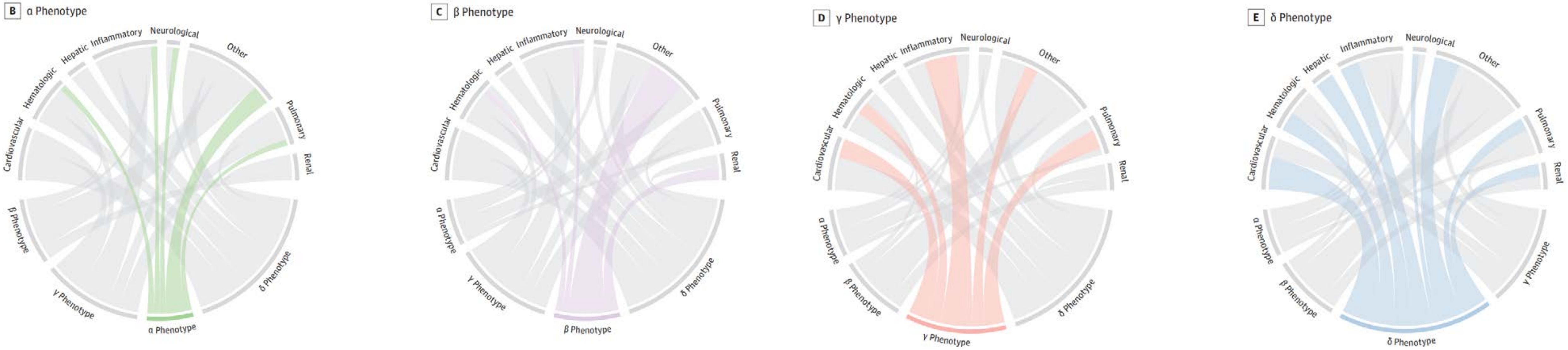


Classifiers/drug	Precision	Precision	Precision	Precision
	CIP	CTX	CTZ	GEN
CNN	0.88 ± 0.04	0.75 ± 0.04	0.81 ± 0.02	0.76 ± 0.03
LR	0.88 ± 0.05	0.71 ± 0.04	0.81 ± 0.03	0.77 ± 0.02
RF	0.92 ± 0.04	0.75 ± 0.03	0.84 ± 0.03	0.79 ± 0.02
SVM	0.85 ± 0.03	0.69 ± 0.02	0.78 ± 0.03	0.75 ± 0.02

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Derivation, Validation, and Potential Treatment Implications of Novel Clinical Phenotypes for Sepsis

Christopher W. Seymour, MD, MSc; Jason N. Kennedy, MS; Shu Wang, MS; Chung-Chou H. Chang, PhD; Corrine F. Elliott, MS; Zhongying Xu, MS; Scott Berry, PhD; Gilles Clermont, MD, MSc; Gregory Cooper, MD, PhD; Hernando Gomez, MD, MPH; David T. Huang, MD, MPH; John A. Kellum, MD, FACP, MCCM; Qi Mi, PhD; Steven M. Opal, MD; Victor Talisa, MS; Tom van der Poll, MD, PhD; Shyam Visweswaran, MD, PhD; Yoram Vodovotz, PhD; Jeremy C. Weiss, MD, PhD; Donald M. Yealy, MD, FACEP; Sachin Yende, MD, MS; Derek C. Angus, MD, MPH



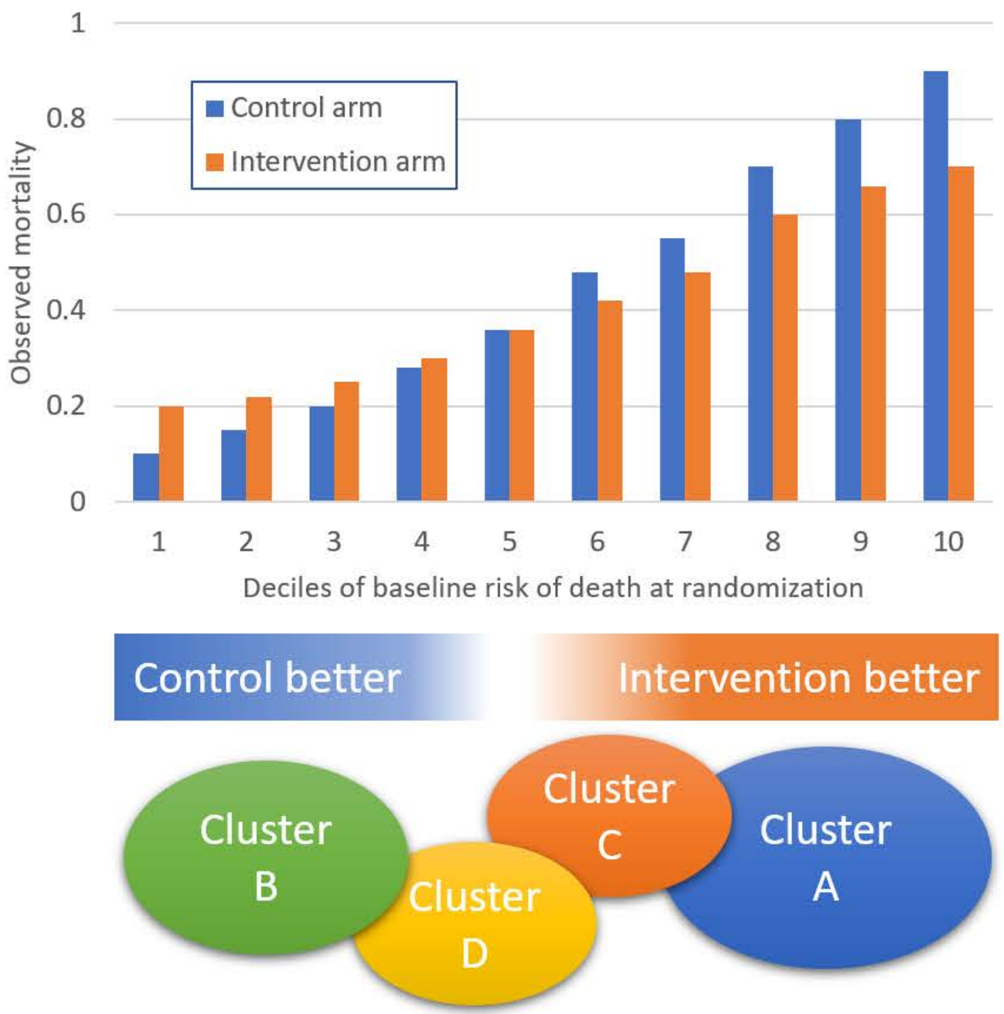
[Aug 2019]

British Journal of Anaesthesia, 123 (1): 14–16 (2019)
doi: 10.1016/j.bja.2019.03.043
Advance Access Publication Date: 7 May 2019

Informing future intensive care trials with machine learning

Matthieu Komorowski[1,2,*] and Malcolm Lemyze[3]

[1]Department of Surgery and Cancer, Faculty of Medicine, Imperial College London, London, UK, [2]Intensive Care Unit, Charing Cross Hospital, London, UK and [3]Intensive Care Unit, Arras Hospital, Arras, France

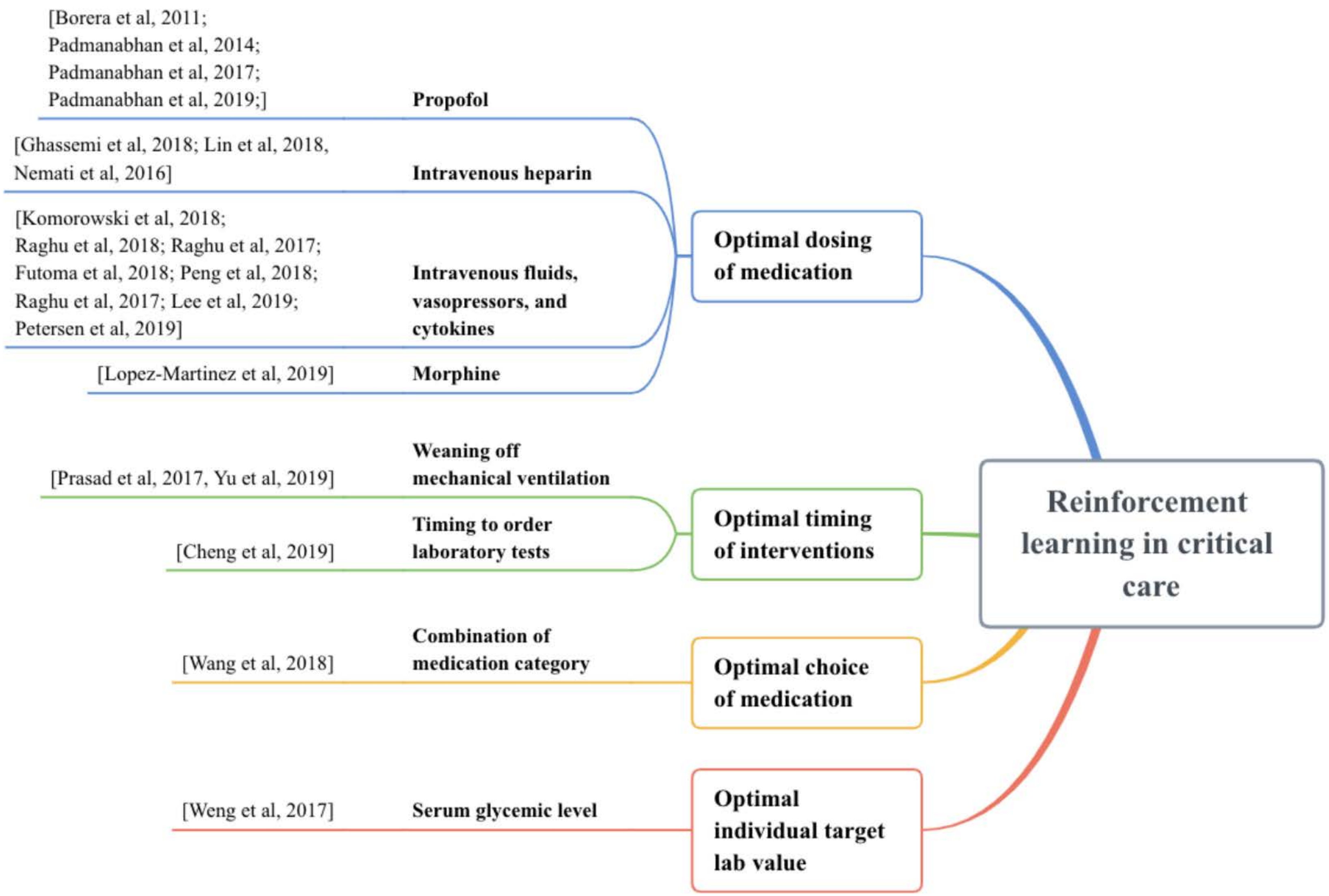


[Adapted with permission from Iwashyna AJRCCM 2015]

Reinforcement learning

[Sutton & Barto 2020, Liu JMIR 2020]

Reinforcement Learning Applications in ICU



[Liu JMIR 2020]

[Feb 2021]

npj Digital Medicine

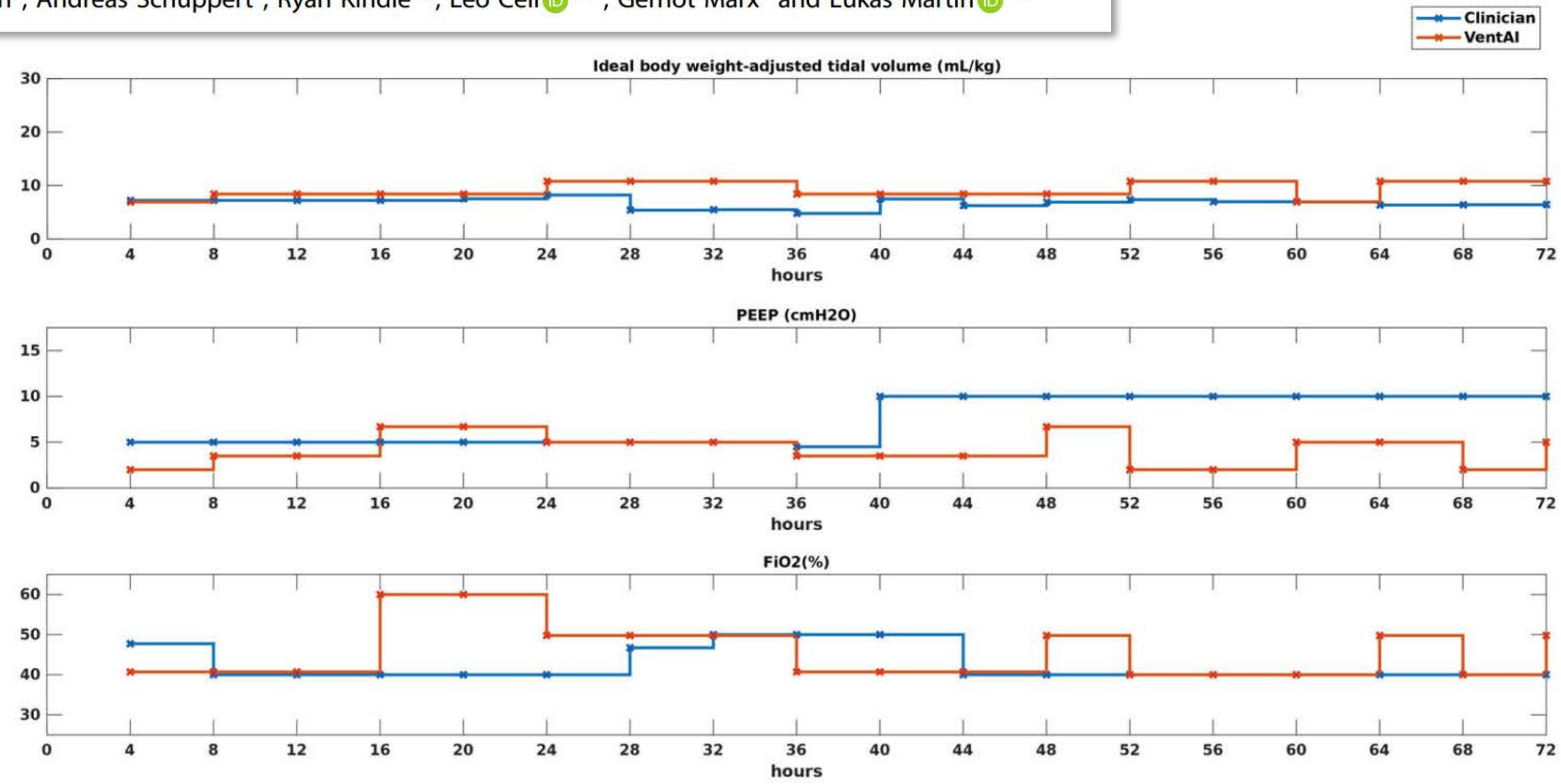
www.nature.com/npjdigitalmed

ARTICLE OPEN

Check for updates

Development and validation of a reinforcement learning algorithm to dynamically optimize mechanical ventilation in critical care

Arne Peine[1,10], Ahmed Hallawa[1,2,10], Johannes Bickenbach[1], Guido Dartmann[3], Lejla Begic Fazlic[3], Anke Schmeink[4], Gerd Ascheid[2], Christoph Thiemermann[5], Andreas Schuppert[6], Ryan Kindle[7,8], Leo Celi[7,8,9], Gernot Marx[1] and Lukas Martin[1]✉

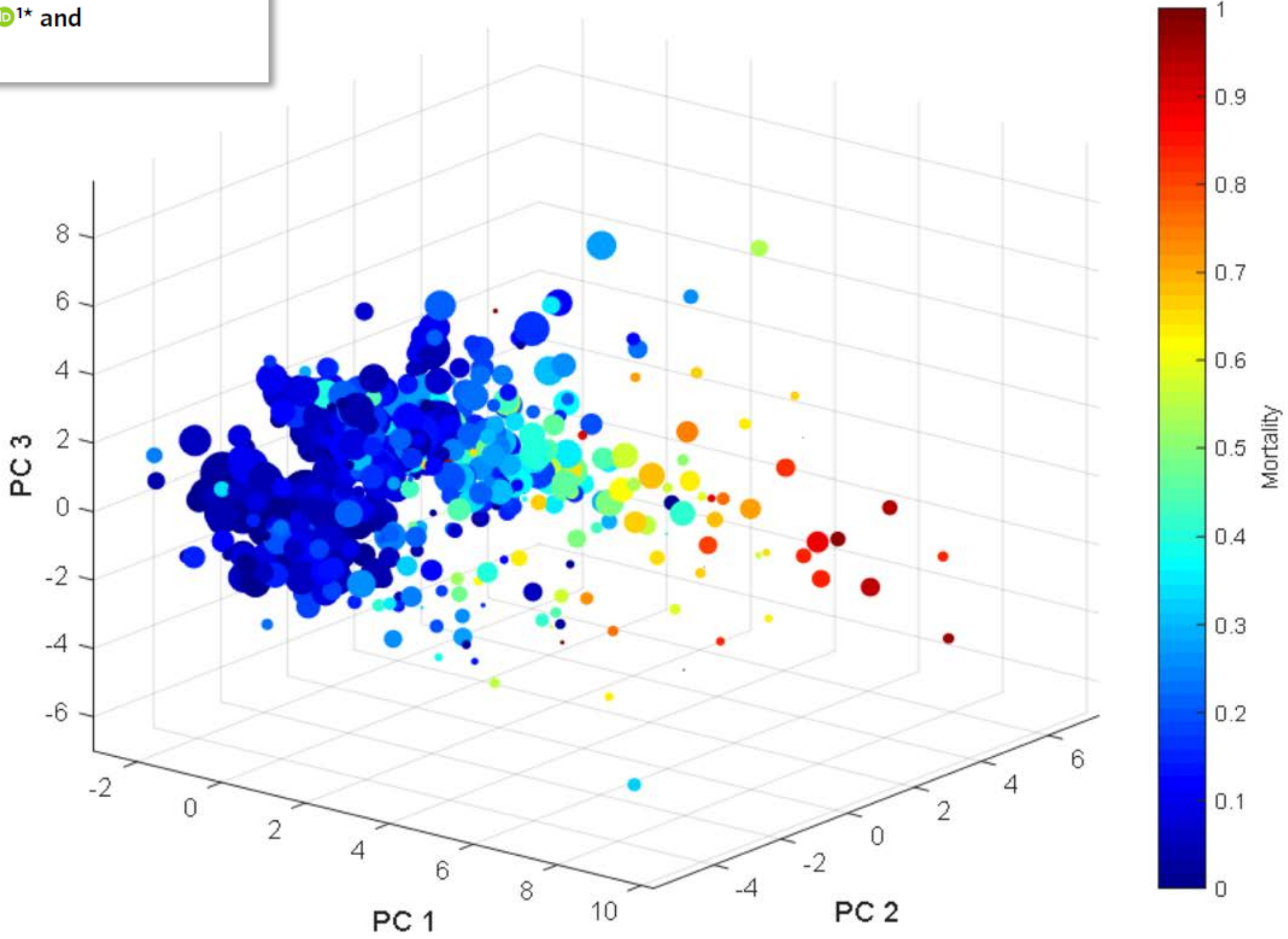


nature medicine
Nov 2018
ARTICLES
https://doi.org/10.1038/s41591-018-0213-5

Imperial College London

The Artificial Intelligence Clinician learns optimal treatment strategies for sepsis in intensive care

Matthieu Komorowski[1,2,3], Leo A. Celi[3,4], Omar Badawi[3,5,6], Anthony C. Gordon[1*] and A. Aldo Faisal[2,7,8,9*]



3D representation of the 750 states of the reinforcement learning model

Independent replication

Amsterdam UMC
University Medical Centers

Artificial Intelligence In Medicine 112 (2021) 102003

Contents lists available at ScienceDirect

Artificial Intelligence In Medicine

journal homepage: www.elsevier.com/locate/artmed

ELSEVIER

Position Paper

Check for updates

Transatlantic transferability of a new reinforcement learning model for optimizing haemodynamic treatment for critically ill patients with sepsis

Luca Roggeveen [a,b,*], Ali el Hassouni [b], Jonas Ahrendt [a], Tingjie Guo [a], Lucas Fleuren [a,b], Patrick Thoral [a], Armand RJ Girbes [a], Mark Hoogendoorn [b], Paul WG Elbers [a]

Microsoft Research
@MSFTResearch

Sept 2021

Announcing a GitHub repo which generates a data cohort for reinforcement learning research on Sepsis. The cohort is produced from the publicly available hospital database, MIMIC III.

Access the improved repo: aka.ms/AAb2dv0
@mefatemi @MarzyehGhassemi @tw_killian

microsoft/
mimic_sepsis

Sepsis cohort from MIMIC dataset

3 · 0 · 32 · 12

Safe Reinforcement Learning for Sepsis Treatment

Yan Jia
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University of York
York, UK
yj914@york.ac.uk

John Burden
Department of computer science
University of York
York, UK
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Tom Lawton
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tom.lawton@bthft.nhs.uk

Ibrahim Habli
Department of computer science
University of York
York, UK
ibrahim.habli@york.ac.uk

2020 IEEE International Conference on Healthcare Informatics (ICHI)

HIS 2022

Check for updates

Learning Optimal Treatment Strategies for Sepsis Using Offline Reinforcement Learning in Continuous Space

Zeyu Wang[1(✉)], Huiying Zhao[2(✉)], Peng Ren[3], Yuxi Zhou[3], and Ming Sheng[3]

[1] Beijing Institute of Technology, Beijing 100081, China
wangzeyu@bit.edu.cn
[2] Peking University People's Hospital, Beijing 100044, China
zhaohuiying109@sina.com
[3] BNRist, DCST, RIIT, Tsinghua University, Beijing 100084, China
{renpeng,yuxi,shengming}@tsinghua.edu.cn

Derived models

PLOS DIGITAL HEALTH

Feb 2022

RESEARCH ARTICLE

Unifying cardiovascular modelling with deep
reinforcement learning for uncertainty aware
control of sepsis treatment

r James Langmead[3],

Learning to Treat Hypotensive Episodes in Sepsis

Return to Blog Home

Microsoft Research Blog

npj | digital medicine

www.nature.com/npjdigitalmed

ARTICLE OPEN

Check for updates

An interpretable RL framework for pre-deployment modeling in ICU hypotension management

Kristine Zhang[1], Henry Wang[1], Jianzhun Du[1], Brian Chu[1], Aldo Robles Arévalo[2], Ryan Kindle[3], Leo Anthony Celi[4] and Finale Doshi-Velez[1]

Ma et al. C
https://do

RESEAR

Indivi
for septic shock formal
modeling and dynami

Penglin Ma[1†], Jingtao Liu[2†], Feng Shen[3], Xuelian Lia
Peng Wang[9], Man Huang[10], Tong Li[11], Meili Duan[12],
Xianyao Wan[17], ZongYu Wang[18], Shusheng Li[19], Jianwei Han[20], Zhenliang Li[21], Guolei Ding[22], Qun Deng[23],
Jicheng Zhang[24], Yue Zhu[25], Wenjing Ma[26], Jingwen Wang[27], Yan Kang[28] and Zhongheng Zhang[29*]

Joseph Futoma, PhD[1,2], Muhammad Masood, PhD[1], Finale Doshi-Velez, PhD[1]
[1] Harvard University, Paulson School of Engineering and Applied Sciences, Cambridge, MA
[2] Duke University, Dept. of Statistical Science, Durham, NC

L RESEARCH
14 April 2022
.2022.766447

Check for updates

on of

s

Based on Reinforcement Learning

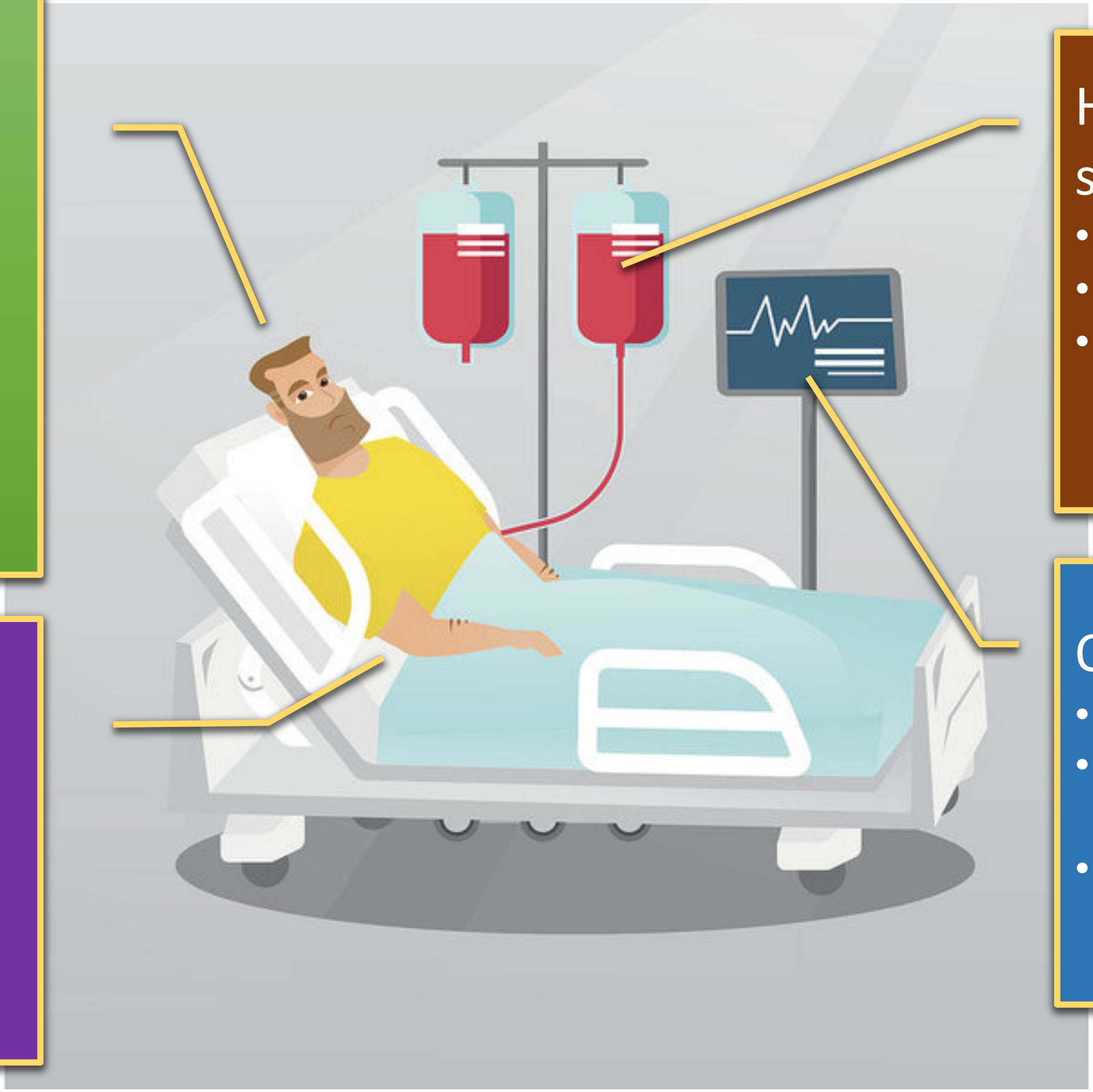
Longxiang Su[1†], Yansheng Li[2†], Shengjun Liu[1†], Siqi Zhang[2], Xiang Zhou[1], Li Weng[3], Mingliang Su[2], Bin Du[3*], Weiguo Zhu[4*] and Yun Long[1*]

Imagine if AI could help us...

- Predict admission
- Predict outcomes
- Identify phenotypes for clinical trial enrolment

In sepsis:

- Predict sepsis
- Predict bacteraemia
- Predict antibiotic resistance
- Discover novel antibiotics



Haemodynamic support:

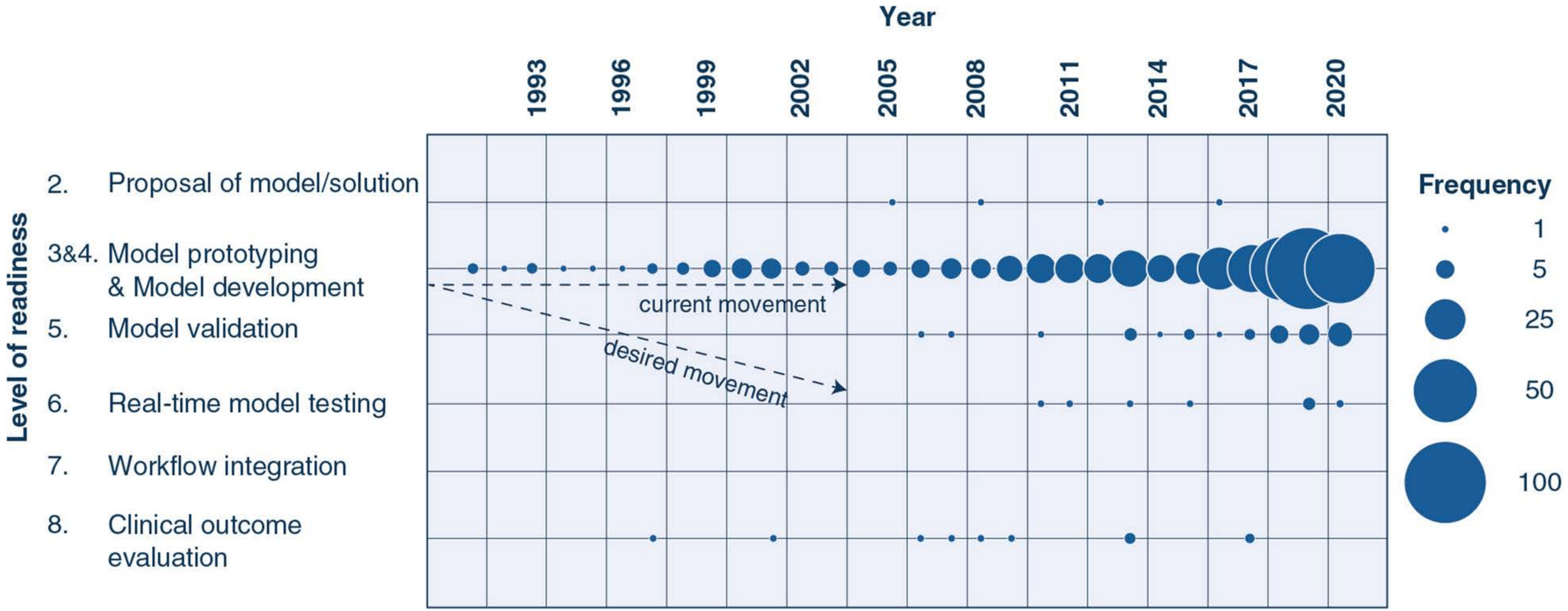
- Predict shock
- Predict hypotension
- Suggest fluids and/or vasopressor dosing

Organ support:

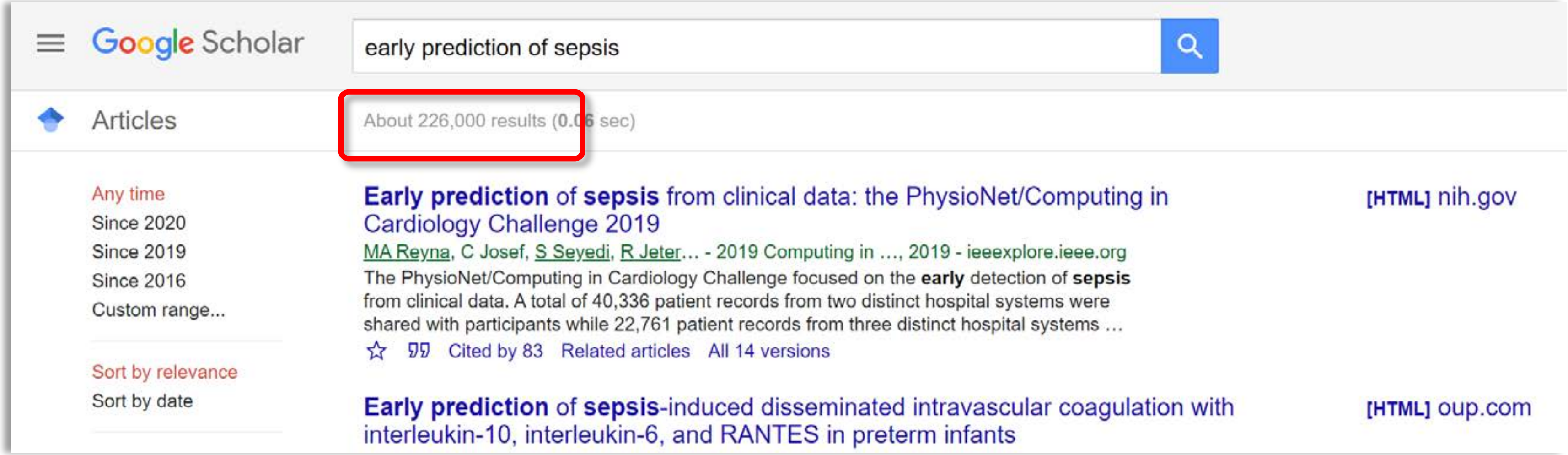
- Predict organ failure
- Sedation / ventilation strategy
- Optimise drug dosing

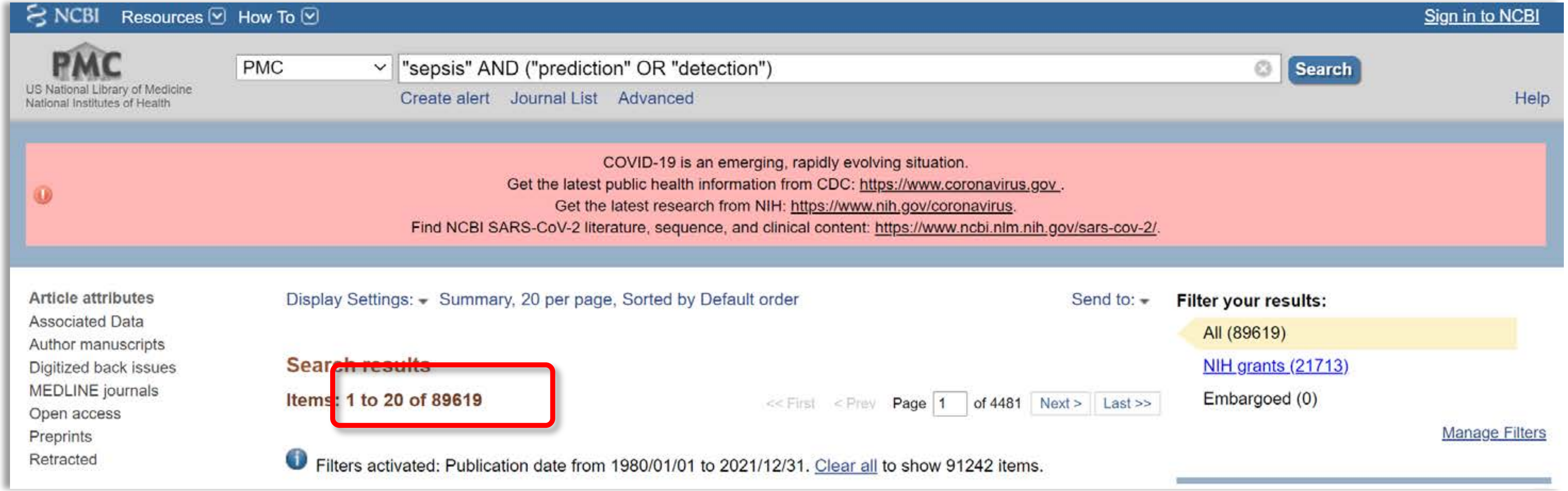
The Reality

Level of readiness of AI Applications in the ICU



[van de Sande, ICME 2021]


Google Scholar
early prediction of sepsis
Articles
About 226,000 results (0.06 sec)
Any time
Since 2020
Since 2019
Since 2016
Custom range...
Sort by relevance
Sort by date
Early prediction of sepsis from clinical data: the PhysioNet/Computing in Cardiology Challenge 2019
[HTML] nih.gov
MA Reyna, C Josef, S Seyedi, R Jeter… - 2019 Computing in …, 2019 - ieeexplore.ieee.org
The PhysioNet/Computing in Cardiology Challenge focused on the early detection of sepsis from clinical data. A total of 40,336 patient records from two distinct hospital systems were shared with participants while 22,761 patient records from three distinct hospital systems …
Cited by 83 Related articles All 14 versions
Early prediction of sepsis-induced disseminated intravascular coagulation with interleukin-10, interleukin-6, and RANTES in preterm infants
[HTML] oup.com


NCBI Resources How To
Sign in to NCBI
PMC
US National Library of Medicine
National Institutes of Health
PMC
"sepsis" AND ("prediction" OR "detection")
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Create alert Journal List Advanced
Help
COVID-19 is an emerging, rapidly evolving situation.
Get the latest public health information from CDC: https://www.coronavirus.gov .
Get the latest research from NIH: https://www.nih.gov/coronavirus.
Find NCBI SARS-CoV-2 literature, sequence, and clinical content: https://www.ncbi.nlm.nih.gov/sars-cov-2/.
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NIH grants (21713)
Embargoed (0)
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Intensive Care Med (2020) 46:383–400
https://doi.org/10.1007/s00134-019-05872-y

SYSTEMATIC REVIEW

Machine learning for the prediction of sepsis: a systematic review and meta-analysis of diagnostic test accuracy

Lucas M. Fleuren[1,2*], Thomas L. T. Klausch[3], Charlotte L. Zwager[1], Linda J. Schoonmade[4], Tingjie Guo[1], Luca F. Roggeveen[1,2], Eleonora L. Swart[5], Armand R. J. Girbes[1], Patrick Thoral[1], Ari Ercole[6,7], Mark Hoogendoorn[2] and Paul W. G. Elbers[1,7]

N=150 Models N=28 Papers

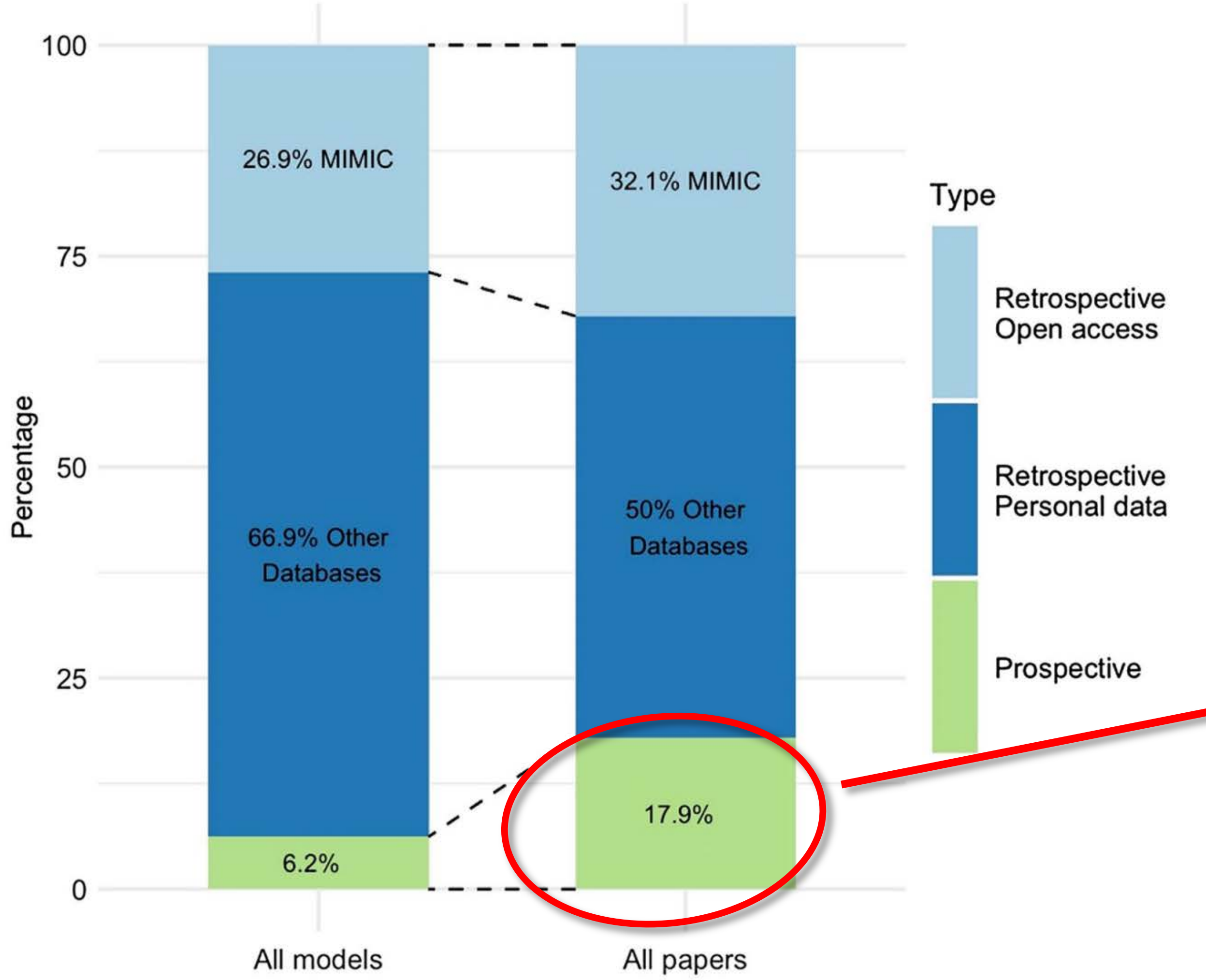


Fig. 3 Prospective versus retrospective models. Percentages specified per paper and for all models

Only 3 prospective trials

Only 1 RCT

[Fleuren ICM 2020]

Critical care

BMJ Open Respiratory Research

Effect of a machine learning-based severe sepsis prediction algorithm on patient survival and hospital length of stay: a randomised clinical trial

2017

David W Shimabukuro,[1] Christopher W Barton,[2] Mitchell D Feldman,[3] Samson J Mataraso,[4,5] Ritankar Das[6]

Table 2 Differences in hospital LOS, ICU LOS, and in-hospital mortality between the experimental and control groups

Outcome	Control (n=75)	Experimental (n=67)	Amount of reduction	P value
Hospital LOS (days)	13.0 (1.23)	10.3 (0.912)	2.30 days	0.042
ICU LOS (days)	8.40 (0.881)	6.31 (0.666)	2.09 days	0.030
In-hospital mortality rate	21.3% (4.76%)	8.96% (3.51%)	12.3%	0.018

The mean and the standard error (in parentheses) for each outcome are noted in the table. All outcomes demonstrate statistically significant reductions when using the machine learning algorithm ($p<0.05$).
ICU, intensive care unit; LOS, length of stay.

- Monocentric
- N=142

nature medicine

Prospective, multi-site study of patient outcomes after implementation of the TREWS machine learning-based early warning system for sepsis

(July 2022)

Roy Adams[1,2], Katharine E. Henry[2,3], Anirudh Sridharan[4], Hossein Soleimani[5], Andong Zhan[2,3], Nishi Rawat[6], Lauren Johnson[7], David N. Hager[8], Sara E. Cosgrove[8], Andrew Markowski[9], Eili Y. Klein[10], Edward S. Chen[8], Mustapha O. Saheed[10], Maureen Henley[7], Sheila Miranda[11], Katrina Houston[7], Robert C. Linton[4], Anushree R. Ahluwalia[7], Albert W. Wu[6,8,12,13,14] ✉ and Suchi Saria[1,3,8,12,15] ✉

590K patients monitored
In 5 hospitals

6,877 patients with sepsis who were identified by the alert before initiation of antibiotics

Alert confirmed by provider within 3h
N =4220

Study

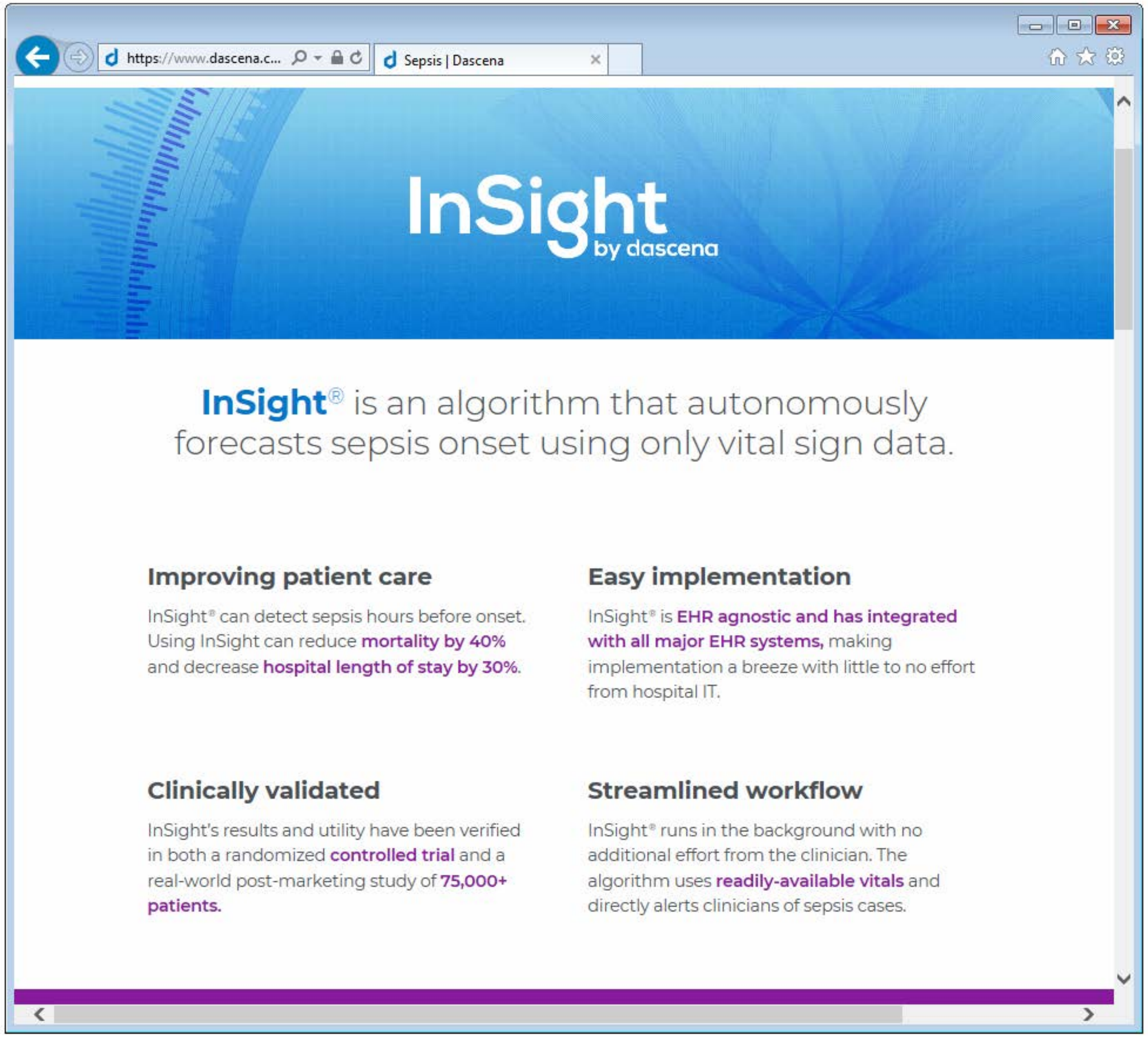
Alert not confirmed
N=2657

Control

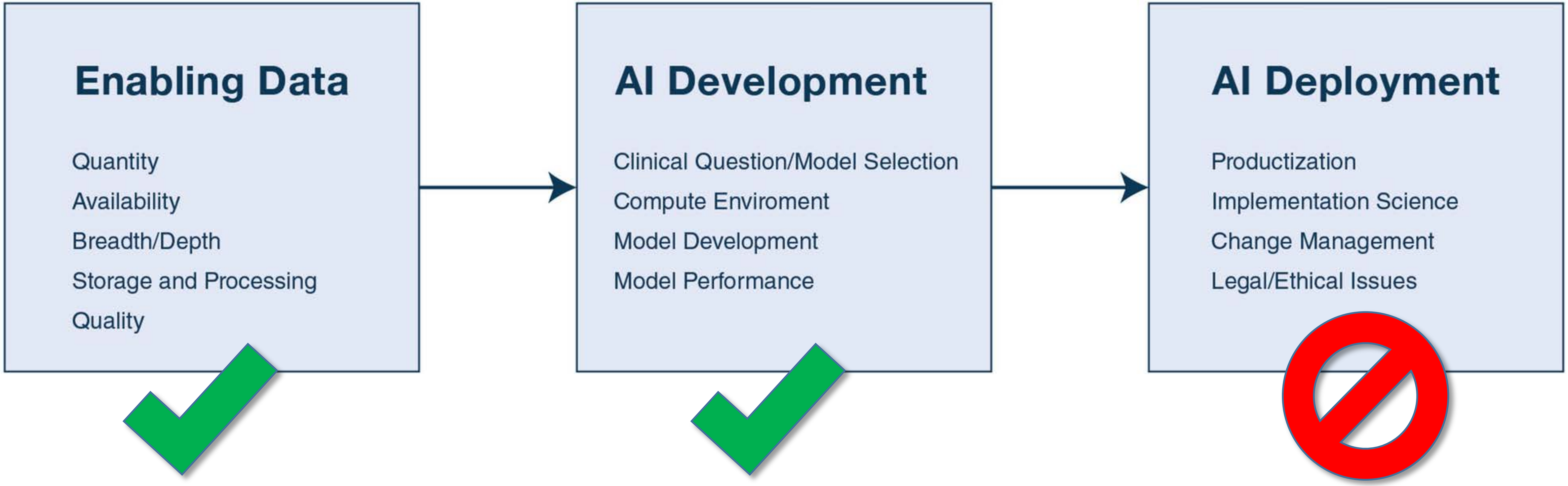
Non randomised

	Study (N=4220)	Control (N=2657)	Adjusted Risk Difference	P value
In-hosp mortality (N,%)	617 (14.6%)	509 (19.2%)	−3.34% (−5.10, −1.67%)	<0.001
SOFA progr. at 72 h	−0.8 ± 2.7	−0.4 ± 2.9	−0.26 (−0.42, −0.11)	0.001
Med. length of stay (h)	156 (99–260)	190 (118–323)	−11.58 (−18.13, −5.03)	0.001

Only product available?

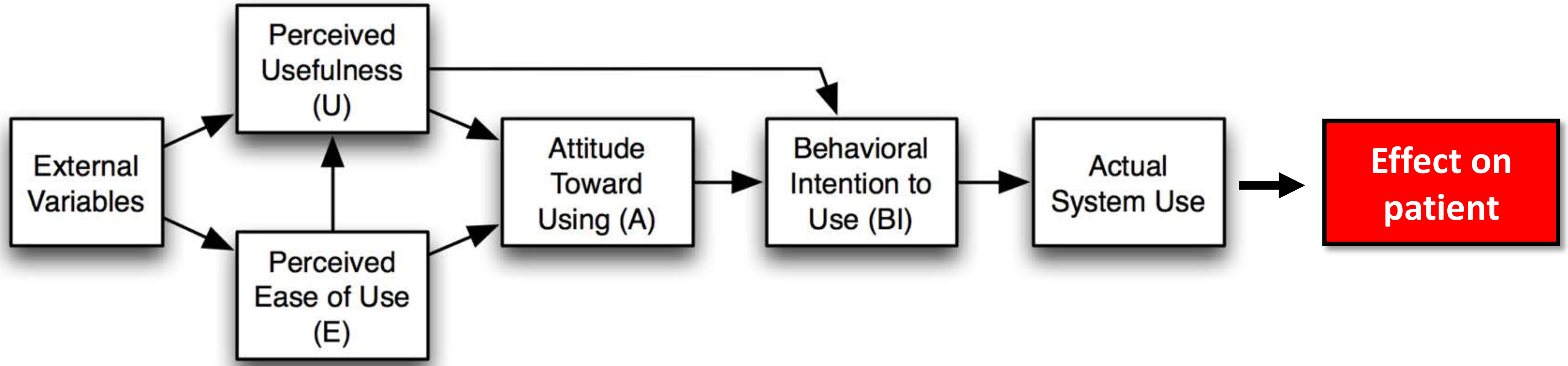


Development & deployment of AI tools into clinical practice



[Mamdani, ICME 2021]

The Technology Acceptance Model (TAM)

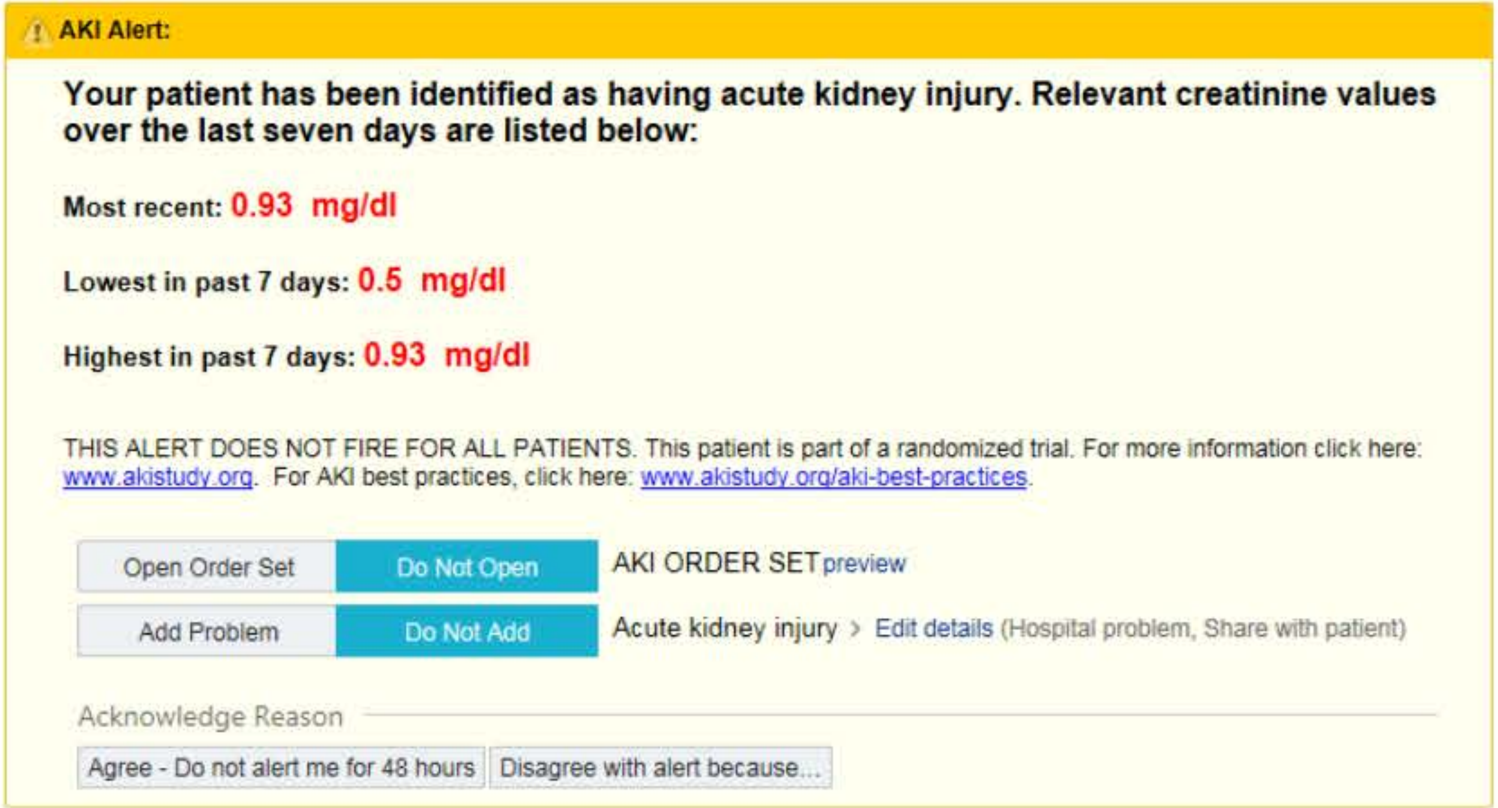


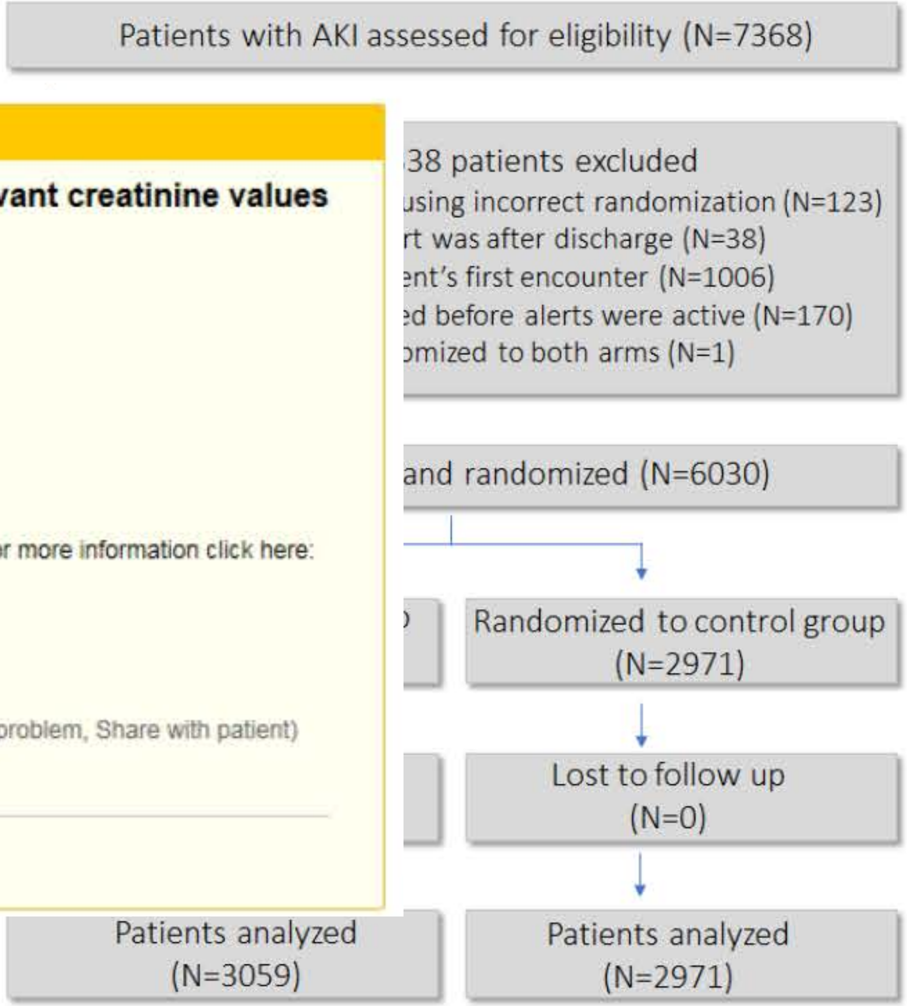
[Davies 1989 ; Holden J Biomed Inf 2010]

RESEARCH

Electronic health record alerts for acute kidney injury: multicenter, randomized clinical trial

F Perry Wilson,[1,2] Melissa Martin,[1,2] Yu Yamamoto,[1,2] Caitlin Partridge,[3] Erica Moreira,[3]
Tanima Arora,[1,2] Aditya Biswas,[1,2] Harold Feldman,[4] Amit X Garg,[5] Jason H Greenberg,[2,6]
Monique Hinchcliff,[7] Stephen Latham,[8] Fan Li,[9] Haiqun Lin,[10] Sherry G Mansour,[1,2]
Dennis G Moledina,[1,2] P
Jeffrey Testani,[13] Ugochu





[Jan 2021]

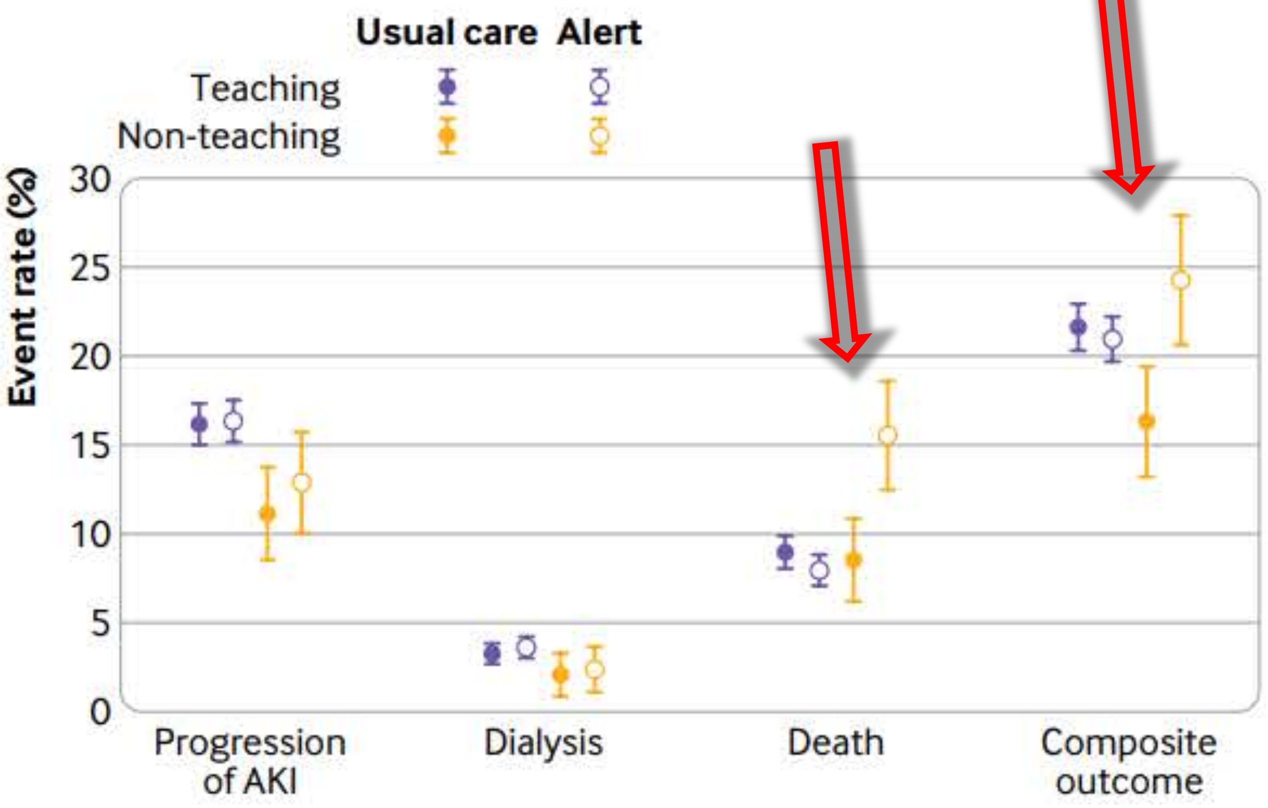
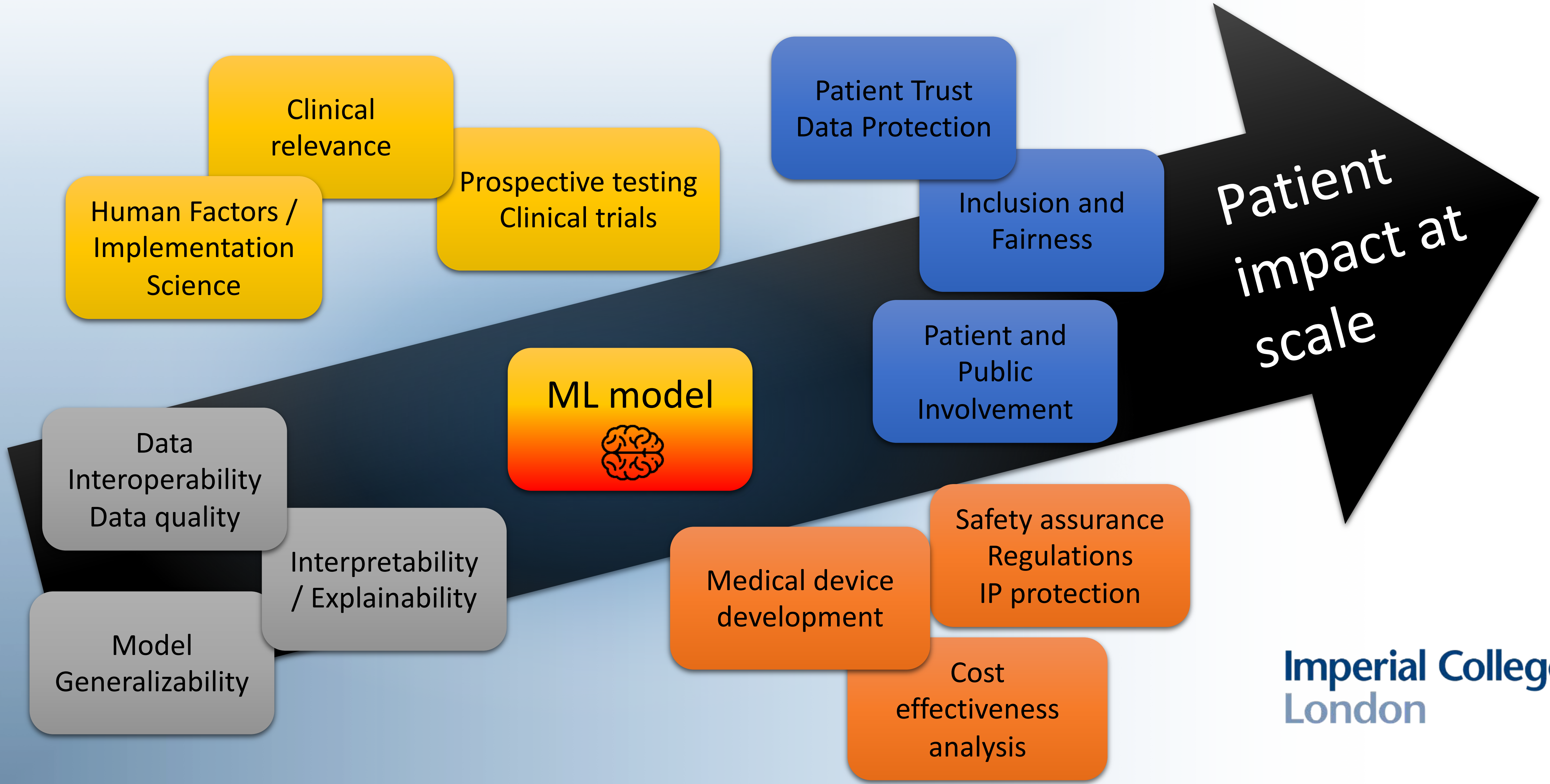


Fig 2 | Primary and secondary outcome events, stratified by hospital type. Error bars are 95% confidence intervals of the observed proportion of events. AKI=acute kidney injury

- **Higher risk of death** at 14 days in non-teaching hospitals with alerts (15.6% vs 8.6%, p=0.003)
- "We are left without a satisfying unifying explanation for the potential harm."

[Wilson BMJ 2021]

Machine learning is only a (small) piece of the puzzle



Imperial College London

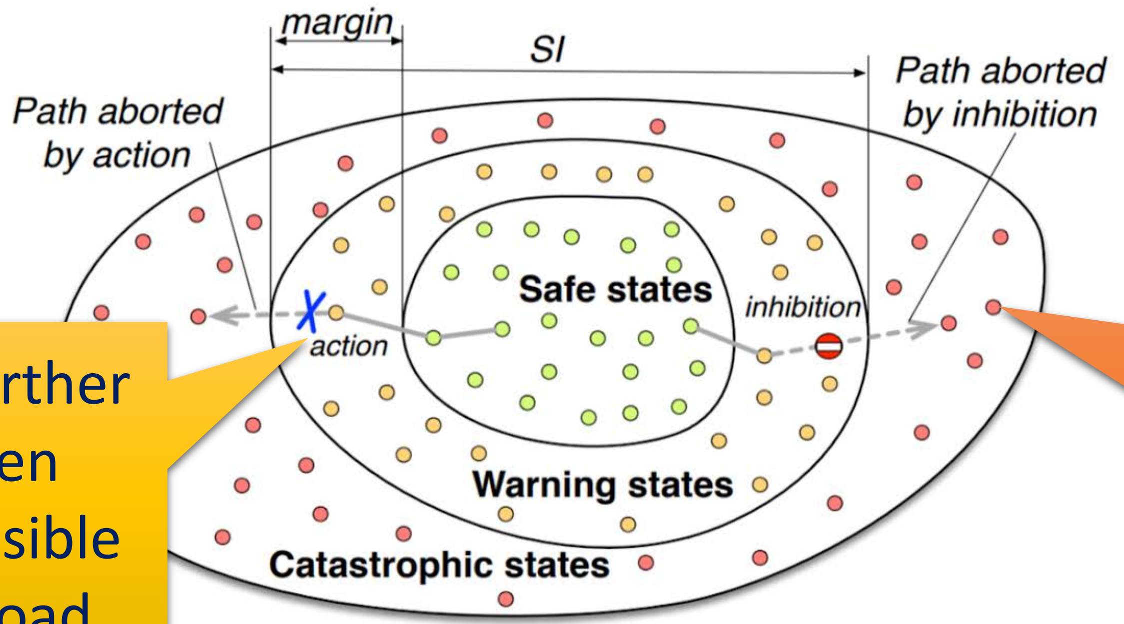
Safety Evaluation

- December 2019 – October 2022
- Co-PI: Prof Ibrahim Habli, Univ of York

ASSURING AUTONOMY
INTERNATIONAL PROGRAMME

UNIVERSITY of York

Safety Monitoring Framework (SMOF) for Autonomous Systems



Example: further fluids given despite possible fluid overload

Example: profound hypotension left untreated

Fig. 1. Partition of system states in catastrophic, warning and safe states.

https://hal.archives-ouvertes.fr/hal-01394139/file/revue9.pdf

Open access | Original research

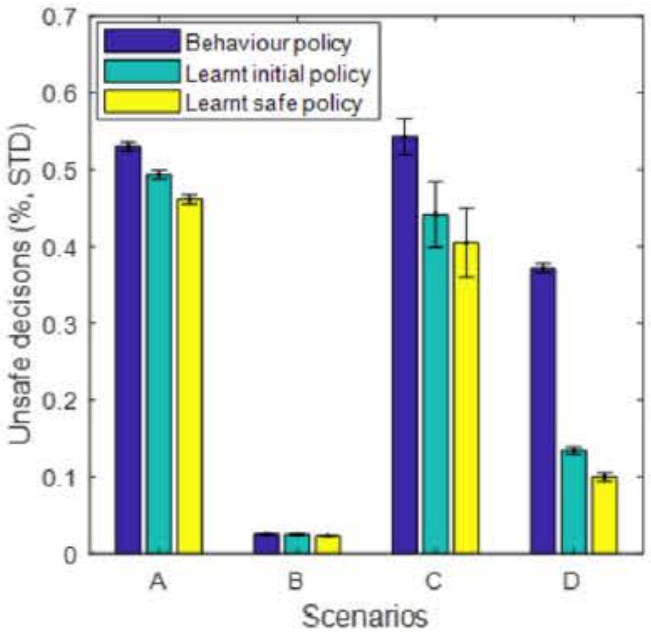
BMJ Health & Care Informatics

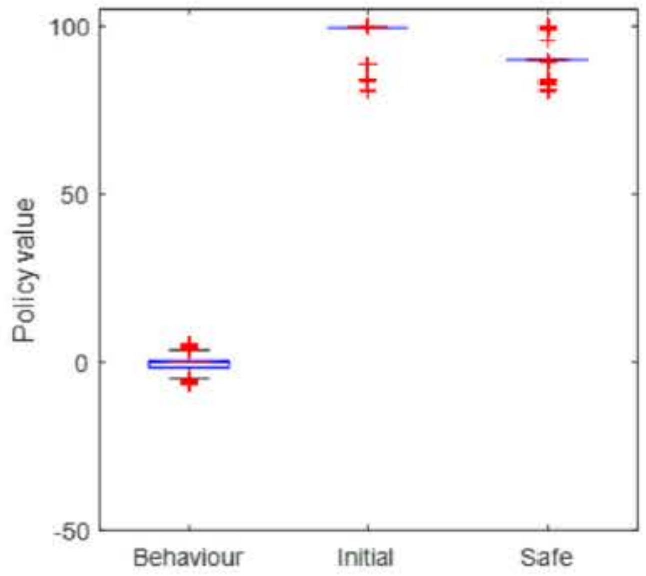
Assuring the safety of AI-based clinical decision support systems: a case study of the AI Clinician for sepsis treatment

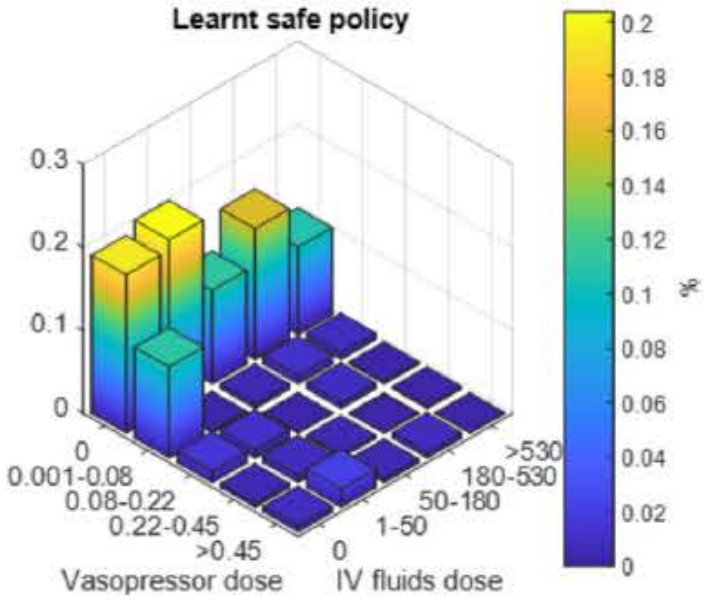
Paul Festor [1,2] Yan Jia [3,4] Anthony C Gordon [5] A Aldo Faisal [2,6]
Ibrahim Habli [3,7] Matthieu Komorowski [1,5]

2022

- We defined 4 unsafe decisions, e.g. hypotension left untreated, fluid overload + more fluids, etc.
- Composite penalty on 90-d mortality + unsafe decisions

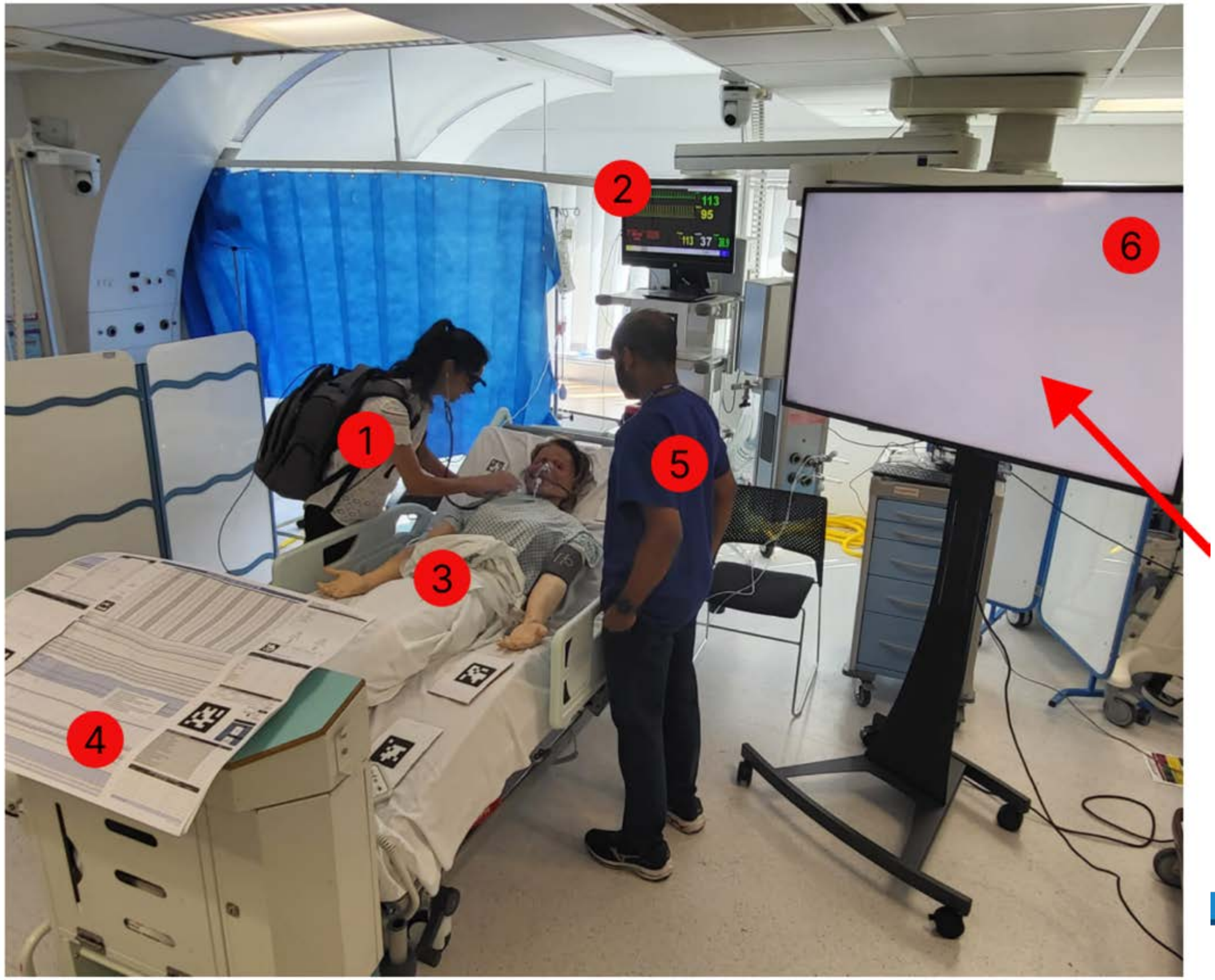






Imperial College London

AI Clinician safety evaluation



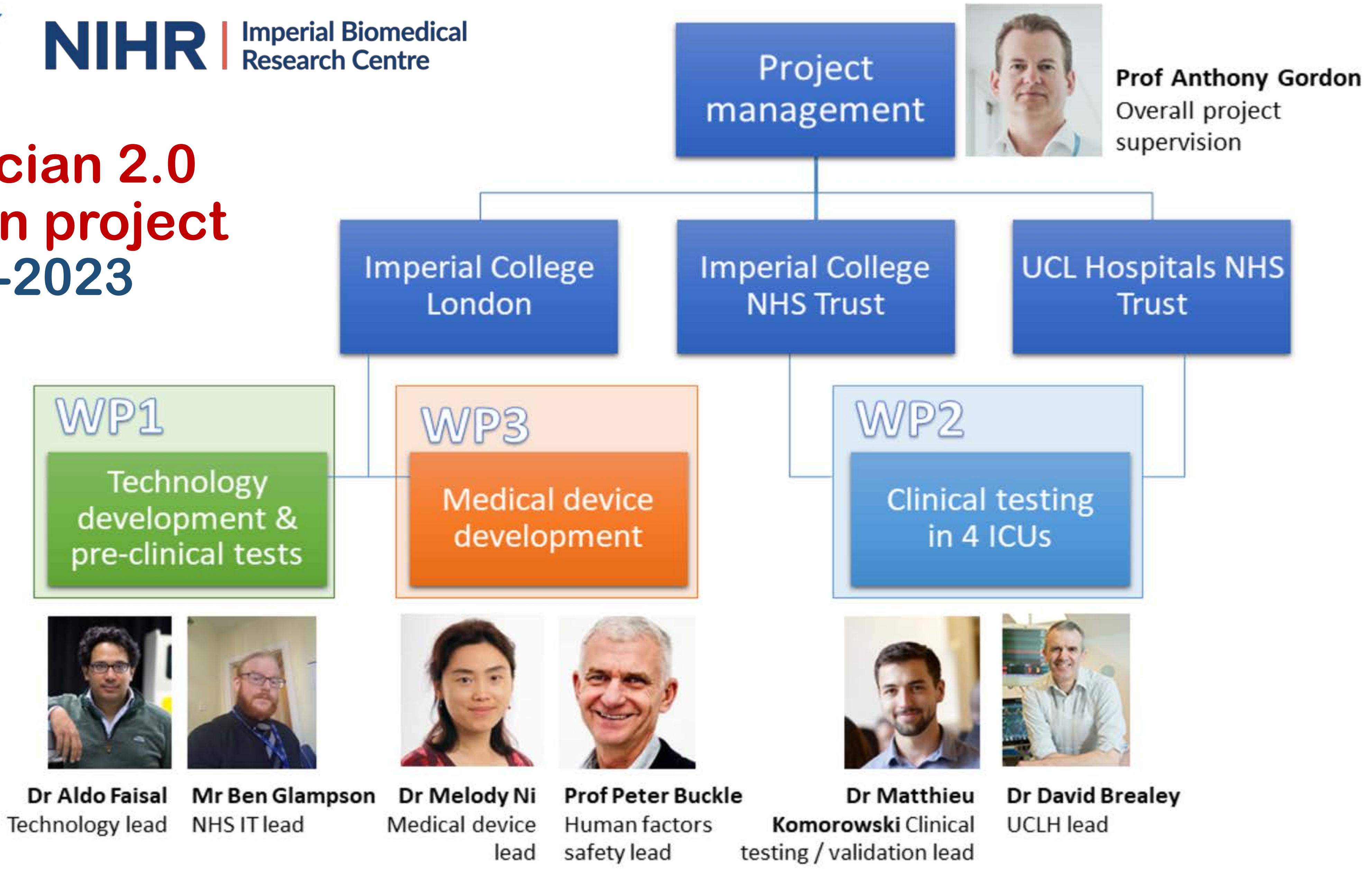
- Simulated ICU ward round of 6 patients with sepsis
- With AI Decision Support System
- 1/3 of AI suggestions voluntarily unsafe
- Eye tracking

(1) Subject
(2) Bedside monitor
(3) Patient mannequin
(4) ICU bedside information chart
(5) Bedside nurse
(6) AI screen.

[Credit: Myura Nagendran, Paul Festor]

NHSX
NIHR | Imperial Biomedical Research Centre

AI Clinician 2.0 validation project 2020-2023



Imperial College London

Early evaluation of the AI Clinician system for sepsis treatment

NHS
University College London Hospitals
NHS Foundation Trust

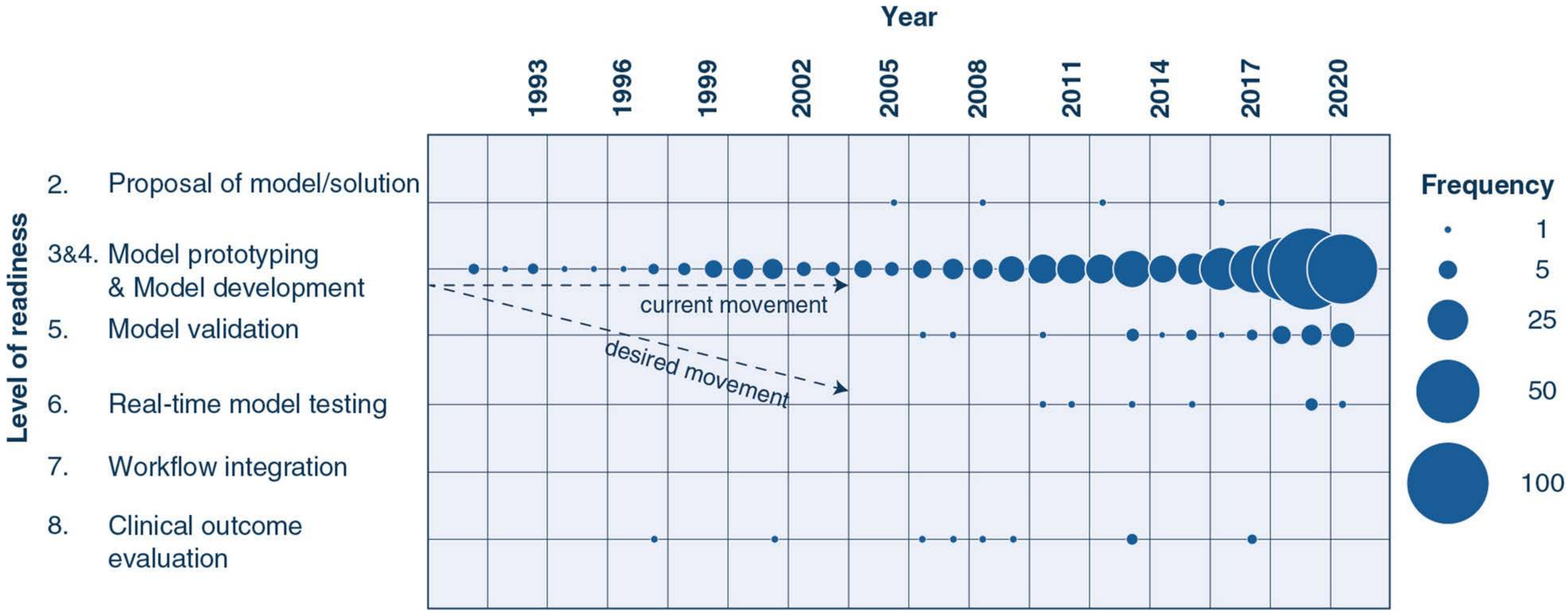
NHS
Imperial College Healthcare
NHS Trust

- XP1 (Oct-Dec 2022)
- “Shadow mode”
- Observational

- XP2 (Jan-June 2023)
- Pilot study at the bedside
- Observational

In 4 ICUs:
- Imperial x3
- UCLH

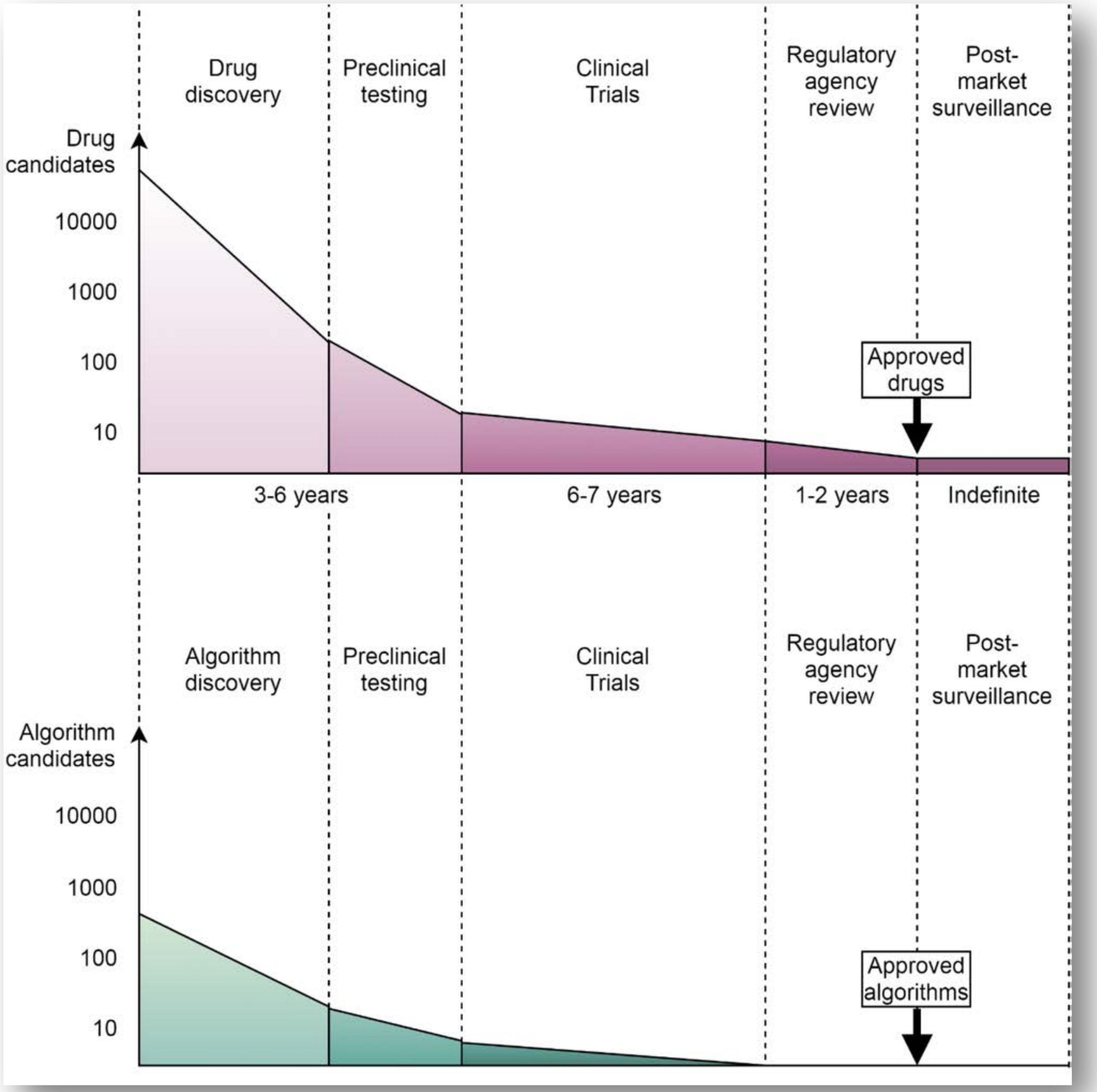
Level of readiness of AI Applications in the ICU



[van de Sande, ICME 2021]

Drugs →

AI systems? →



[Komorowski, ICME 2019]

Thank you

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[Sept 2021]

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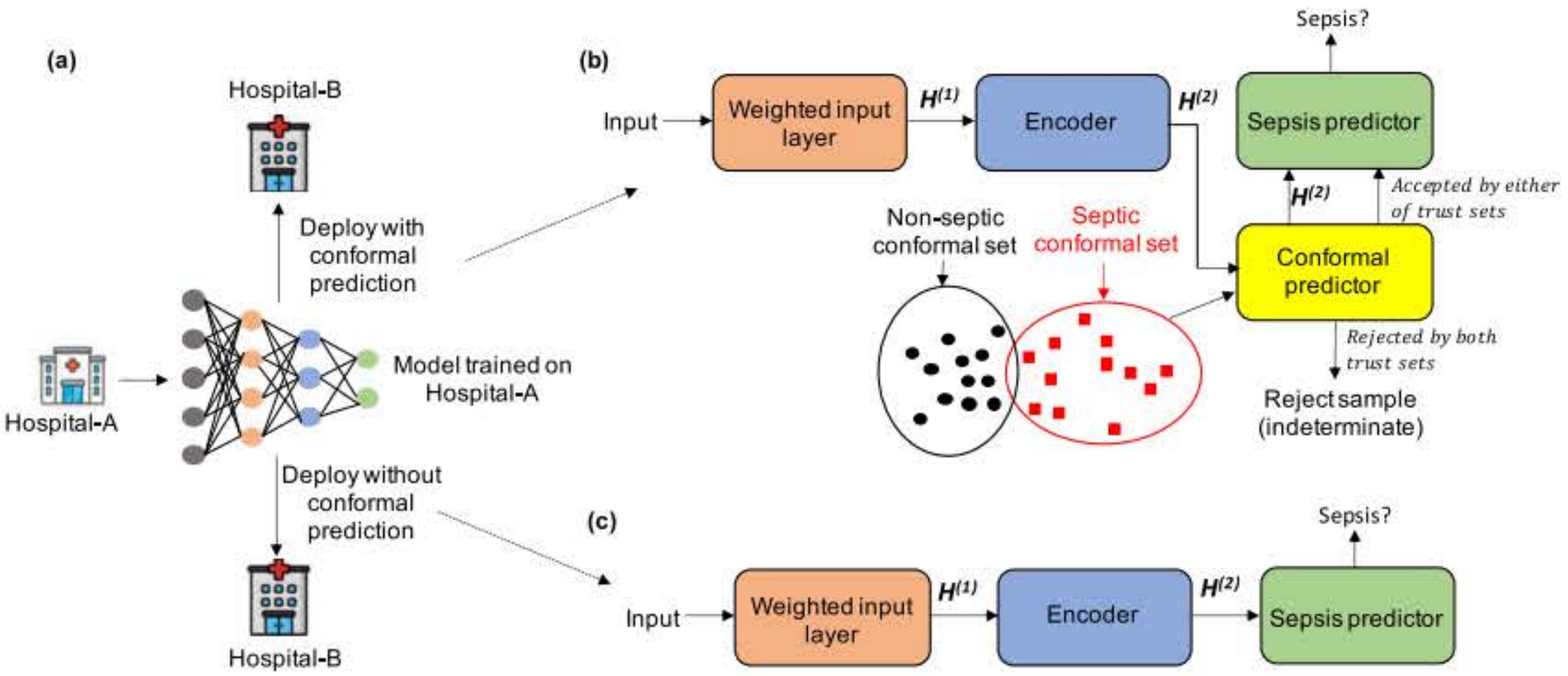
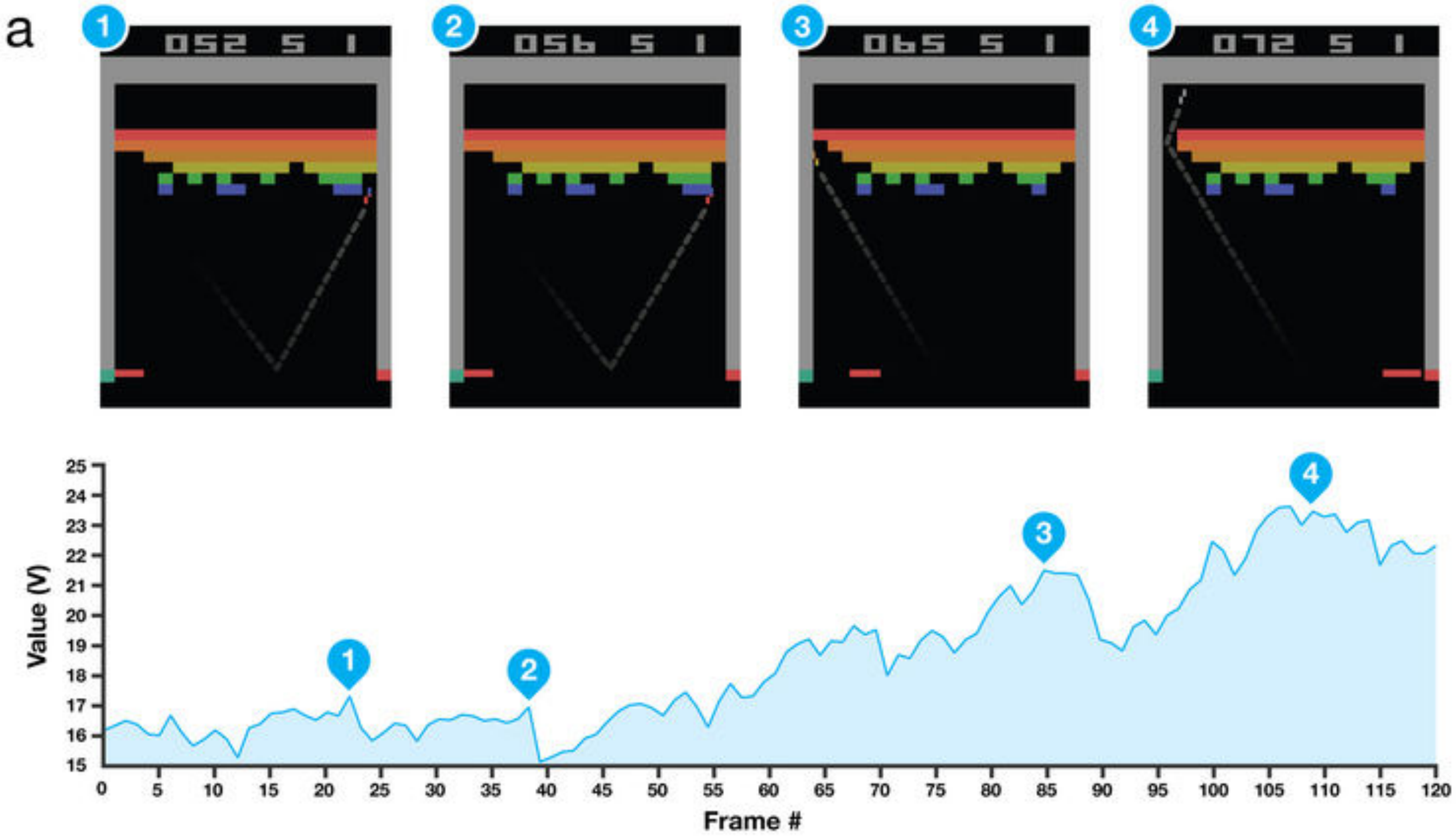
Artificial intelligence sepsis prediction algorithm learns to say "I don't know"

Supreeth P. Shashikumar[1]✉, Gabriel Wardi[2,3], Atul Malhotra[3] and Shamim Nemati[1]✉



"Pixel to Action" Reinforcement Learning



[Mnih Nature 2015]

Laï et al. J Transl Med (2020) 18:14
https://doi.org/10.1186/s12967-019-02204-y

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Translational Medicine

RESEARCH

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Perceptions of artificial intelligence in healthcare: findings from a qualitative survey study among actors in France

M.-C. Laï[1*], M. Brian[2] and M.-F. Mamzer[1]

Abstract

Background: Artificial intelligence (AI), with its seemingly limitless power, holds the promise to truly revolutionize patient healthcare. However, the discourse carried out in public does not always correlate with the actual impact. Thus, we aimed to obtain both an overview of how French health professionals perceive the arrival of AI in daily practice and the perception of the other actors involved in AI to have an overall understanding of this issue.

Methods: Forty French stakeholders with diverse backgrounds were interviewed in Paris between October 2017 and June 2018 and their contributions analyzed using the grounded theory method (GTM).

Results: The interviews showed that the various actors involved all see AI as a myth to be debunked. However, their views differed. French healthcare professionals, who are strategically placed in the adoption of AI tools, were focused on providing the best and safest care for their patients. Contrary to popular belief, they are not always seeing the use of these tools in their practice. For healthcare industrial partners, AI is a true breakthrough but legal difficulties to access individual health data could hamper its development. Institutional players are aware that they will have to play a significant role concerning the regulation of the use of these tools. From an external point of view, individuals without a conflict of interest have significant concerns about the sustainability of the balance between health, social justice, and freedom. Health researchers specialized in AI have a more pragmatic point of view and hope for a better transition from research to practice.

Conclusion: Although some hyperbole has taken over the discourse on AI in healthcare, diverse opinions and points of view have emerged among French stakeholders. The development of AI tools in healthcare will be satisfactory for everyone only by initiating a collaborative effort between all those involved. It is thus time to also consider the opinion of patients and, together, address the remaining questions, such as that of responsibility.