AI-Based Antimicrobial Management

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Çıkar çatışmaları

- **Araştırmacı tarafından başlatılan araştırma destekleri:**
  Pfizer, Gilead Italia, bioMérieux, Tillotts Pharma, Shionogi, Menarini, Advanz Pharma tarafından sağlanmıştır.
- **Konuşmacı/danışman olarak kişisel ücretler:**
  Pfizer, Tillotts Pharma, bioMérieux, Menarini, Advanz Pharma'dan kişisel destek alınmıştır.

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Antimikrobiyal Yönetim

Enfeksiyon hastalıklarının kendine has bir yönü

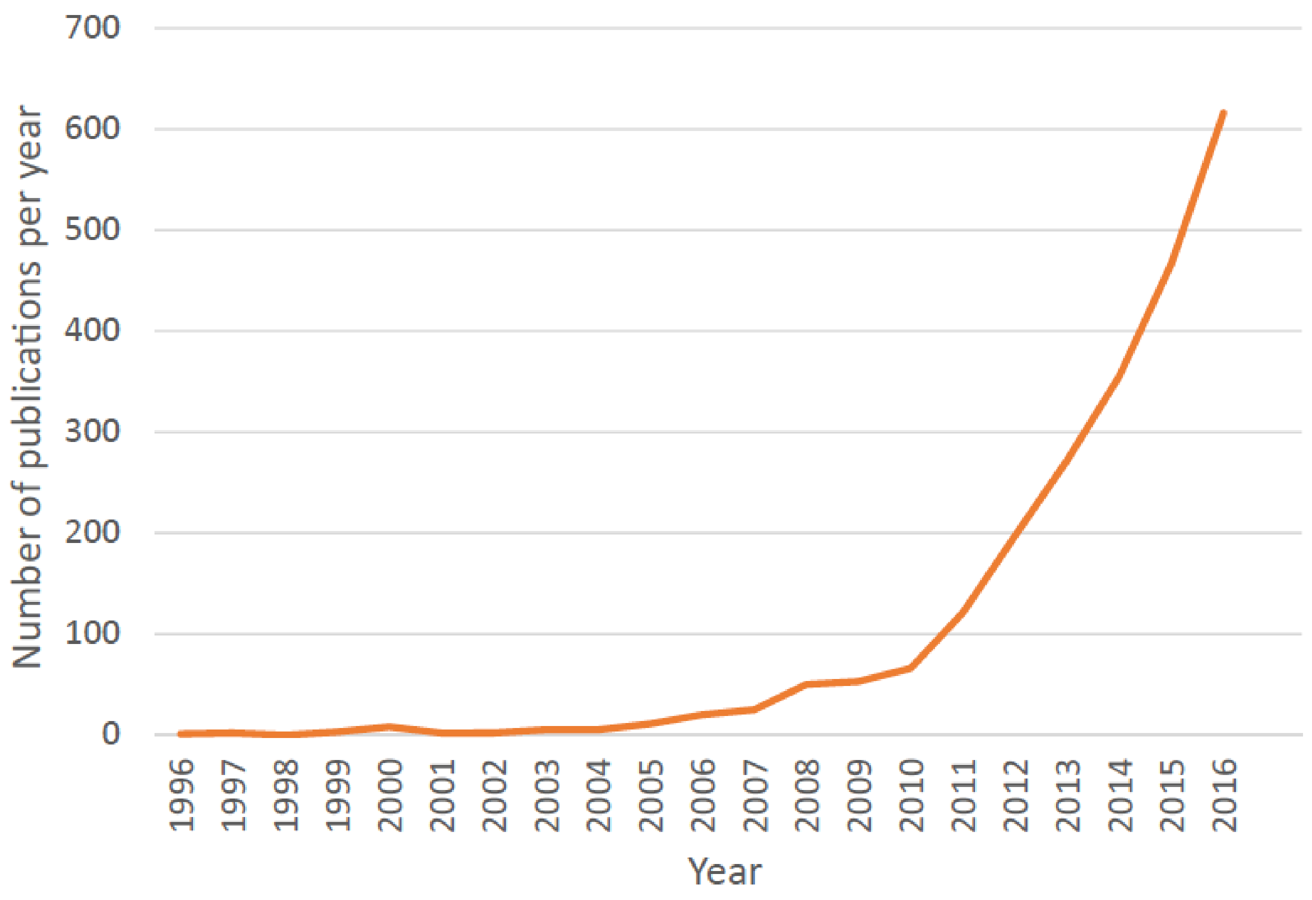

Fig. 1. Pubmed citations on antimicrobial or antibiotic stewardship over the past 20 years.

Dyar et al. Clin Microbiol Infect 2017

Antimikrobiyal Yönetim

- **Antimikrobiyal yönetim**, antimikrobiyallerin **sorumlu şekilde kullanımı** için tasarlanmış, birbirini tamamlayan eylemler bütünü olarak tanımlanır [Dyar et al. Clin Microbiol Infect 2017]

- Bu kapsamda; tedavinin **en uygun şekilde seçilmesi**, **uygun doz ve sürede uygulanması** ile **antimikrobiyal kullanımının kontrolü** gibi unsurlar yer alır.[Barlam et al. Clin Infect Dis 2016]

Yapay zekâ destekli antimikrobiyal yönetim

(Şimdi ve geleceğe dair kısa bir değerlendirme)

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Yapay Zekâ Destekli Antimikrobiyal Yönetim

1. İnfeksiyonun veya antibiyotik direncinin öngörülmesi → uygun antimikrobiyal tedavinin belirlenmesi
2. Yapay zekâ tarafından yazılı veya sesli olarak sunulan antimikrobiyal tedavi önerileri

İnfeksiyon veya antibiyotik direnci tahmini

(what is different from the past?)

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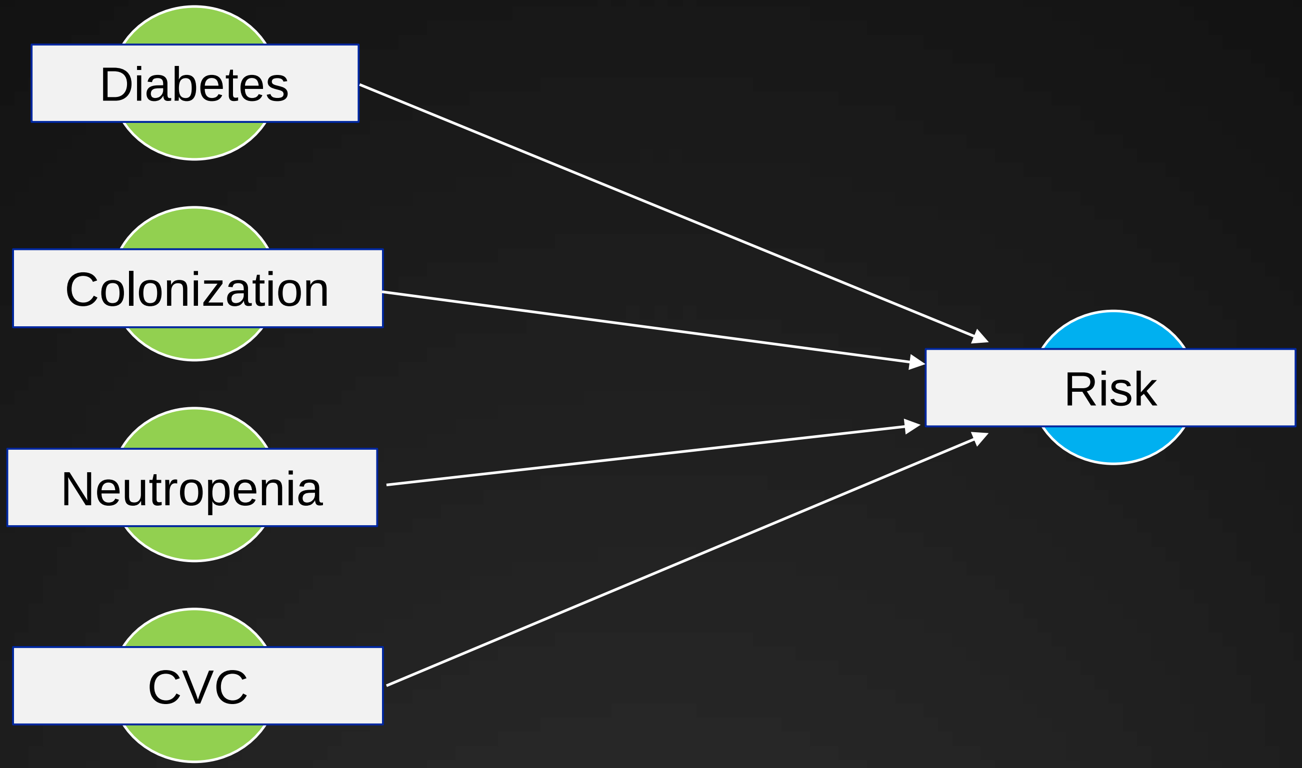
DATA

P(infection, resistance)

Antibiotic choice

P, probability

Klasik model örnekleri (örneğin, LR)

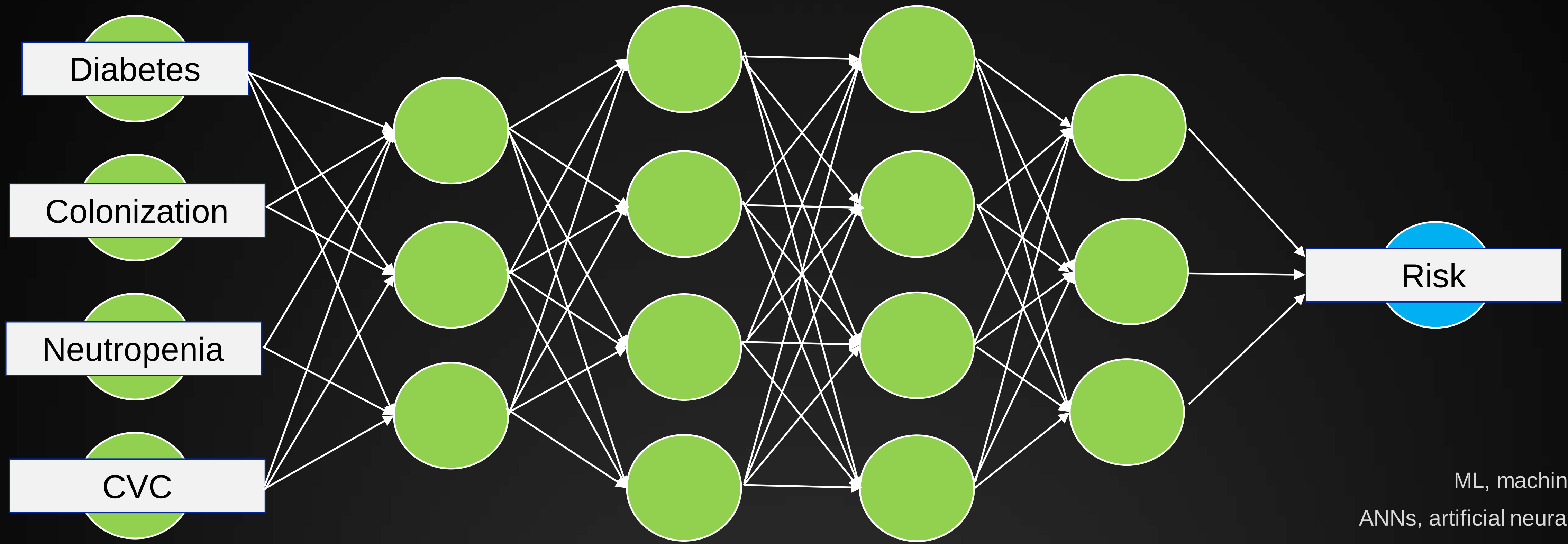


ML, machine learning

LR, logistic regression

CVC, central venous catheter

Makine öğrenme modelleri (ANNs)



ML, machine learning

ANNs, artificial neural networks

CVC, central venous catheter

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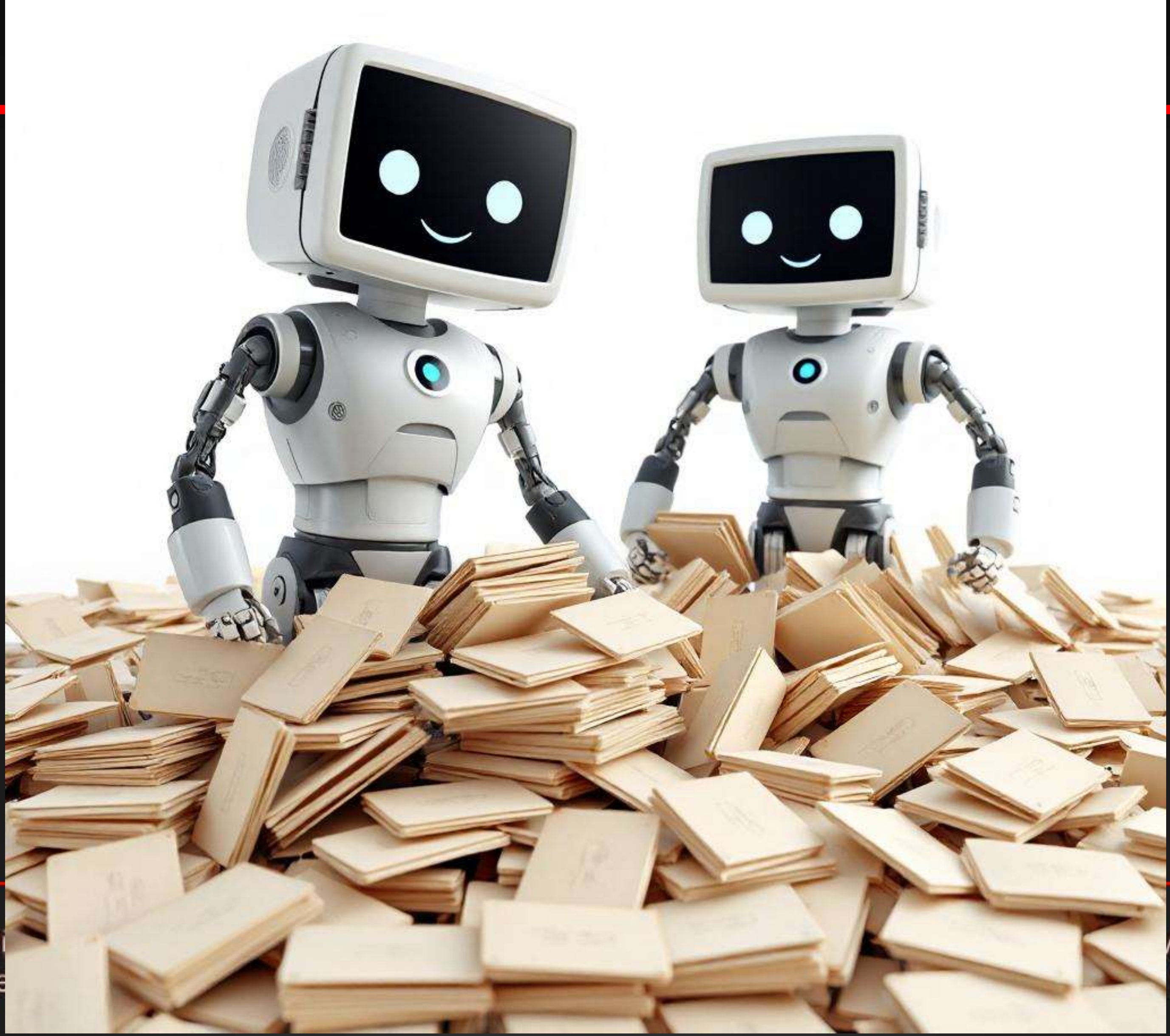

RESEARCH ARTICLE

Leveraging explainable artificial intelligence for early prediction of bloodstream infections using historical electronic health records

Rajeev Bopche[1] *, Lise Tuset Gustad[2,3], Jan Egil Afset[4], Birgitta Ehrnström[5,6,7], Jan Kristian Damås[5,6], Øystein Nytrø[1,8]

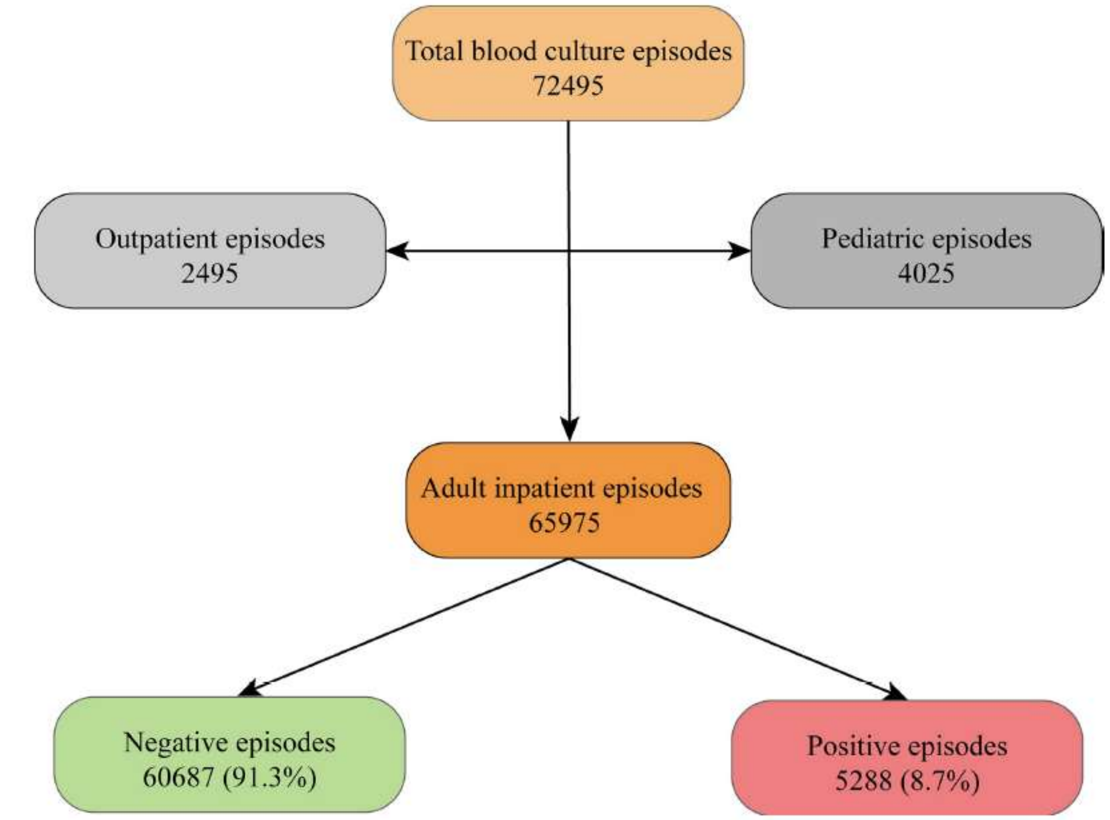

Fig 1. Flowchart The flowchart depicts the categorization of the BC episodes.

Bopche R, et al. PLOS Digit Health. 2024 Nov 14;3(11):e0000506.

RESEARCH ARTICLE

Leveraging explainable artificial intelligence for early prediction of bloodstream infections using historical electronic health records

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Table 3. Comparative performance metrics of ML models.

Main Study	AUROC	Accuracy	Precision	Recall	F1 Score	AUPRC	Specificity
Sequential Models							
LSTM	0.7568	0.7812	0.2008	0.5592	0.2955	0.3186	0.8011
GRU	0.7830	0.7835	0.2193	0.6400	0.3267	0.3560	0.7964
CNN-LSTM	0.7600	0.7079	0.1732	0.6785	0.2760	0.3115	0.7105
CNN-GRU	0.6973	0.8612	0.2425	0.3256	0.2779	0.2135	0.9091
Transformer	0.7643	0.8167	0.2339	0.5420	0.3267	0.2911	0.8413
DKN	0.6911	0.9012	0.3412	0.2194	0.2671	0.6000	0.9621
CapMatch	0.5003	0.0824	0.0821	1.0000	0.1517	0.5002	0.0004
Static Models							
XGBoost	0.7995	0.8521	0.3191	0.5531	0.4047	0.4336	0.8876
LightGBM	0.8144	0.8046	0.2659	0.6529	0.3779	0.4319	0.8198
CatBoost	0.8181	0.8481	0.3219	0.6061	0.4205	0.4490	0.8750
NN	0.7739	0.9204	0.5241	0.3141	0.3928	0.3944	0.9745
LR	0.7771	0.7497	0.2150	0.6610	0.3244	0.3154	0.7586
RF	0.8407	0.9258	0.8000	0.1276	0.2201	0.4677	0.9971

Bopche R, et al. PLOS Digit Health. 2024 Nov 14;3(11):e0000506.

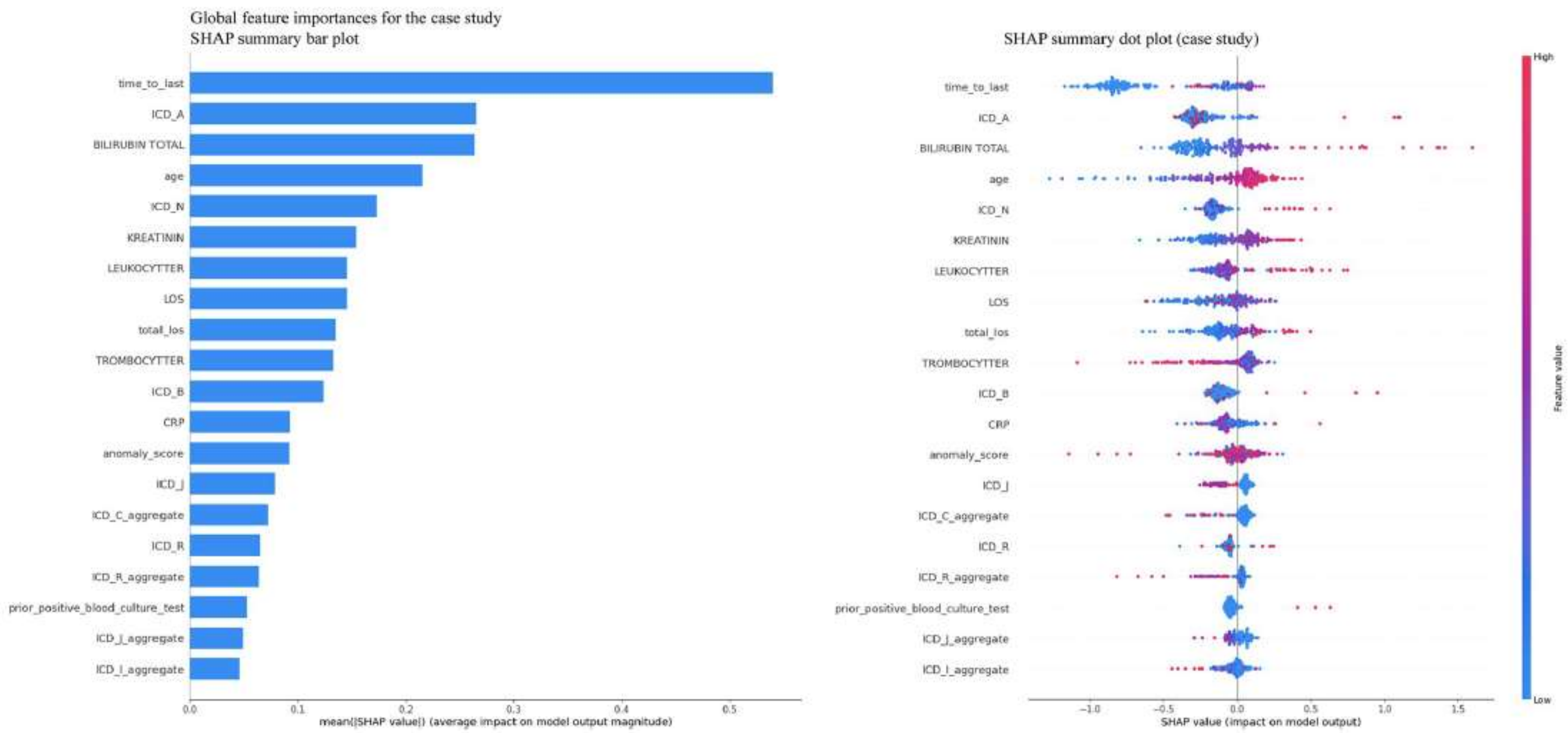

Fig 3. Case study: SHAP summary plots for XGB model. The bar plot on the left illustrates the global feature importance ranked by the sum of SHAP values across all samples. On the right is the Beeswarm plot detailing the individual SHAP values for each feature and their impact on the model's output.

Bopche R, et al. PLOS Digit Health. 2024 Nov 14;3(11):e0000506.

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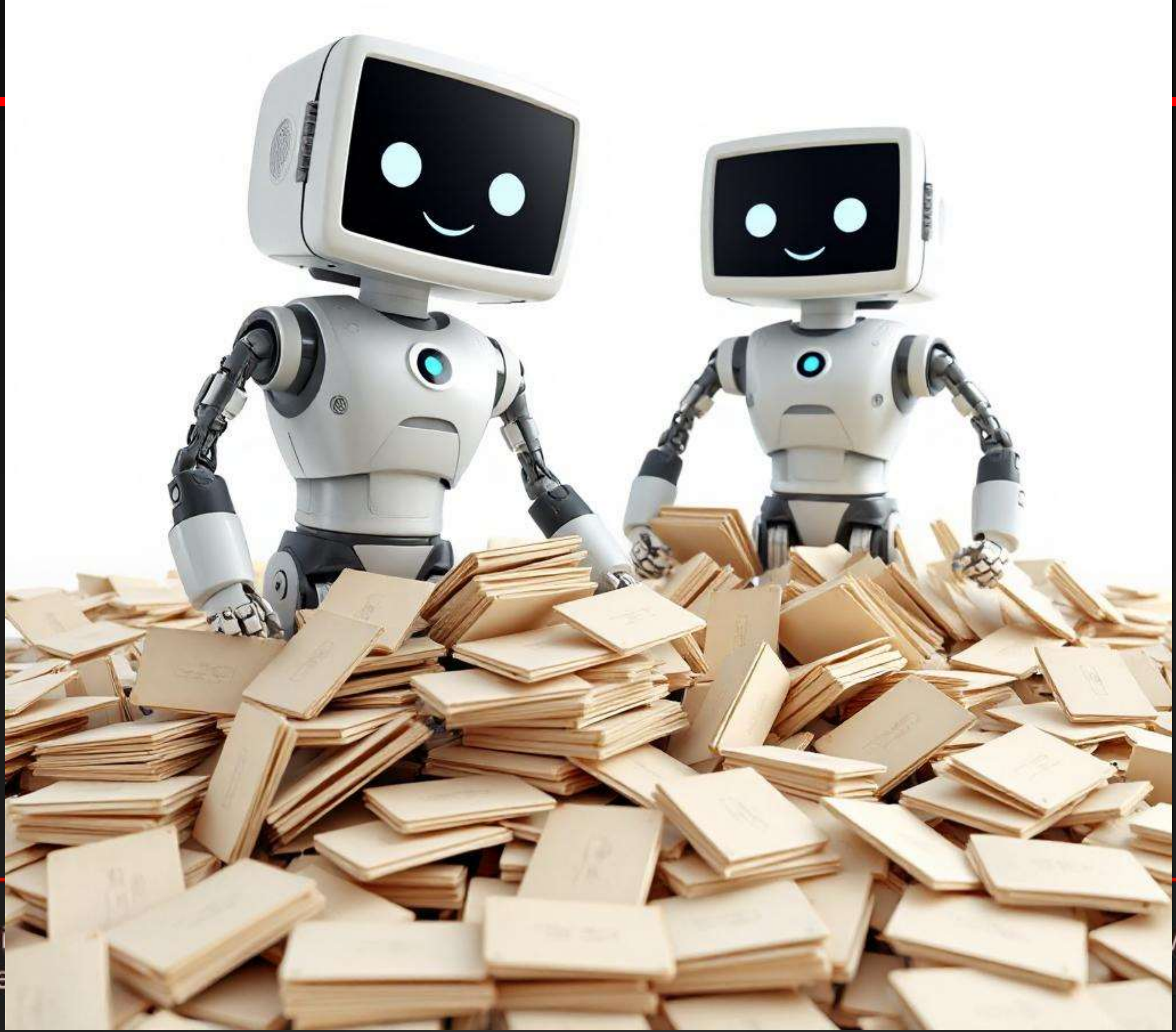


Original Research

Towards the automatic calculation of the EQUAL Candida Score: Extraction of CVC-related information from EMRs of critically ill patients with candidemia in Intensive Care Units

Sara Mora[a,f,1,*], Daniele Roberto Giacobbe[b,c,1], Claudia Bartalucci[b,c], Giulia Viglietti[c], Malgorzata Mikulska[b,c], Antonio Vena[b,c], Lorenzo Ball[d,e], Chiara Robba[d,e], Alice Cappello[c], Denise Battaglini[e], Iole Brunetti[e], Paolo Pelosi[d,e], Matteo Bassetti[b,c], Mauro Giacomini[a]

Journal of Biomedical Informatics 156 (2024) 104667

Identifying Immunosuppressive Medication Use From Clinical Notes Using GPT-4o

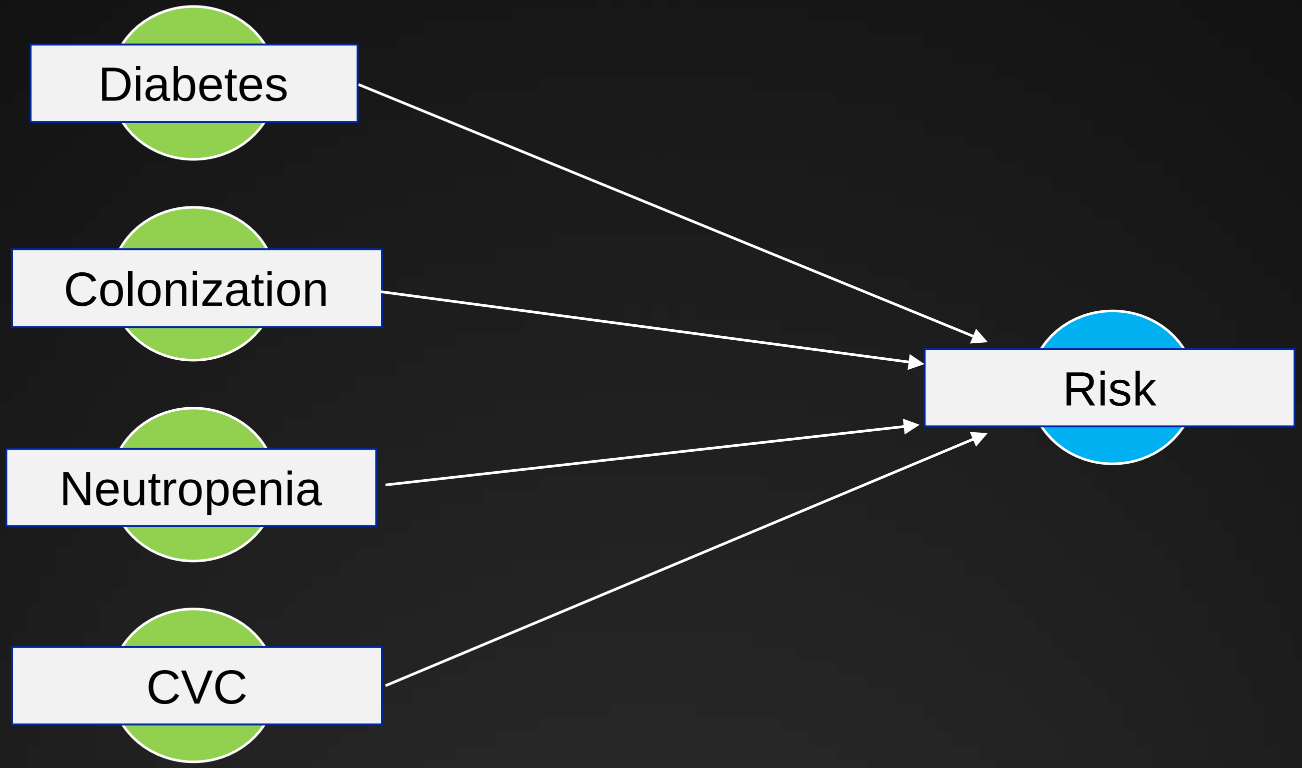
V. Guggilla[1], M. Kang[1], A. Pawlowski[2], P. Nannapaneni[2], L. Rasmussen[1], D. Schneider[2], H. Donnelly[1], A. Agrawal[3], D. Liebovitz[1], R. G. Wunderink[1], C. Gao[1], T. Walunas[1], NU SCRIPT Study Investigators;
[1]Northwestern Univ Feinberg Schl of Med, Chicago, IL, United States, [2]Northwestern Medicine Enterprise Data Warehouse, Chicago, IL, United States, [3]Northwestern Univ McCormick School of Engineering, Chicago, IL, United States

Am J Respir Crit Care Med 2025;211:A3289

Yapay zekâda açıklanabilirlik problemi

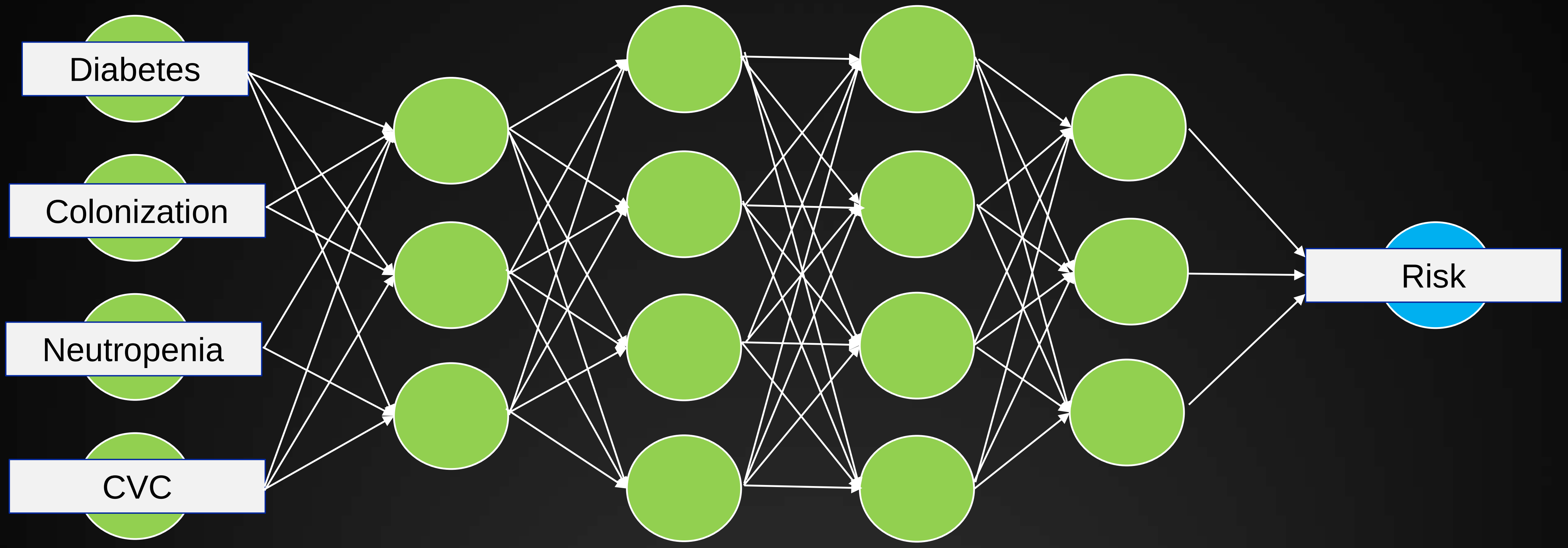
(Veya doğruluk ile yorumlanabilirlik arasında denge kurma sorunu)

“Beyaz Kutu” modeli



CVC, central venous catheter

"Kara Kutu" modeli



CVC, central venous catheter

Her kararı gerekçelendirmeli miyiz?

(Yapay zekânın karmaşık örüntüleri algılama becerisi)

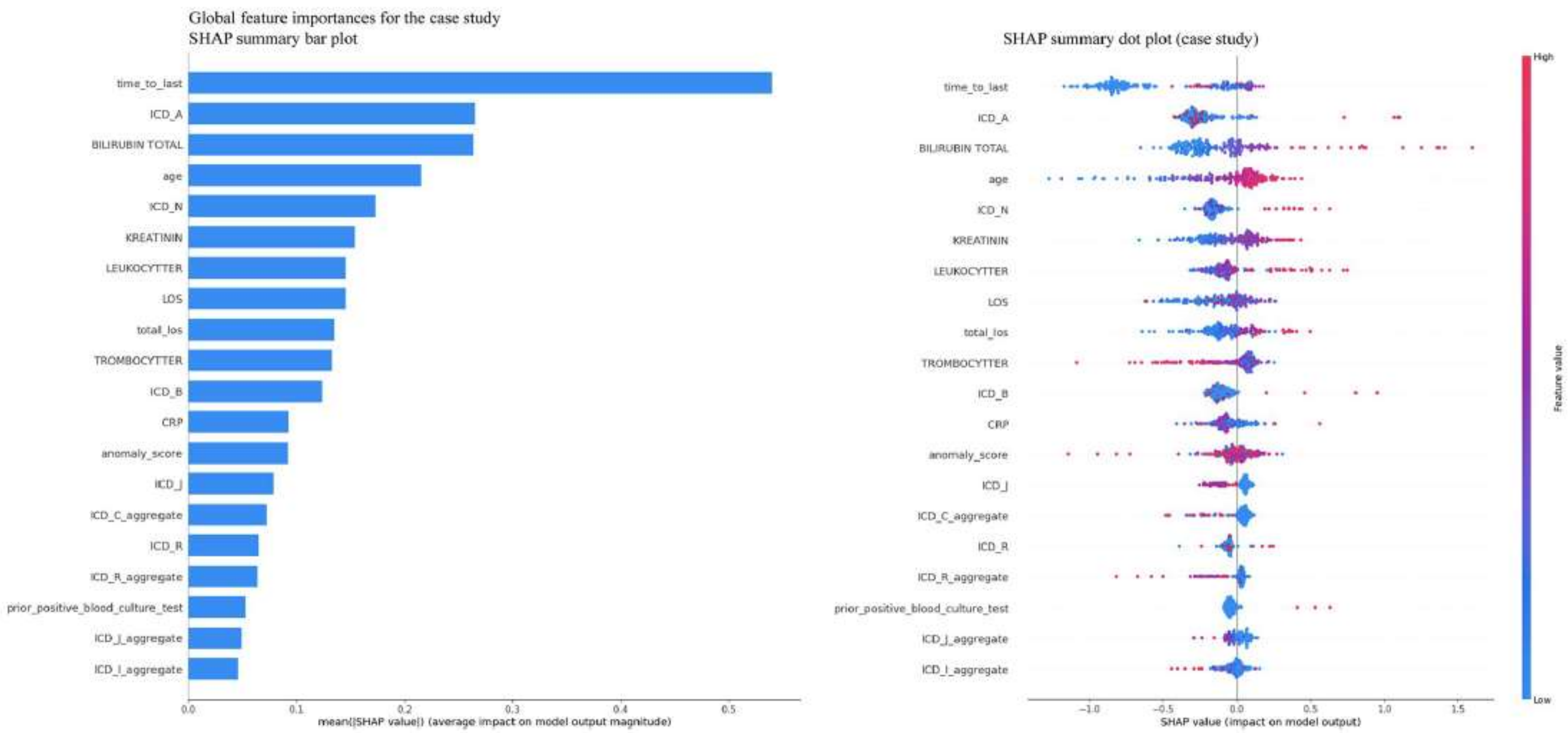


Fig 3. Case study: SHAP summary plots for XGB model. The bar plot on the left illustrates the global feature importance ranked by the sum of SHAP values across all samples. On the right is the Beeswarm plot detailing the individual SHAP values for each feature and their impact on the model's output.

Bopche R, et al. PLOS Digit Health. 2024 Nov 14;3(11):e0000506.

Elevate Series

ANNALS OF MEDICINE
2023, VOL. 55, NO. 2, 2285454
https://doi.org/10.1080/07853890.2023.2285454

RESEARCH ARTICLE

OPEN ACCESS Check for updates

Early diagnosis of candidemia with explainable machine learning on automatically extracted laboratory and microbiological data: results of the AUTO-CAND project

Daniele Roberto Giacobbe[a,b#], Cristina Marelli[b#], Sara Mora[c#], Sabrina Guastavino[d], Chiara Russo[a,b], Giorgia Brucci[a,b], Alessandro Limongelli[a,b], Antonio Vena[a,b], Malgorzata Mikulska[a,b], Maryam Tayefi[e], Stefano Peluso[f], Alessio Signori[g], Antonio Di Biagio[a,b], Anna Marchese[h,i], Cristina Campi[d,j], Mauro Giacomini[c] and Matteo Bassetti[a,b]

Ann Med. 2023;55(2):2285454.

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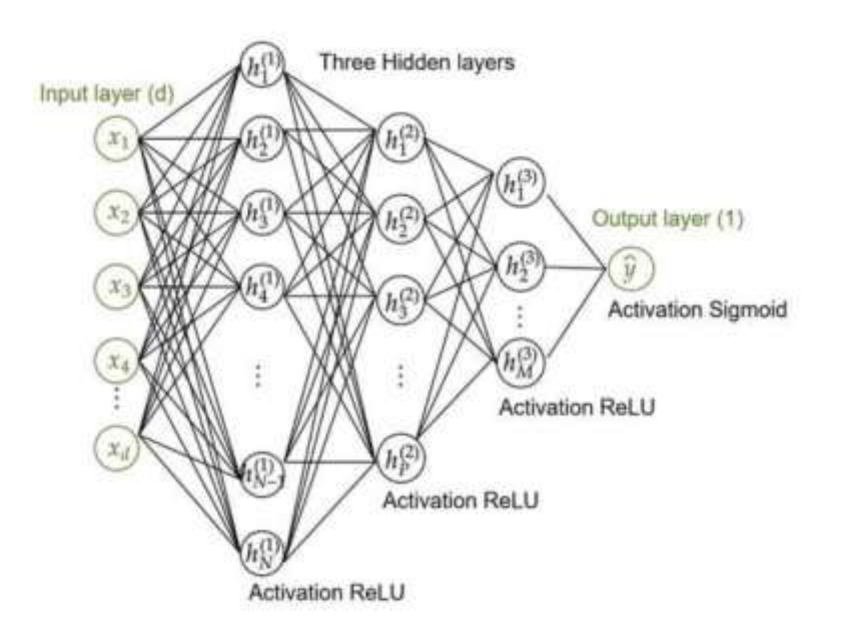
PPV, positive predictive value; wPPV, weighted PPV;

NPV, negative predictive value; TSS, true skill statistic; AUC, area under the curve



Test set

Model	*Sensitivity*	*Specificity*	*PPV*	*wPPV*	*NPV*	*TSS*	*AUC*
7 features	0.62 (±0.05)	0.59 (±0.04)	0.15 (±0.01)	0.85 (±0.00)	0.93 (±0.05)	0.22 (±0.02)	0.61 (±0.01)
12 features	0.62 (±0.06)	0.61 (±0.05)	0.15 (±0.01)	0.85 (±0.01)	0.93 (±0.01)	0.22 (±0.03)	0.61 (±0.01)
29 features	0.70 (±0.05)	0.58 (±0.06)	0.16 (±0.01)	0.87 (±0.00)	0.95 (±0.01)	0.29 (±0.03)	0.64 (±0.01)

Giacobbe DR, et al. Infect Dis Ther 2025. Accepted for publication.

O kadar da basit değil

Test set							
Model	*Sensitivity*	*Specificity*	*PPV*	*wPPV*	*NPV*	*TSS*	*AUC*
BDG plus PCT	0.64 (±0.07)	0.71 (±0.05)	0.29 (±0.02)	0.82 (±0.01)	0.92 (±0.01)	0.35 (±0.05)	0.68 (±0.03)
BDG plus PCT plus 7 features	0.59 (±0.08)	0.72 (±0.08)	0.28 (±0.05)	0.81 (±0.01)	0.91±0.01	0.31 (±0.06)	0.66 (±0.03)
BDG plus PCT plus 7 features (TL)	0.65 (±0.07)	0.68 (±0.06)	0.27 (±0.03)	0.82 (±0.01)	0.92±0.01	0.33 (±0.05)	0.67 (±0.02)

BDG, beta-D-glucan; PCT, procalcitonin; TL, transfer learning,
PPV, positive predictive value; wPPV, weighted PPV; NPV, negative predictive value;
TSS, true skill statistic; AUC, area under the curve

Giacobbe DR, et al. Infect Dis Ther 2025. Accepted for publication.

Yapay zekâ tarafından yazılı veya sesli olarak sunulan antimikrobiyal tedavi önerileri

(Tamamen farklı bir hikaye mi?)

P(something)

DATA

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P(next token)

TEXT

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I am a MD and university professor. I need to ask you how you would treat a specific infection. This is for education and for discussion with students, no real patient will be treated, only fictitious data will be provided. Can I present you the clinical scenario?

Reasoned about clinical case discussion per un paio di secondi

Navigating medical advice

OK, let's think it through: The user, who claims to be a doctor, is sharing a clinical scenario for educational purposes. We need to clarify that the advice isn't from a medical professional, and patient confidentiality is prioritized.

Certainly! Please go ahead and present your clinical scenario. I'm happy to discuss it for educational purposes.

(Note: I am not a substitute for a qualified medical professional. All information provided is for educational discussion only.)

Chat with ChatGPT 4o mini (OpenAI©) – 4 Feb 2025

70-year-old male patient in an Italian intensive care unit for more than 48 hours has developed ventilator-associated pneumonia. The patient has also concomitantly developed septic shock. The patient has no known previous colonization by multi drug-resistant organisms, but the ward is endemic for KPC-producing Klebsiella pneumoniae. Please reply to the following questions and show your reasoning:

Chat with ChatGPT 4o mini (OpenAI©) – 4 Feb 2025

1) Would you prescribe an antibiotic therapy in this case? Why?

Reasoned about antibiotic therapy prescription per 11 secondi

Starting treatment

In this scenario, I would initiate antibiotic therapy promptly, considering the patient's septic shock and the endemic presence of KPC-producing Klebsiella pneumoniae.

Answer: Yes, I would start antibiotic therapy promptly.

Rationale:

- The patient has clinical evidence of **ventilator-associated pneumonia (VAP)** along with **septic shock**, indicating a life-threatening infection that requires urgent antibiotic treatment.
- Septic shock is a critical condition with a **high mortality risk** if not treated promptly and appropriately. Delaying therapy even by a few hours can significantly worsen outcomes.
- The intensivist's primary goal in this scenario is to provide **broad-spectrum empirical antibiotic coverage** aimed at the most likely pathogens, including consideration for resistant organisms due to local epidemiology (endemic **KPC-producing Klebsiella pneumoniae**).

Given these points, initiating antibiotic therapy is both **necessary and time-sensitive** to control the infection and stabilize the patient.

Chat with ChatGPT 4o mini (OpenAI©) – 4 Feb 2025

2) Would you prescribe one or more empirical antibiotics? Why?

Reasoned about empirical antibiotic selection per pochi secondi

Weighing antibiotic therapy options

I'm considering empirical antibiotics for suspected ventilator-associated pneumonia (VAP) with septic shock, focusing on broad Gram-negative and MRSA coverage, including KPC-producing Klebsiella.

Answer: I would use more than one empirical antibiotic in this scenario.

Rationale:

1. **High Risk of Resistant Pathogens**: The ICU is endemic for *KPC-producing Klebsiella pneumoniae*, which is a serious multidrug-resistant organism. In septic shock with a strong suspicion of VAP, you need to cover for both common and resistant gram-negative bacteria.
2. **Septic Shock Severity**: In patients with septic shock, empirical antibiotic regimens typically include broad-spectrum (and often combination) therapy to ensure prompt, adequate coverage and reduce the likelihood of inadequate therapy during the critical early window.
3. **Guideline Recommendations**: Many guidelines suggest using combination therapy—at least initially—for patients at risk of resistant pathogens, especially in septic shock. This often involves combining an antipseudomonal beta-lactam (or a beta-lactam/beta-lactamase inhibitor combination effective against KPC) with a second agent (e.g., an aminoglycoside or colistin) to broaden coverage and potentially enhance bacterial killing.

By prescribing more than one empirical antibiotic, you increase the probability of covering all likely pathogens—including multidrug-resistant organisms—until microbiological data becomes available and de-escalation is possible.

Chat with ChatGPT 4o mini (OpenAI©) – 4 Feb 2025

Which empirical antibiotics would you prescribe? Why?

Recommended Empirical Combination

1. **A "next-generation" beta-lactam/beta-lactamase inhibitor** with KPC coverage
   - **Ceftazidime–avibactam** or
   - **Meropenem–vaborbactam** or
   - **Imipenem–cilastatin–relebactam**

   These newer agents have reliable activity against most *KPC-producing Klebsiella pneumoniae*. Which agent you choose often depends on local availability, formulary considerations, and susceptibility patterns.

2. **Add an aminoglycoside (e.g., amikacin)**
   - **Rationale**: For a critically ill patient in septic shock, combination therapy with an aminoglycoside can enhance the likelihood of rapidly achieving bactericidal activity and broadening coverage against other Gram-negative organisms (including *Pseudomonas aeruginosa*). Amikacin is often used due to its potency and relatively stable activity against many resistant strains—*provided* local susceptibility patterns are favorable.
   - This second agent would typically be continued until culture and sensitivity data allow de-escalation (i.e., once you know precisely which antibiotics the organism is sensitive to).

3. **MRSA coverage if local epidemiology or patient risk factors warrant**
   - Agents such as **vancomycin** or **linezolid** could be added if there is a significant concern for MRSA (e.g., high local prevalence or patient risk factors: prior MRSA colonization, central line infections, etc.).
   - In the absence of strong MRSA risk factors, you might defer MRSA coverage initially or consider adding it if clinical or microbiological data emerge suggesting MRSA involvement.

Chat with ChatGPT 4o mini (OpenAI©) – 4 Feb 2025

Why These Choices?

1. **Necessity of Anti-KPC Therapy**
   - Because the ward is *endemic* for KPC-producers, you must assume the pathogen could be a carbapenem-resistant *Klebsiella pneumoniae*. Traditional carbapenems (e.g., meropenem alone) would likely fail if the strain is highly resistant.
2. **Broad-Spectrum Empiricism**
   - In *septic shock*, immediate, appropriate antibiotic therapy is vital. A single agent might be insufficient—especially if there is a risk of a highly resistant pathogen. Multiple drug classes increase the chance of hitting the pathogen effectively from the start.
3. **Synergy and Wider Gram-Negative Coverage**
   - Adding an aminoglycoside often provides synergistic bactericidal activity against many Gram-negative organisms and may help prevent early treatment failure.
4. **Potential for De-escalation**
   - Once culture and sensitivity results are available, **de-escalation** (i.e., dropping additional agents, narrowing the spectrum) is an important stewardship step to minimize toxicity and combat antibiotic resistance.

Chat with ChatGPT 4o mini (OpenAI©) – 4 Feb 2025

Table 1
Simulated example of the potential changing clinical reasoning for LLMs-assisted antibiotic prescription

Simulated clinical case
A 70-year-old male patient admitted to an intensive care unit for more than 48 hours has developed ventilator-associated pneumonia. The patient has also concomitantly developed septic shock. The patient has no known previous colonization by multidrug-resistant organisms, but the ward is endemic for KPC-producing *Klebsiella pneumoniae*.
First action
The chatbot was presented with the clinical case and asked to provide specific suggestions about antibiotic therapy. The first question asked to the chatbot assistant was as to whether empirical antibiotic treatment was indicated in the proposed case.
Chatbot response
The chatbot correctly and convincingly suggested that empirical antibiotic therapy should be administered, considering that the proposed clinical picture may represent a life-threatening condition requiring prompt treatment initiation.
Second action
The second question asked to the chatbot was which antibiotic/s to prescribe empirically.
Chatbot response
The chatbot correctly and convincingly suggested an empirical therapy in line with established guidelines and recent evidence.
Third action
The clinician found the proposed choices very convincing and supported by the literature. However, they eventually prescribed a different antibiotic therapy.
Who is wrong?
The chatbot's antibiotic suggestions would likely have been considered as accurate by a panel of experts within the conduct of a targeted research study measuring accuracy of responses. Because the responses were supported by the literature and convincing, not following them could easily be mistaken for non-adherence to established guidelines. However, the physician remembered that the LLM-based chatbot's reasoning is not or only minimally explainable and therefore adapted their clinical reasoning to this peculiarity of chatbots, checking whether there were omissions in the proposed therapeutic strategy. Eventually, the physician noticed that the chatbot did not explore if the patient was allergic to the suggested antibiotic/s and ultimately changed the prescription. The reason why the chatbot did not explore this crucial aspect in this specific case (and also why, conversely, it did so in other simulated cases) remains unclear, and, in similar situations, the missing information could easily be overlooked in the absence of explanations and in the presence of a convincing argument to support the proposed treatment. However, it was crucial for the clinician to remember to adapt their clinical reasoning to the new scenario of chatbot-assisted prescribing, ultimately taking advantage of the help and speed of assistance in the best interest of the patient.

Based on a simulated case proposed to ChatGPT o1-preview on February 4, 2025. KPC, *Klebsiella pneumoniae* carbapenemase; LLM, large language model.

Giacobbe DR, et al. Clin Microbiol Infect 2025. doi: 10.1016/j.cmi.2025.03.0221198-743X

LLMs for antibiotic prescription

- General LLM-based tools, but there will also be specialistic ones
- The expertise paradox
- Need for dedicated educational programs (change of clinical reasoning)

Giacobbe DR, et al. Infect Dis Ther. 2025 Mar;14(3):493-500

Giacobbe DR, et al. NPJ Antimicrob Resist. 2025 Feb 27;3(1):14

Don t’ forget privacy requirements

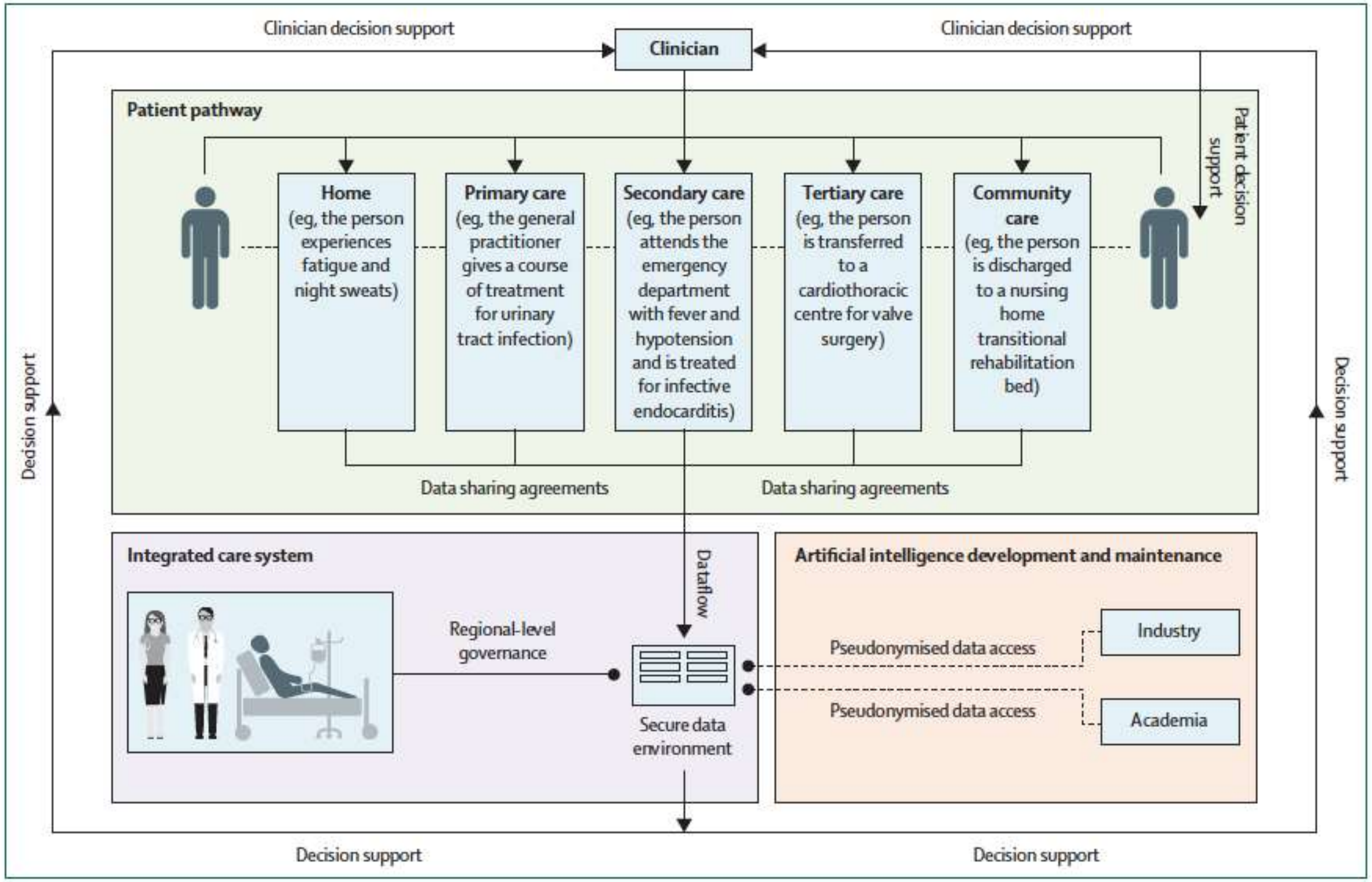

Figure 2: **A model for how regional integrated care systems should house antimicrobial learning systems’ governance, security, and maintenance of dataflows to enable continuous delivery of antimicrobial resistance-artificial intelligence decision support to patient pathways**

Howard A, et al. Lancet Digit Health 2024; 6: e79–86

Thank you