



**HEIDELBERG
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HOSPITAL**

eahp BOOST

1st EDITION



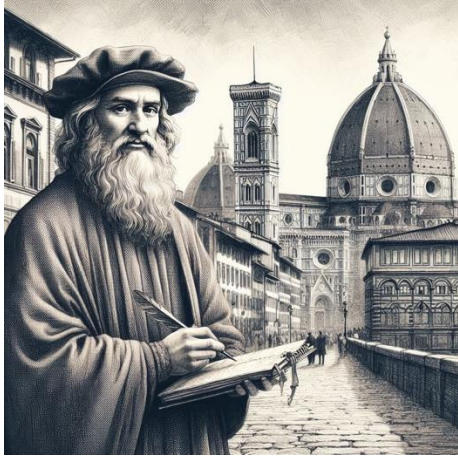
Bedside dispensing services and pharmaceutical care

Automation and AI at Bedside - Is the future now?

Dr. Benedict Morath
Hospital Pharmacy Heidelberg
Heidelberg University Hospital



Advanz Pharma (Speaker)



Traditional ward dispensing



Semi-automated Dispensing



Automated Dispensing



Traditional ward dispensing



High risk of medication errors
Workload on nurses
Increasing risk depending on staffing

Automated Dispensing



50 % reduction of medication administration errors

90 % reduction of clinical errors

Workload shift into hospital pharmacy

Additional data on cost-effectiveness needed

Dispensing errors occur rarely

Automated dispensing



New risks

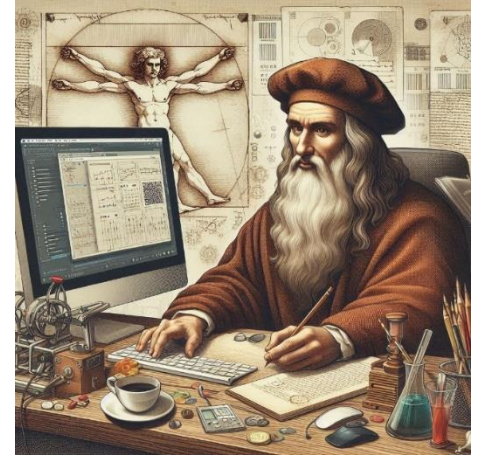
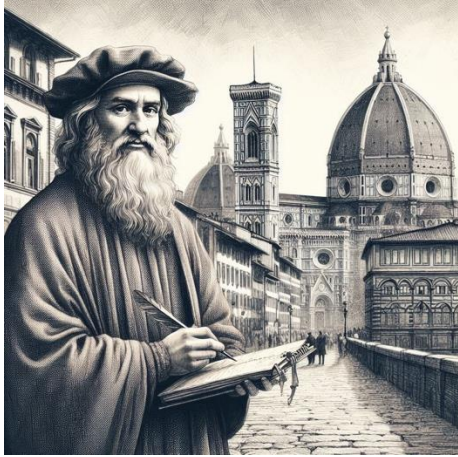
Fading ink on the package

Device outage and technological issues

Late changes in medication increase risk for errors

Scanning is priority as pouches and bags have a look a like risk

Automated dispensing has the potential to move the pharmaceutical care at bedside on a new level.



A brief history of Artificial Intelligence mostly complete
starting around the cybernetics movement

From cybernetics to AI
The idea that humans and machines are essentially the same gives rise to a project where scientists began seriously considering what it would take to develop machines with human-like intelligence.

1942: Accelerated code breaking Alan Turing used the Bombe machine to decode messages encrypted using the Enigma machine of an accelerated pace during WWII.

1949: "The Manchester Baby" runs its first program

1952: Program that can play Checkers is developed by Arthur Samuel

1956: "Giant Brains: Or Machines That Think" Edmund Berkeley compares AI machines to human brains if they were made of "hardware and wire instead of flesh and nerves."

1958: LISP (List Processing) First Programming Language Created by John McCarthy

1959: "Machine Learning" Introduced into the nomenclature by Arthur Samuel at IBM

1956: "AI will beat a human at chess within the next 10 years" -Herbert Simon

1955: First AI Workshop Proposed to be held at Daltmouth in 1956 McCarthy, Minsky, Rochester, Shannon

1956: DENDRAL Expert System: hypothesis formation and science Inferences & Logical Conclusions Feigenbaum & Lederberg

1958: The Imitation Game Computing Machinery and Intelligence by Alan Turing

1957: The Perception learns to identify shapes, an early form of machine learning Created by Frank Rosenblatt

1959: ELIZA Chatbot Natural Language Processing Created by Weizenbaum

1961: UNIMATE First Industrial Robotic arm available commercially Created by George Devol

1962: "Cybernetics" the study of control and communication in the animal and the machine by Norbert Wiener

1964: ELIZA Chatbot Natural Language Processing Created by Weizenbaum

1965: First National Conference on Artificial Intelligence Held at Stanford University, August 18-21

1966: SHAKEY First robot to perceive its surroundings, navigate, plan a route, adjust for errors, and improve its abilities using English language communication Stanford Research Institute

1968: WABOT-1 The first "android" Walked, communicated in Japanese and gripped objects Waseda University

1968: EXPERTISE Linear Algebra is used to advance racial recognition programs Strach & King

1968: ELIZA Chatbot Natural Language Processing Created by Weizenbaum

1969: GAMMADIC leads champion of back-gammon Created by Hans Berliner

1969: The Stanford Cart successfully navigates a room without human assistance

1970: "Machine Learning" Introduced into the nomenclature by Arthur Samuel at IBM

1970: "From three to eight years we will have a machine with the general intelligence of an average human being" -Marvin Minsky

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1971: Reduced funding for AI due to lack of promised progress in Britain

1972: WABOT-1 The first "android" Walked, communicated in Japanese and gripped objects Waseda University

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1976: Physical Symbol System Hypothesis "Computer science as empirical inquiry Symbols and Search" by Newell & Simon

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1977: "Winter is Coming" -Schanck & Minsky

1977: XCON First expert system on the commercial market

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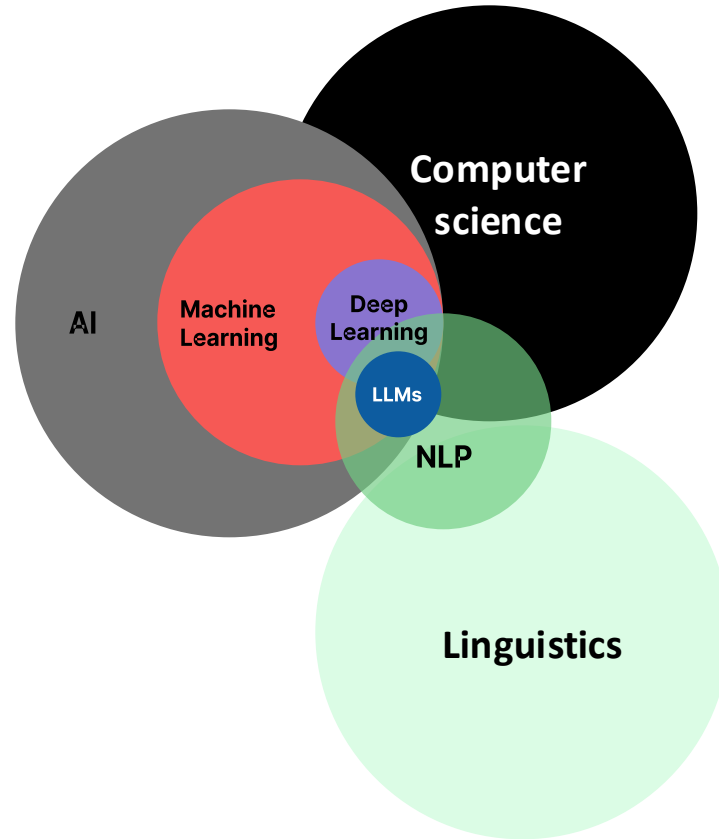
September 2024 | Morath

Danielle J. Williams, A brief history of AI

Shown on the vertical axis is the training computation that was used to train the AI systems.



Large computing power enables new technologies



The dose makes —

The dose makes ...

The dose makes a ^{*P* ≈ 0,04}

The dose makes the ^{*P* ≈ 0,93}

The dose makes the _____

The dose makes the ...

The dose makes the joy $P \approx 0,06$

The dose makes the ^{*P ≈ 0,92*}poison

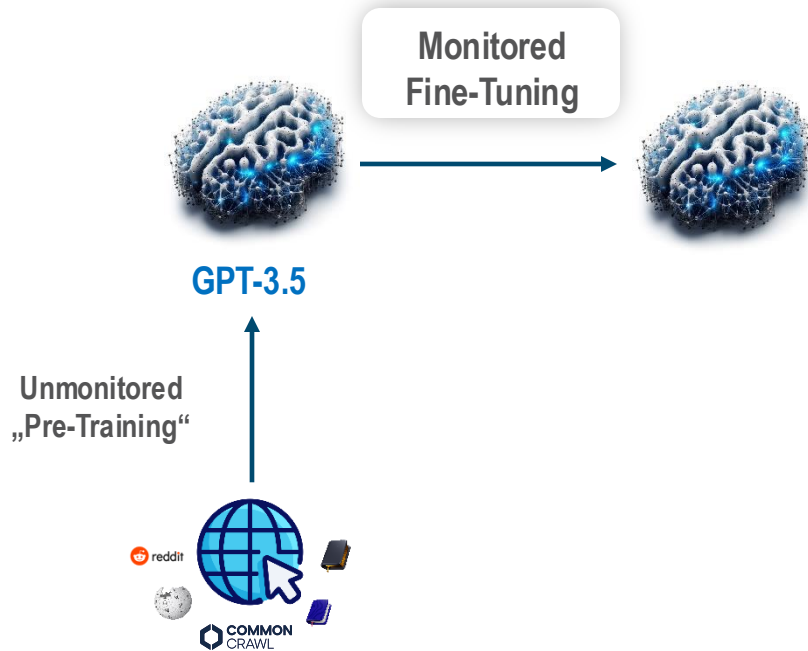
Large datasets

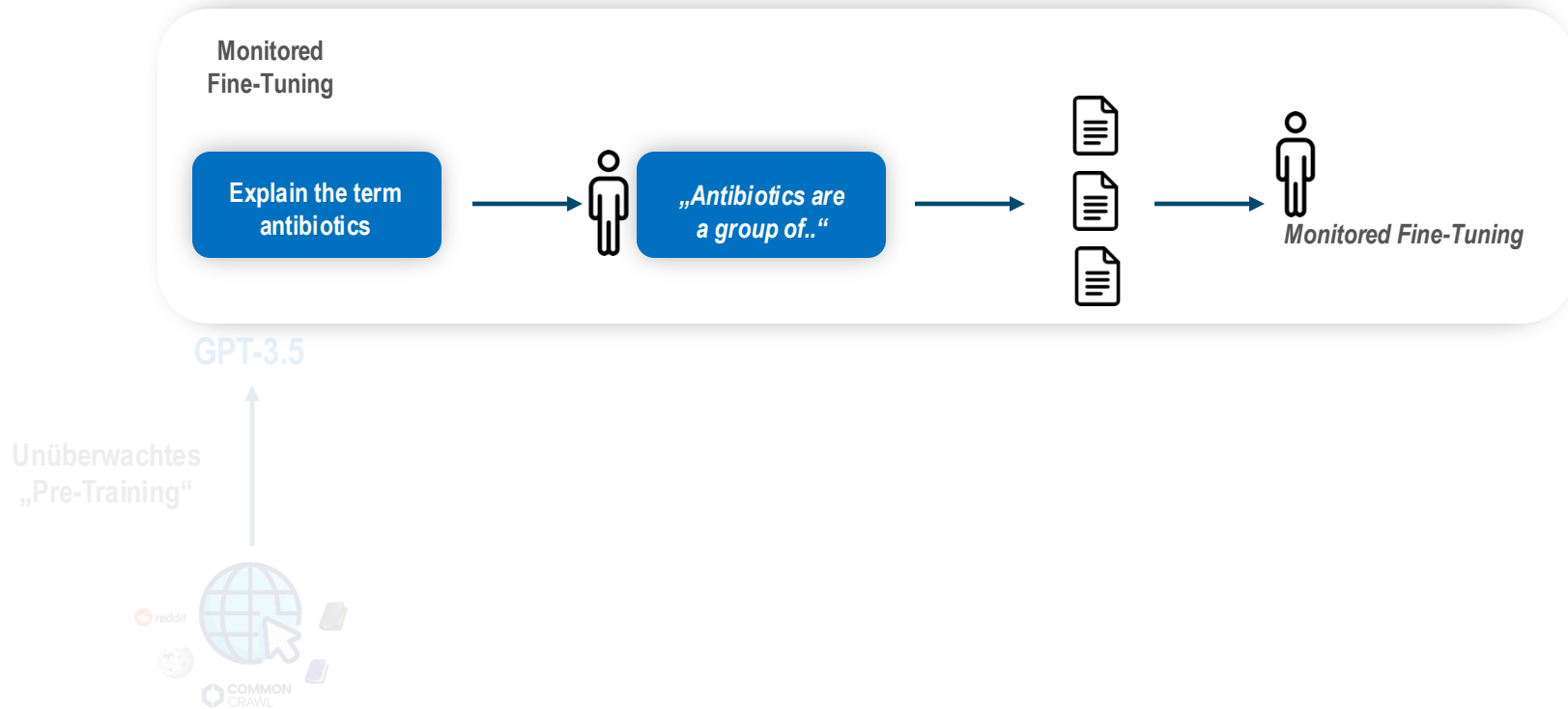


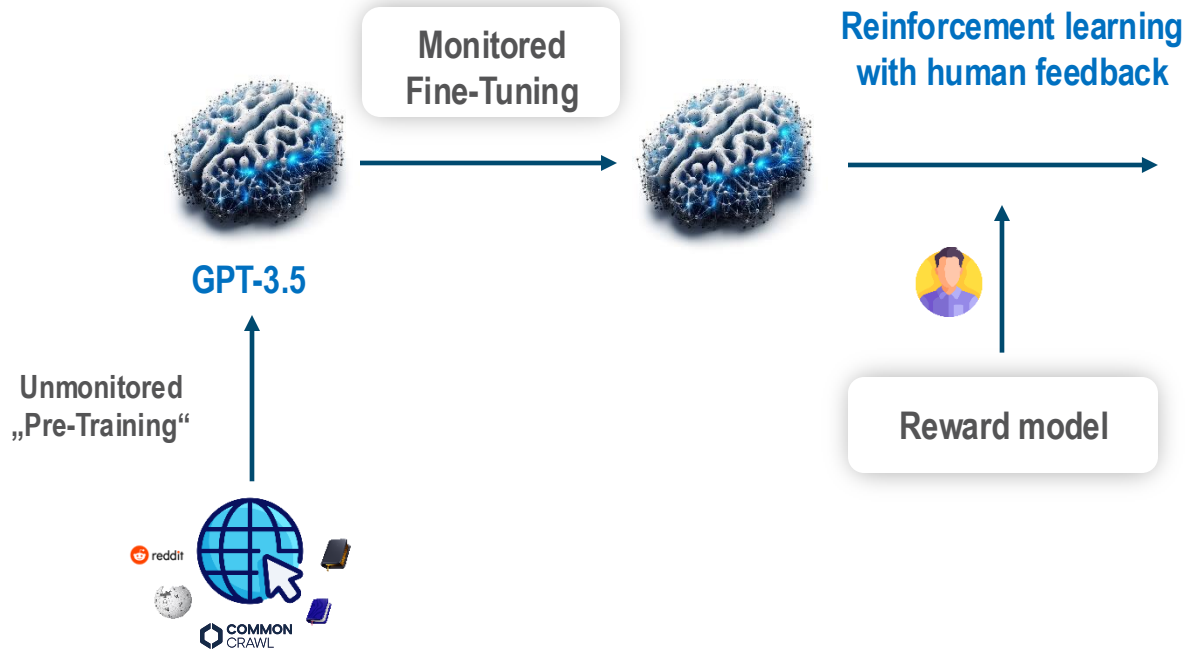
Books1

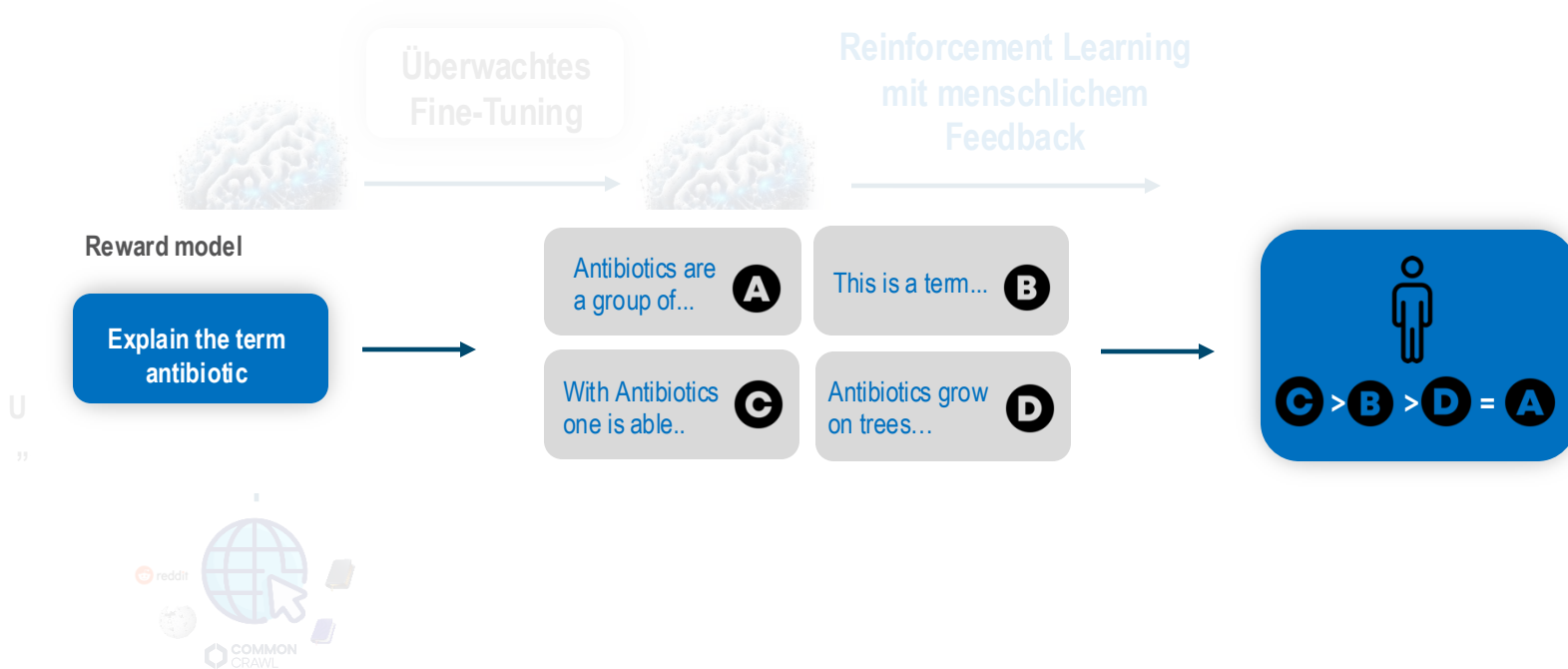


Books2

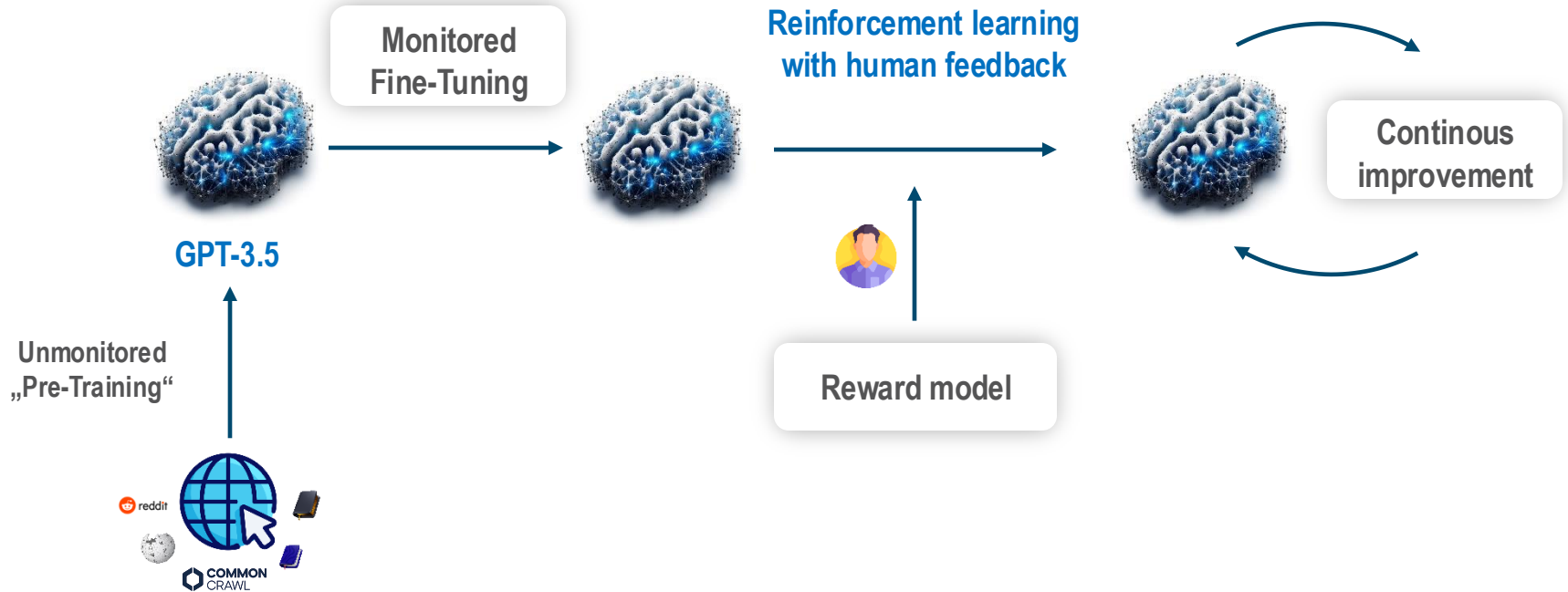









How was ChatGPT developed?



Performance and risks of ChatGPT used in drug information: an exploratory real-world analysis

Benedict Morath , Ute Chiriac, Elena Jaszowski, Carolin Deiß, Hannah Nürnberg, Katrin Hörth, Torsten Hoppe-Tichy, Kim Green

BMJ Journals




**50 questions from
clinical routine**



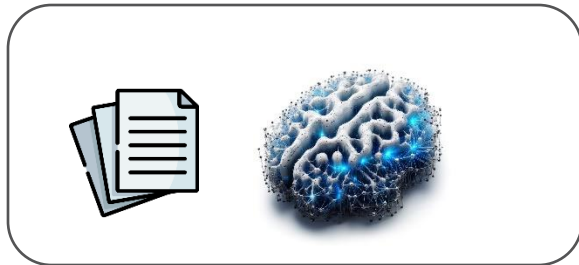
**Rating of answers
according complexity**

- I:** Open-Access: e.g. SmPC
- II:** Guidelines, standard literature
- III:** Commercial databases
- IV:** Individual answers, knowledge transfer

Performance and risks of ChatGPT used in drug information: an exploratory real-world analysis

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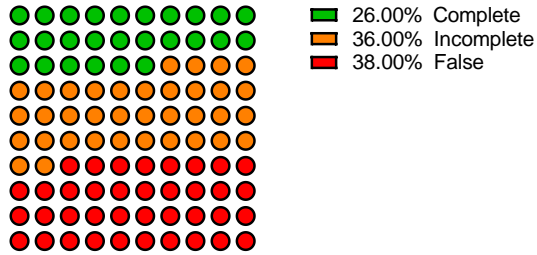
**Rating of ChatGPT-3.5
answers by 7 trained clinical
pharmacists**

Content: Complete ● | Incomplete/Inconsistent ● | False/Not applicable ●

Management: Possible ● | Insufficient ● | Not possible ●

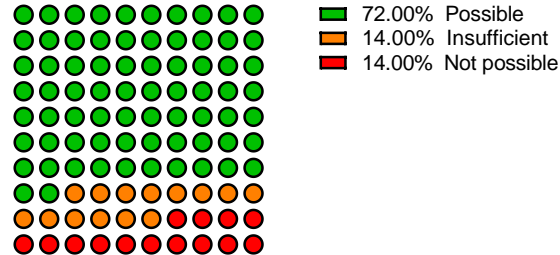
Risk: No risk of patient harm ● | low risk ● | no risk ●

Content



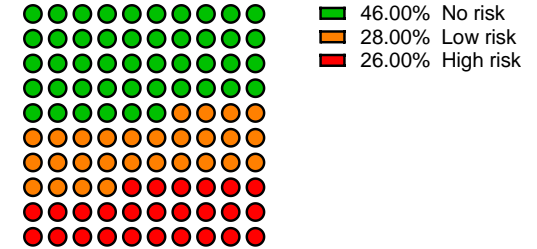
n = 50 questions

Management



n = 50 questions

Risk



n = 50 questions

11 answers had a high risk combination:

False content + possible management + high risk of patient harm

Table 2 Questions entered in ChatGPT that were rated either completely correct or completely wrong, that is, rated in the highest or lowest category of all three domains

Answer category	Question to ChatGPT	Overall rating
I	What is the labelled standard dose of apixaban in atrial fibrillation?	●
I	What is the labelled standard dose of apixaban in a patient with CrCl 20 mL/min and atrial fibrillation?	●
I	Can a patient who reacted with a rash to penicillin in the past be treated with cephalosporins?	●
I	Should the caspofungin dose be adjusted in a patient with bilirubin of 17 mg/dL, AST of 400 U/L and ALT of 100 U/L?	●
I	When should empagliflozin be paused before surgery?	●
I	What is the maximum recommended daily dose of diclofenac?	●
I	How should caspofungin be diluted prior to infusion?	●
I	What is the maximum daily dose of amlodipine?	●
I	What is the standard dose of carbamazepine for trigeminal neuralgia?	●
II	How should aztreonam be dosed on a CVVHD with dialysis flow rate of 2 L/h?	●
II	How is tinzaparin therapeutically dosed in a patient on intermittent hemodialysis?	●
III	What is the recommended initial dose of insulin glargine in a patient with steroid-induced diabetes?	●
IV	Which painkiller should be used in a patient on lithium therapy?	●
III	Which interactions can occur in patient treated with nirmatrelvir/ritonavir (Paxlovid), atorvastatin, trazodone, paroxetine, acetylic salicylic acid, and candesartan and how should these be managed?	●
IV	How much vitamin K can be used to lower the INR to two in a LVAD patient before surgery currently with an INR of 3.5?	●

Legend: ● : Content, patient management, and risk rated in the highest category. ● : Content, patient management, and risk rated in the lowest category.
 ALT, Alanine transaminase; AST, Aspartate transaminase; CrCl, Creatinine clearance; CVVHD, Continuous veno-venous hemodialysis; INR, International normalised ratio; LVAD, Left ventricular assist device; U, Unit.

Question II	What is the dosing weight for aminoglycosides in a patient with a body weight of 190 kg and a height of 165 cm?	
Answer ChatGPT day 1	The dosing weight for aminoglycosides in a patient with a body weight of 190 kg and a height of 165 cm would typically be calculated using the patient's ideal body weight (IBW). The most commonly used formulas for calculating IBW are the Devine formula for males ($IBW=50 + 2.3(\text{height (in)} - 60)$) and the Robinson formula for females ($IBW=45.5 + 2.3(\text{height (in)} - 60)$). Since we don't know the gender of this patient, we would use the Devine formula. $165 \text{ cm}=64.96 \text{ inches}$, $IBW=50 + 2.3(64.96-60) = 72.986 \text{ kg}$.	N/A



Correct answers possible, if information was openly accessible

No use in drug information currently:

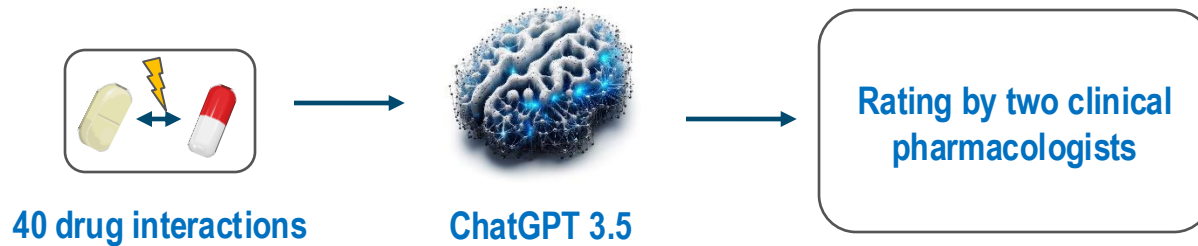


- Answers were unspecific with a high risk of patient harm
- No reproducibility
- No references and no transparency
- From a legal point of view within the MDR?

The Capability of ChatGPT in Predicting and Explaining Common Drug-Drug Interactions

Monitoring Editor: Alexander Muacevic and John R Adler

Ayesha Juhj,¹ Neha Pipil,² Soumya Santra,³ Shaikat Mondal,⁴ Joshil Kumar Behera,⁵ and Himel Mondal^{✉1}



✓ 39 von 40 answers were correct.

50 % were rated as inconclusive

The reading level needed for understanding was determined as „college-level“

Can I take ritonavir and ticagrelor?



ChatGPT

I am not a doctor, but I can provide some general information. It's important to consult with a healthcare professional for advice tailored to your specific situation.



Disclaimer

Ritonavir is primarily used as a medication for the treatment of HIV infection, and it is also sometimes used to boost the levels of other medications. Ticagrelor is an antiplatelet medication commonly prescribed to reduce the risk of cardiovascular events.

There is a potential for drug interactions between ritonavir and ticagrelor. Ritonavir can affect the metabolism of other drugs by inhibiting certain enzymes in the liver, particularly those from the cytochrome P450 family. This inhibition can lead to increased levels of drugs that are metabolized by the same enzymes, potentially resulting in adverse effects or reduced efficacy.



Interaction identified

Combining ritonavir with ticagrelor may increase the risk of bleeding, as both medications can independently cause this side effect. Therefore, it is crucial to inform your healthcare provider about all medications, including over-the-counter drugs and supplements, that you are taking. Your doctor can assess the potential interactions and determine the best course of action for your specific medical condition.



**No contraindication
Reasoning false**

Never make changes to your medication regimen without consulting your healthcare provider, as they can provide personalized advice based on your health history and current medications.



Disclaimer

Performance of ChatGPT on Factual Knowledge Questions Regarding Clinical Pharmacy

The Journal of Clinical Pharmacology
2024, 0(0) 1–6
© 2024, The American College of
Clinical Pharmacology.
DOI: 10.1002/jcph.2443

Merel van Nuland, PharmD, PhD¹ , Abdullah Erdogan, BSc¹, Cenkey AÇar, PharmD¹, Ramon Contrucci, PharmD², Sven Hilbrants, PharmD³, Lamyae Maanach, PharmD⁴, Toine Egberts, PharmD, PhD^{5,6}, and Paul D. van der Linden, PharmD, PhD¹

Better performance as hospital pharmacists

RESEARCH



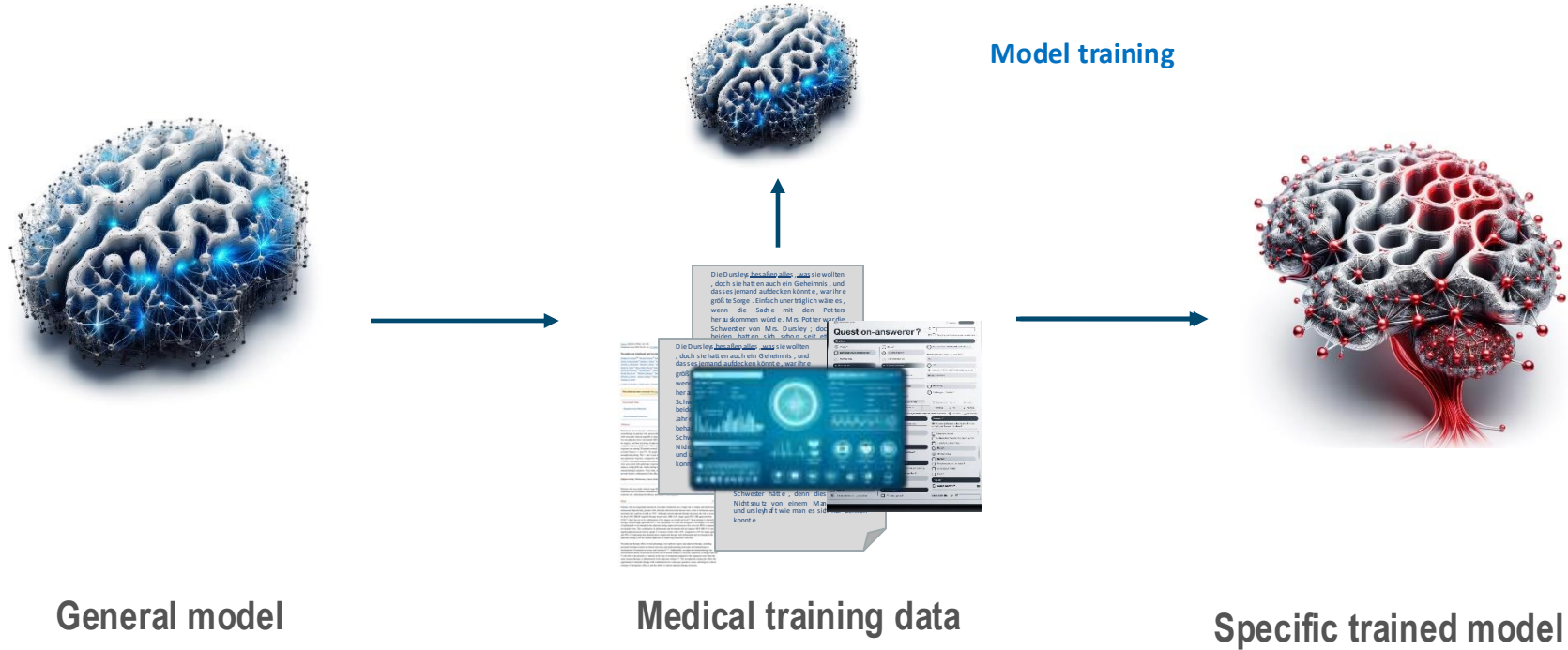
Poor performance of ChatGPT in clinical rule-guided dose interventions in hospitalized patients with renal dysfunction

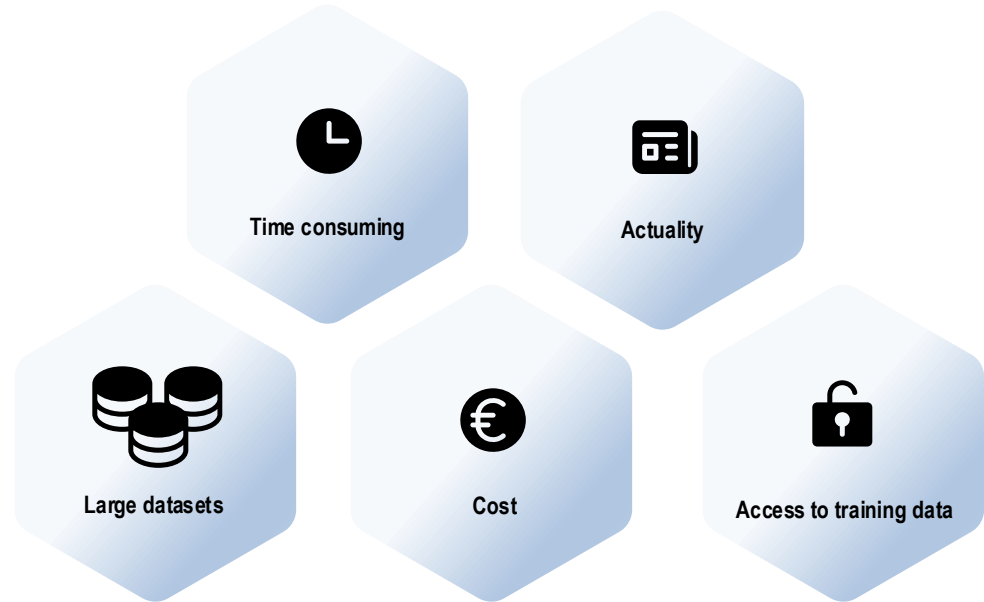
Merel van Nuland¹  · JaapJan D. Snoep² · Toine Egberts^{3,4} · Abdullah Erdogan¹ · Ricky Wassink¹ · Paul D. van der Linden¹

Integration in CDSS possible
All questions on dialysis wrong

~ 50 % of questions on renal insufficiency incorrect



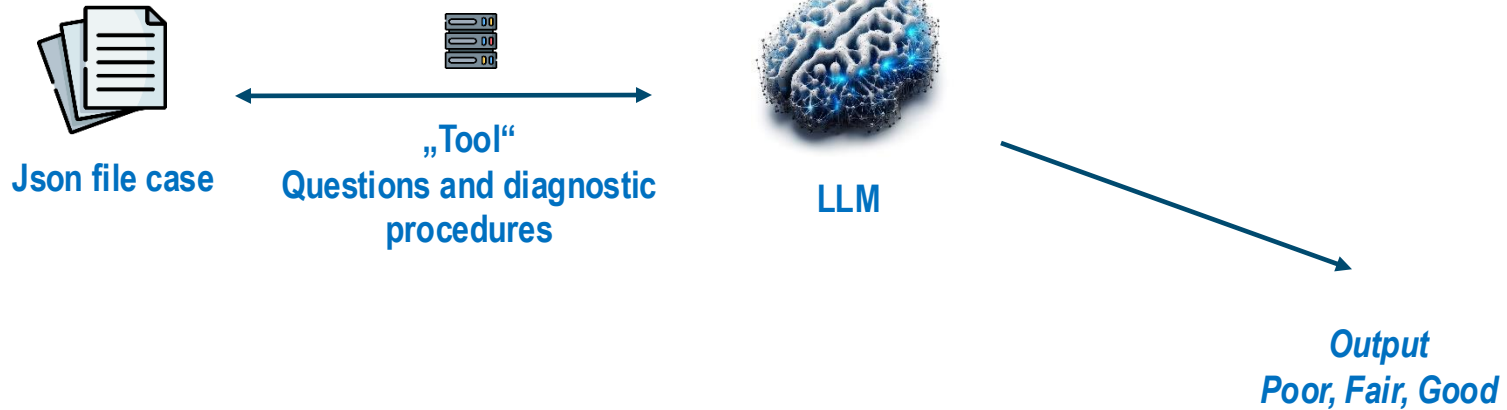


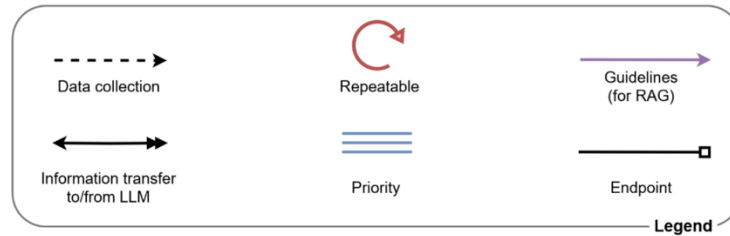
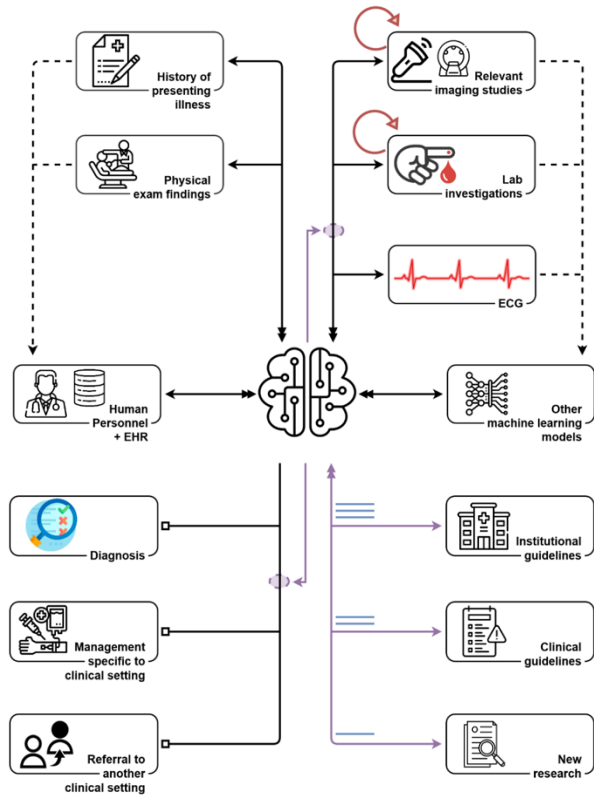


Generative Large Language Models are autonomous practitioners of evidence-based medicine

Akhil Vaid MD^{1,2}, Joshua Lampert* MD³, Juhee Lee* MD^{4,5}, Ashwin Sawant* MD^{1,6}, Donald Apakama* MD^{1,7}, Ankit Sakhuja* MD^{1,2,8}, Ali Soroush MD^{1,9}, Denise Lee MD^{1,10}, Isotta Landi PhD^{1,2}, Nicole Bussola PhD¹, Ismail Nabeel MD¹¹, Robbie Freeman RN¹, Patricia Kovatch BS¹², Brendan Carr MD MS⁷, Benjamin Glicksberg PhD¹³, Edgar Argulian MD^{14, 15}, Stamatios Lerakis MD PhD^{14, 15}, Monica Kraft MD⁶, Alexander Charney MD PhD^{1,16}, Girish Nadkarni MD MPH^{1,2,17}

**Contributed equally*





Question	What is the next best step in management?
Observation	To determine the next best step in management, I first need to understand the patient's symptoms and clinical presentation.
Action + Action Input	Symptom tool (<i>No input</i>)
Tool response	Patient reported 1 hour ago with left sided chest pain, sweating, nausea, vomiting, shortness of breath.
Observation	The symptoms suggest a possible cardiac event, such as a myocardial infarction. I need to gather more information about the patient's past medical history and physical exam findings to further narrow down the differential diagnosis.
Action + Action Input	Past medical history tool (<i>No input</i>)
Tool response	No past medical history available.
Observation	The lack of past medical history makes it difficult to assess the patient's risk factors for cardiac disease. However, given the patient's symptoms, I should proceed with a physical exam to gather more information.
Action + Action Input	Sign tool (<i>No input</i>)
Tool response	S3 gallop
Observation	An S3 gallop is often associated with conditions that cause rapid ventricular filling, such as congestive heart failure. This finding, in combination with the patient's symptoms, further supports the possibility of a cardiac event. I should use the machine learning tool to predict the likelihood of a low ejection fraction, which is often seen in heart failure.

→ *Medical history*

→ *Assessment*

→ *Physical examination*

Observation	An S3 gallop is often associated with conditions that cause rapid ventricular filling, such as congestive heart failure. This finding, in combination with the patient's symptoms, further supports the possibility of a cardiac event. I should use the machine learning tool to predict the likelihood of a low ejection fraction, which is often seen in heart failure.
Action + Action Input	Machine learning tool (<i>Low ejection fraction (<40%) model</i>)
Tool response	Low ejection fraction (<40%): 0.9
Observation	The high probability of a low ejection fraction suggests that the patient may be experiencing heart failure. However, to confirm this diagnosis, I need to order relevant lab investigations and an ECG.
Action + Action Input	Lab investigation tool (<i>SERUM TROPONINS</i>)
Tool response	SERUM TROPONINS: 0.1 ng/mL (Elevated)
Observation	The elevated troponin levels are indicative of myocardial injury, which is consistent with a myocardial infarction. This, in combination with the patient's symptoms and the S3 gallop, strongly suggests a cardiac event. I should now order an ECG to further confirm this diagnosis.
Action +	ECG tool

→ **Determination LVEF**

→ **Lab investigation**

→ **ECG**

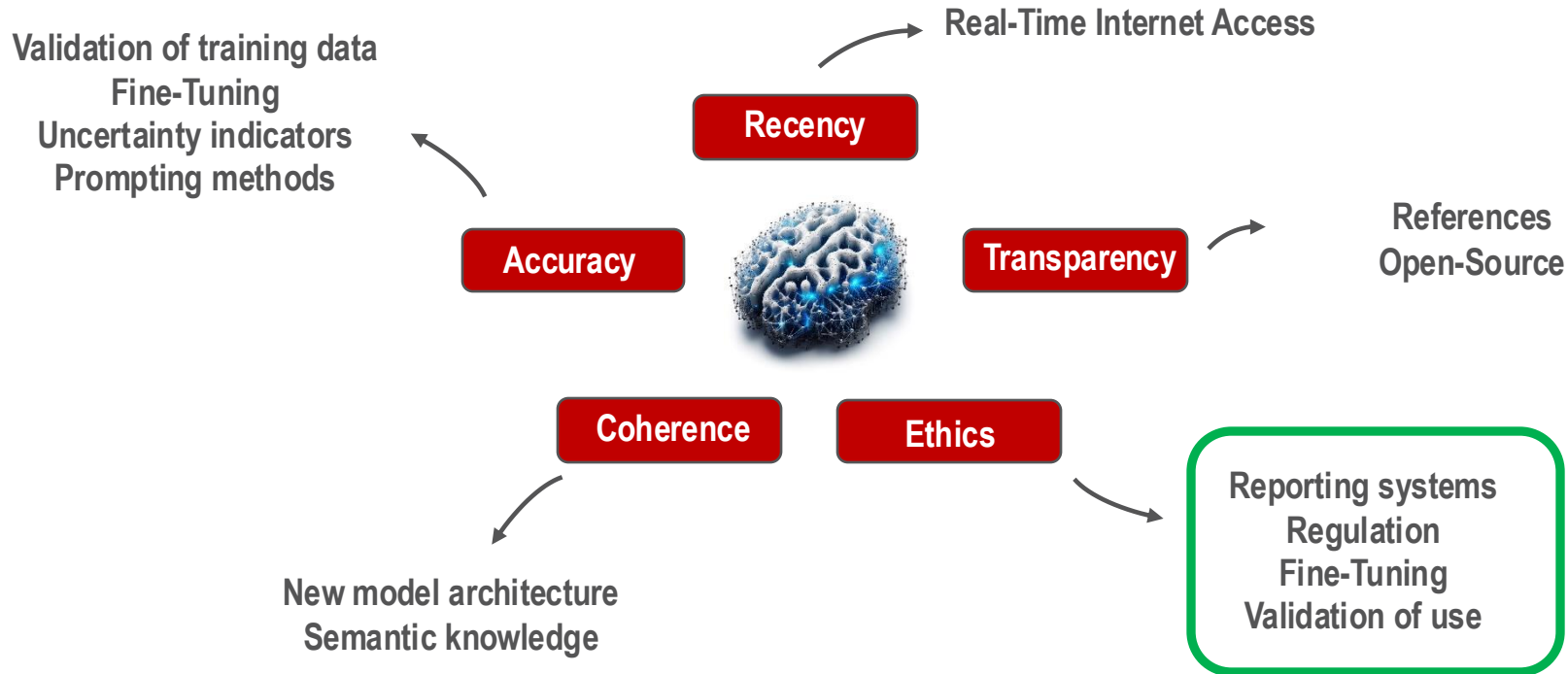
Action Input	
Tool response	ST elevation in leads V1-V4
Observation	The ST elevation in leads V1-V4 is consistent with an anterior wall myocardial infarction. This, along with the patient's symptoms, elevated troponins, and the S3 gallop, confirms the diagnosis of a myocardial infarction. I should now use the guidelines tool to determine the most appropriate next steps in management.
Action + Action Input	Treatment guidelines tool (<i>Acute myocardial infarction</i>)
Tool response	<Guidelines about general management of Acute MI> <i>According to institutional (Institutional guidelines): The institution does not accept STEMI patients beyond initial evaluation. Patient must be immediately transferred to another facility.</i>

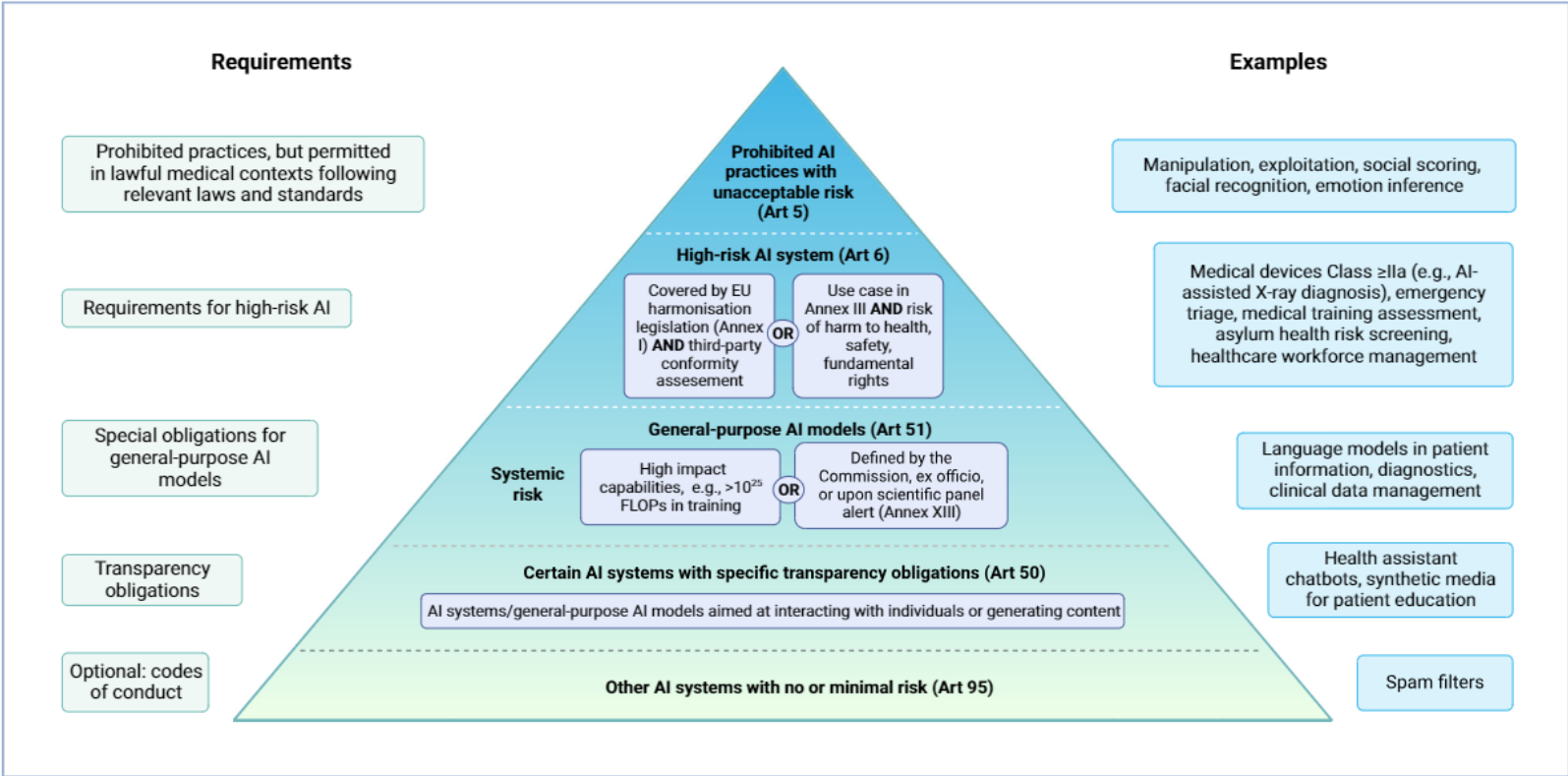
→ RAG

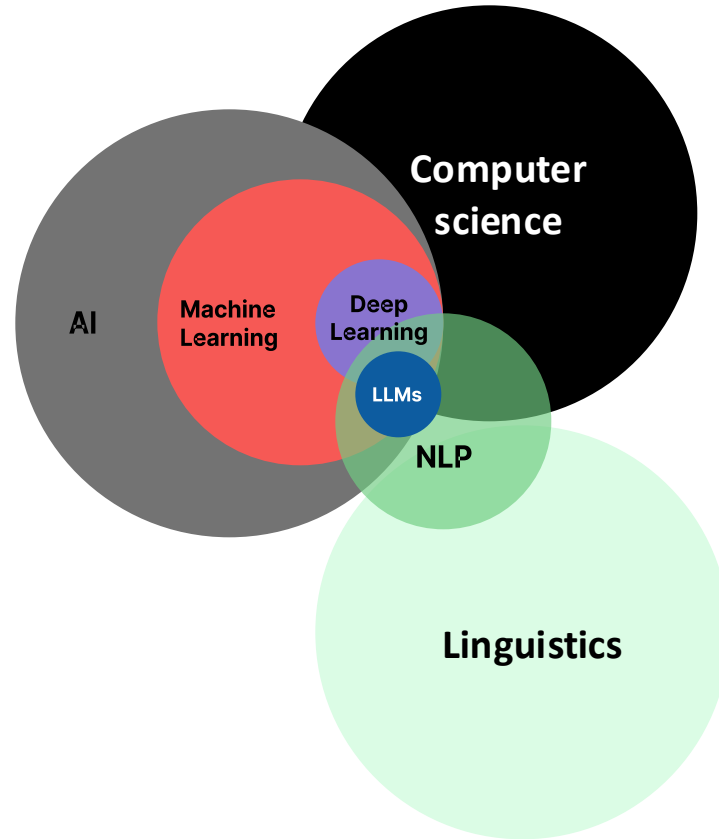
Final answer	The next best step in management is to immediately start the patient on aspirin, a P2Y12 inhibitor, and an anticoagulant. The patient should also be started on a beta blocker, an ACE inhibitor, and high-intensity statin therapy within the first 24 hours, unless there are contraindications. Pain relief with opioids can be given if required. <i>However, given the institutional guidelines, the patient must be immediately transferred to another facility for further management, including reperfusion therapy.</i>
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Performance by speciality



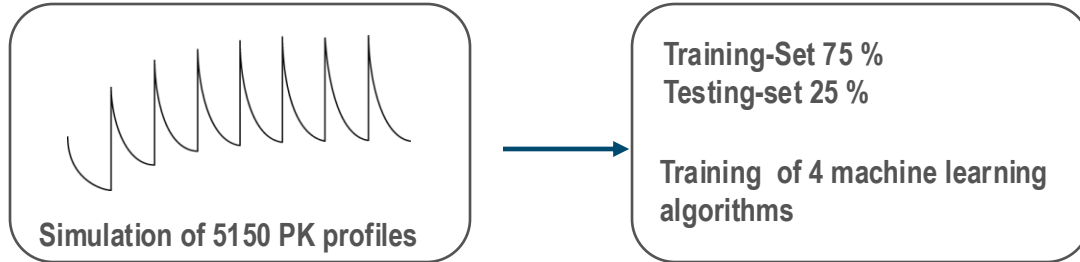






A machine learning approach to predict daptomycin exposure from two concentrations based on Monte Carlo simulations

Cyrielle Codde¹, Florence Rivals², Alexandre Destere³, Yeleen Fromage², Marc Labriffe^{2,4}, Pierre Marquet^{2,4}, Clément Benoist⁴, Laure Ponthier⁴, Jean-François Faucher¹, Jean-Baptiste Woillard^{2,4}



Very good AUC estimation

Use for TDM possible with C0, C1 and covariates

Exposure estimation and dose adjustment possible


Clinical Pharmacokinetics (2024) 63:1137–1146

<https://doi.org/10.1007/s40262-024-01405-z>

ORIGINAL RESEARCH ARTICLE



A Machine Learning Algorithm to Predict the Starting Dose of Daptomycin

Florence Rivals¹ · Sylvain Goutelle^{2,3,4} · Cyrielle Codde^{5,6} · Romain Garreau^{2,3,4} · Laure Ponthier⁶ · Pierre Marquet^{1,6} · Tristan Ferry^{4,7,8} · Marc Labriffe^{1,6} · Alexandre Destere⁹ · Jean-Baptiste Woillard^{1,6} 

Accepted: 16 July 2024 / Published online: 31 July 2024

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Use for lowering the administrative workload is conceivable, but application of generative models is limited by the model architecture



AI applications can help to digitize processes faster (quick wins)



The more complex the facts and the context, the less applicable the models are



ChatGPT is primarily a chatbot, LLM for medical applications are being tested. The combination with guidelines & context information appears promising (RAG). However, regulation increases and might slow down development.



Thank you for your attention



**Auditorium and
Exhibition**

**Workshop Rooms
1 and 2**

Participants' Entrance
(Piazza Adua)