

HALLUCINATIONS IN LARGE LANGUAGE MODELS: A CRITICAL THREAT TO MEDICATION SAFETY AND EVIDENCE-BASED PHARMACY PRACTICE

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ABSTRACT

Background: LLMs have recently received considerable attention as potential applications within the realm of healthcare, notably pharmacy practice and databases of medications information. However, the utility of LLMs in a clinical context is severely limited due to the possible generation of factually untrue or invented output that is highly risky to patients' safety. **Objectives:** In this paper, there is a comprehensive analysis of the typology of hallucinations that are generated by LLMs, dangers associated with hallucinations in relation to medications, and the impact of hallucinations on evidence-based pharmacological data sets. **Methods:** Literature narrative synthesis has been performed on the subject, emphasizing the frequency of hallucinations, the methodology of their assessment for clinical safety, and risk mitigation

strategies in AI-enabled clinical apps. **Results:** LLM hallucinations manifest themselves as facts-dissonant fabrications, inappropriate clinical advice, and significant omissions. It has been proven that LLMs generate fabricated medication instructions and disregard important aspects of patients' medical data, such as having an allergy to prescribed medication, when engaging in clinical reasoning and planning processes. Additionally, LLMs demonstrate serious deficiencies when synthesizing scientific evidence, making up references, and providing unsubstantiated therapeutic suggestions. These issues raise concerns over the ability of LLMs to make evidence-based pharmacological recommendations. **Conclusion:** The unsupervised application of LLMs within the field of pharmacy practice is highly

dangerous from a clinical standpoint. To ensure the safe application of LLMs in pharmacy practice, a controlled approach needs to be employed.

KEYWORDS: Large Language Models (LLMs), AI hallucinations, Clinical decision support, Medication errors, LLM Hallucinations.

1. INTRODUCTION

1.1] Introduction to Large Language Models in the Healthcare Industry: Large Language Models (LLMs) are being used in the healthcare sector to ease manually tedious processes like clinical documentation or patient inquiry.

However, large language models may create serious problems when it comes to their accuracy and reliability in some cases.^[3,8] These models are adept at problem-solving. Besides, they excel in linguistic situations. Despite these advantages, the large language models cannot be trusted in terms of reliability in critical situations of the field of medicine.^[5,3]

1.2] Why LLM hallucinations matter in Pharmacy: In the context of LLMs, hallucinations refer to the generation of outputs that are either factually incorrect, fictitious or unfaithful to the source material provided. This poses a significant barrier to the reliability and implementation of these models in high-risk clinical settings.^[3,8] The reason being, LLMs string together words based on probability rather than factual data, due to which the outputs may deviate away from the original sources. These risks are unacceptable in pharmacy practice as absolute precision is key to ensure patient safety and well-being.^[5,3]

1.3 Impact in clinical settings: Various critical errors by LLMs have been demonstrated by research, such as fabricating citations and references, omission of clinically validated data, contradicting suggestions, or missing important patient details.^[5] Research has illustrated a lapse in the past medical history of patients, current medications, known allergies and family history.^[8] Incorrect medicine-related instructions contradicting known knowledge have also been observed and documented.^[5] These outputs could potentially be the reason for disastrous errors in treatment plans and even hazardous adverse drug reactions.^[5,8] These LLMs also disturb traditional drug information systems, which have been proven to be reliable and backed by evidence. Pharmacists have high faith in these systems to assist with clinical practice and support. LLMs have proven to generate misleading and unverified claims not scientifically backed with a high sense of

confidence, despite being unfactual or unfaithful to the source material. The convincing and confident tone of these outputs are particularly misleading. Due to the same, reliance on such information could compromise evidence-based information derived from traditional drug information systems and derange decision making based on these, while also potentially spreading misinformation.^[5]

1.4 Scope and objectives of the review This review emphasises on the effect of LLM hallucinations in pharmacy, the risks they pose in a clinical setting and to traditional drug information systems and explores various mitigation strategies and frameworks.^[5,9]

2] Hallucinations in LLMs

In my opinion, there are many possible approaches to using Large Language Models (LLMs) to keep records of clinical information and communicate effectively. Nevertheless, there are several restrictions in its use in clinical pharmacy. Among them, I would note the problem called "LLM Hallucinations". As you may guess from the name, it means the possibility of receiving information which is false and not real. Pharmacists should take into account that precision is important while prescribing medicines. If the provided information by the AI is incorrect or misleading, it can lead to mistakes related to the prescription of medicines.^[7,8,13]

2.1] Definition and Important Concepts As far as LLM models are concerned, the term "hallucinations" stands for a LLM providing the user with information which is not grounded on facts. Thus, one should distinguish the three notions connected with AI hallucinations. They are misinformation, omission and fabrications. To put it differently, the first one means failure of the AI to extract information presented in the initial text. In the case of omission, the information will simply be omitted. In its turn, hallucinations means the creation of non-existent information. LLMs may be confident that it provides you with reliable information, although not true.^[7,8]

2.2] Types of Hallucinations As for the types of LLM hallucinations in clinical pharmacy, it may contradict some facts. For example, the model may state that there is an interaction between two drugs. However, in fact, they do not influence each other, or the contrary. The second type of hallucination includes creation of the information about the author, article title and journal. Besides, the LLM may provide you with omission of such information as medical history or information about drug interaction. Furthermore, LLMs may provide you with some assertions which have no grounds at all. Finally, during long talks, the model may

contradict itself, for instance, advising to prescribe medicine which should not be provided.^[9,10]

2.3] Reason for Occurrence of Hallucinations

The reason why AI hallucinations occur is related to how LLMs work. To put it differently, such hallucinations occur because LLM is generated based on probabilities. The information produced is not checked for credibility. Context of prompts may also influence responses of AI. Hallucinations in LLMs are rather dangerous since they may lead to clinical errors in clinical pharmacy.^[11,12]

3. Why Pharmacy Practice Is High-Risk

Pharmacy practice is a high-stakes and professional field where patient safety depends on the accuracy of clinical and pharmacological information.^[1,5] The introduction of generative AI, specifically the large language models (LLMs), produces new risk because these systems can produce reliable but false data, known as Hallucination.^[1,5] In high-stakes healthcare settings, such errors are the greatest barrier to safe technology.^[8]

3.2] Effects of Inaccurate Drug Information

There can be several dire effects of inaccurate drug information on patients. Doctors might make errors in their treatment procedures due to inaccurate information about drugs. They might not be able to diagnose patients, and prescribe treatments accordingly. Patients might think they are receiving treatments; however, there will be no significant improvement. Therefore, the patient will not receive any medical assistance. The second adverse effect of inaccurate drug information can be a major issue for doctors and patients. It might confuse them, which might mislead them into prescribing certain medications. This would be very harmful to patients.^[1,5,8]

3.3] Medication safety as a patient-safety priority: Maintaining medication safety is a top priority in healthcare systems, requiring careful validation of all drug-related documentation.^[1] Due to Documentation error, major safety risks often arise, such as the deletion of allergy histories or current medication. For instance, failing to record that a patient has "no known allergies" or missing details of a patient's anti-epileptic regimen can lead to life-threatening clinical errors or fatal issues. Ensuring a complete and faithful pharmacological record, protects the patient outcomes and hence, ensures patient's safety.

3.4] High-stakes pharmacy tasks vulnerable to hallucinations: Several complex

professional duties are highly susceptible to fabrication, negation, and incorrect reasoning errors.

- Prescription review and drug interaction screening are vulnerable to "causality" hallucinations, where a model may incorrectly assume a relationship between two independent clinical events.
- Dose interpretation is at risk of omissions, such as failing to document a missed dose of a critical medication.
- Adverse drug reaction assessment and therapeutic recommendation generation may involve negations, where clinical facts are omitted or contradictions are introduced into the treatment plan.
- Counseling support can be compromised when models provide generic advice that lacks the specificity required for safe medication use or misinterprets the severity of reported symptoms.^[1,5,8]

4. Clinical Risks of Hallucinations in Medication Management

4.1] Overview

Language models can be used to assist with administrative chores in health systems. But these models have an issue.^[1,5] They are capable of making errors. Provide false information. We refer to this as hallucinations. Pharmacists may give patients the incorrect medication or dosage while using these models. Patients may be harmed by this.^[10,4] It might be challenging to determine who is at fault when something goes wrong. Liability and trust issues may result from this.

Giving patients the incorrect medication or overlooking crucial information are two issues that might arise from hallucinations. To ensure patient safety, we must comprehend the Clinical Risks of Hallucinations in Medication Management.^[19,20]

4.2] Definitions and Mechanisms: When information is provided by an artificial intelligence system, hallucinations occur. This may be due to the system's imperfections or the fact that data was used to train it. Occasionally, the system simply invents things. Pharmacists need to know what to give patients, hence this is bad.^[1,5]

4.3] Clinical Implications and Pharmacy-Specific Relevance

Many issues can arise from hallucinations. Here are a few of them

- Patients may receive the incorrect medication. This may occur when the medication or

dosage is recommended by the model.

- It is possible to overlook crucial information regarding allergies or cautions. If a patient has a medication allergy, this could be quite dangerous.
- Certain patients are more susceptible to injury, such as adults or toddlers. Their needs may not be understood by the model.
- Patients and physicians may not take action to assist if the model indicates that everything is fine when it is not. This may lead to issues.
- Errors could occur throughout the entire medication procedure if the model provides information. Patients may end up receiving the medication as a result.

Giving patients the incorrect medication or overlooking crucial information are two issues that might arise from hallucinations. To ensure patient safety, we must comprehend the Clinical Risks of Hallucinations in Medication Management.^[19,20]

5. Influence on Drug Information Systems and how they are affected

In pharmacy practice, it is crucial to ensure that the drug information is reliable, accurate, and trustworthy. Modern information systems have shifted from being conventional static and rule-based systems to becoming dynamic generative models, introducing various obstacles to practitioners. While these information systems allow faster processing and retrieving information, they pose certain dangers since they can produce information that is not reliable and is termed hallucination, posing serious concerns regarding information consistency.^[5,2]

5.1] Non-transparent reasoning

There are many large language models that generate outputs without any relation to the original source, making it impossible to verify them through original sources.

The difficulty of finding connections in the information source makes it hard to trust the evidence produced.^[6,11]

5.2] Fictitious references

LLMs generate scientific contents and summaries for non-existent or fake references.^[6,2] Such models are deceptive in nature since they use scientific language and could confuse even experienced clinical scientists.^[6,13] This could be hazardous since they present false information in a highly assertive manner and thus making it difficult to refute.^[2]

5.3] Threats to Evidence-Based Pharmacotherapy

Wrong dissemination of information regarding drug efficacy and clinical statistics directly poses threats to evidence-based pharmacotherapy.^[2] Clinicians may end up prescribing drugs to patients relying on fabricated data, resulting in inappropriate medication. In addition, these models, when trained using average data, could promote poor reviews and outdated methods, resulting in unnecessary research wastes. Clinicians will prescribe patients medications based on information that is untrue and generated through artificial intelligence. Moreover, in case these models get trained using average or mediocre data, they might proliferate inferior reviews and outdated practices, generating research waste.

6. Large Language Model Hallucinations within Pharmacist Workflows

6.1] Introduction

The integration of large language models into healthcare opens up avenues for improving administrative tasks, writing clinical notes, and communicating with patients.^[1,2] The propensity of such models to generate hallucinations—that is, producing misleading, conflicting, or unanchored medical knowledge—is highly dangerous when applied in clinical pharmacy.^[3,4] Given the importance of accuracy in medication administration, inaccuracies generated by AI systems may lead to incorrect prescription of medications and serious drug side effects.^[2,5]

6.2] Methods and Clinical Consequences: LLM hallucinations can be attributed to text prediction based on probability, training on skewed datasets, and a failure to incorporate validated medical information.^[3] The resulting mistakes can occur either through deliberate fabrication of clinical data or omission of crucial patient information, and both cases represent a significant hazard to pharmacists' decisions.^[4,5]

6.3] Prescription Validation, Screening, and Medication Reconciliation: As for medication reconciliation and prescription screening, the use of LLMs presents a serious threat because of the omission of critical clinical information. Models may not include key components of patients' medical history, prescribed medications, and drug allergies.^[5] Moreover, there is a high risk of generating mistakes labeled as "Medicine Related Instructions" when the instructions provided by the model significantly diverge from the actual clinical notes.^[4] The omission of an allergy or approval of a fabricated dose, in case of prescription validation with the use of LLM-generated summaries, may cause fatal medication dispensing errors.^[4,5]

6.4] LLMs and Hospital, Clinical, and Community Pharmacy Practices: In hospital and

community pharmacy practice, research has been done exploring the use of LLMs to document clinical encounters, such as Subjective, Objective, Assessment, and Plan (SOAP) notes.^[2] Nevertheless, empirical studies indicate that the most common hallucinations by LLMs occur in the "assessment and plan" segments of patient documents.^[5] Since the planning segment is where pharmacists and other healthcare professionals document patient therapy, drug interactions, and dosage recommendations, any hallucination here poses a threat to medical decision-making and pharmacotherapy safety.^[2,5]

6.5] LLMs in Discharge Counseling, Monitoring of Patients, and Evidence-Based Practice

Pharmacists depend on clinical documentation during discharge counseling, as well as for monitoring therapeutic drug use. Although LLMs help in summarizing information in discharge summaries and patient education documents, they have been found to overlook important instructions for follow-up after discharge.^[1,4] Moreover, due to difficulties with analyzing complex patient history or multiple conditions, LLMs cannot be safely used in more advanced clinical monitoring, including ward practice.^[7] Lastly, LLMs have shown themselves capable of making up information about nonexistent clinical trials and statistics, thus creating illusions regarding the reliability of treatment plans.^[3,6]

6.6] LLM Help in Relevant Areas vs. Areas Where LLM Help Should Not Rely On

LLMs show their practical application value in alleviating administrative burdens in pharmacy procedures, including the translation of clinical language into coding and the generation of preliminary drafts for patient interaction purposes.^[2] However, considering that these models cannot evaluate themselves regarding their factual truthfulness and tend to create realistic but erroneous information, they should never become autonomous agents in a clinical setting.^[1,3]

While LLMs can efficiently support administrative and drafting tasks within pharmacy workflows, their severe risks of hallucinating medication instructions and omitting drug allergies mandate that they only be used as assistive tools under continuous, expert pharmacist supervision.^[2,3]

7. LLM Safety Evaluation in Pharmacy

Evaluation of the LLMs' safety and reliability is an essential step before implementing these models in pharmacy work. It is necessary to check whether they are safe to use in

pharmacotherapy and will not cause patient harm or lead to therapeutic errors. Recently there has been a trend to assess not only language skills but also clinical safety of the model.

We have to consider the safety and reliability of LLMs before implementing them in safety-related tasks, particularly, managing medications.^[4,5,6,16]

7.1] Evaluating Hallucination Rate

Hallucination rate means the extent to which the output of the LLM is inaccurate or inconsistent with the content of the source documents. There may be different levels of evaluating hallucinations, ranging from sentences to data objects. The method of ACHMI (Assessment of Caption Hallucinations in Medical Imagery) allows measuring the ratio of unsupported clinical details.^[5,4,8]

The rate of hallucinations is evaluated at the sentence and object level. For instance, ACHMI metric measures the share of clinical components in the generated output. When applying LLM to pharmacy, we should check whether the model produces invented therapeutic indications for the drugs.^[5,10]

7.2] Output Validity against Source Text

Validity can be determined by examining whether the generated text contains information that cannot be part of the output based on the source text. In pharmacy, the groundedness of LLMs during data extraction from records and synthesis of complex scientific texts needs to be assessed. It is necessary to point out errors such as specific to general because they can cause drug interactions.^[16,19,20]

7.3] Toxicity and Unsound Advice

LLMs need to be tested for toxicity and unadvisable suggestions that may pose safety hazards. CARES serves as a framework for model benchmarking based on the principles of safety and level of harm as well as their response to difficult questions. Models have provided suggestions that include approval of suicide.^[4,5,8]

7.4] Human expert review as the gold standard

The human-in-the-loop testing process serves as the gold standard for the safety evaluation of large language models in the context of pharmacy practice. This involves the creation of a team of experts comprising pharmacists, physicians, and ethicists who will judge the output with regard to its clinical utility, tone, and empathy. While the computer has shown

effectiveness, only humans can bring nuance to the output.^[4,5,16,20]

8. Mitigation Strategies The integration of language models into pharmacy practice needs to be carefully considered so as not to contribute to the dissemination of misinformation regarding drugs. This is necessary in order to ensure medication safety, facilitate decision-making processes, and ultimately achieve positive patient outcomes.^[4,9]

8.1] Expert-in-the-Loop and Pharmacist Oversight: Since the probability of making errors while generating results from LLMs is relatively high, the element of humans becomes necessary. Pharmacists can be regarded as the validators of outputs produced by those models. By using the expert-in-the-loop approach, it becomes possible to achieve considerable progress with regards to drug discoveries. All validation procedures that take place within the process led by pharmacists always include the assessment of outputs from the model.^[5,15,18]

8.2 Risk Management Cannot Protect against Every Potential Risk

Risk management is not all about protection against potential risks. Mistakes may also sometimes occur while operating LLMs. Before using these models, risk management should be considered carefully. Without which, key elements such as data recall, audits and human involvement could be affected adversely. Due to the same, additional actions must be taken to prevent risks involved in producing data.^[7,13]

9. Governance, Regulation, and Ethical Considerations

The implementation of LLMs in pharmaceutical practices creates complex issues of regulation and ethical implications that should be taken into consideration to guarantee the clinical safety of such integration. Effective governance mechanisms must be developed to control the associated risks of automated decision-making while preserving the standards of evidence-based pharmacotherapy. Proactive governance on both institutional and governmental levels is crucial to counteract systemic risks to accountability and integrity of pharmacy practice in high-stakes situations.^[2]

9.1] Accountability in the use of pharmacy: AI One of the main issues arising with the clinical application of LLMs is the absence of the relevant legislative acts that would establish the professional liability framework in case of adverse events related to the usage of AI technology.^[1,2] Existing standards of medical practice are ambiguous in assigning liability

between the pharmacist, the software vendor, and the institution.^[2,6] To uphold the standard of care, a licensed pharmacist must keep the final decisional authority over medication prescriptions.^[15]

9.2] Requirements for transparency and explainability: The black box approach employed in some LLMs makes it difficult for a pharmacist to validate AI-generated therapy recommendations. Specific mechanisms of governance need to be developed to facilitate the provision of transparent justification of the proposed courses of treatment to allow for clinical decision-making. From an ethical perspective, informed consent requires informing patients about the fact that an AI is generating their medication plans.^[2,15]

9.3] Expectations of clinical AI regulators: At present, the regulatory standards of medical software do not cover the specific characteristics of LLMs, such as open-endedness and the probabilistic nature of the results.^[2,10] Regulators move toward establishing tiered risk frameworks that will allow for distinguishing low-stake information services and high-stakes activities of recommending therapies.^[2] Specific evaluation procedures should be standardized in light of constant model updating.^[16]

9.4] Ethical boundaries of autonomous medication advice: The autonomy that some LLMs enjoy may be dangerous as it may result in incorrect self-diagnosis and the subsequent complications of patients' conditions. LLMs are supposed to be a copilot of clinicians, not a substitute for their experience and professional judgment. Currently existing autonomous clinical systems lack sufficient reasoning and are incapable of aligning with medical truths.^[15,6]

10. Practical Recommendations for Pharmacy Practice

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10.1 Implementation Prerequisites and SOPs

Before implementing large language models (LLMs) in drug information services or clinical care settings, there are a certain number of implementation prerequisites that need to be addressed. Local testing in the setting of standardized clinical scenarios needs to be performed to define the base error rate and possible dataset bias of the LLM used.^[15] Also, Standard Operating Procedures (SOPs) need to emphasize the role of LLMs as assistive “copilots” as opposed to independent clinical decision-makers. The content generated by AI needs to be properly labeled and always go through mandatory human validation before any

clinical decisions are taken.^[2,15]

10.2 Education and the Red-Flag Checklist For the safe use of AI in clinical settings, pharmacists need to obtain targeted education on different types of hallucinations performed by the LLM, such as fact-conflicting or context-conflicting internally inconsistent messages.^[7] For this purpose, a standardized "red-flag checklist" needs to be implemented to identify the signs of potential LLM hallucinations.^[16,2,4] Specifically, when performing a review of the output generated by the system, pharmacists need to pay attention to several signs:

- A strong confident therapeutic recommendation without sufficient backing;
- Citations from sources with unclear origins or fabricated authors;
- Absence of key patient data, especially existing contraindications or drug allergies;
- Internal inconsistencies and contradictions in the LLM message.

10.3 Workflow and Verification Protocols As far as ongoing medication safety is concerned, the proposed workflow for LLM should rely on an "expert-in-the-loop" approach. Specifically, a pharmacist formulates a query or document, and an LLM generates a draft answer, which should be followed by active verification of all facts stated against relevant pharmacological databases (e.g., drug monographs or literature). Documentation should require that no AI-generated therapeutic plan is approved and included in a patient's electronic medical record without expert verification.^[15,18,16]

11. Future Directions

The development of generative AI in pharmacy practice is contingent upon shifting from the creation of general-purpose tools to those which are both clinically competent and focus on drug safety.^[7] Future research should not be limited to language fluency but should incorporate the rigorous demands placed upon pharmacists by patient well-being.^[9,10] Benchmarking, hybridization, and regulation will play crucial roles in ensuring that AI serves as a resource and not a source of erroneous clinical information.^[13,15]

The usage of large language models (LLMs) in health care institutions allows optimizing the processes of administration and patient interaction. Regrettably, the implementation of LLMs in the sphere of clinical pharmacy is fraught with numerous risks since LLMs always generate AI hallucinations. Due to the necessity to observe maximum accuracy when issuing prescriptions and dispensing medications, any mistakes that may occur in the operation of AI

systems are extremely risky not only for patients' safety but also for the decision-making process of pharmacists.^[1,6,16]

12.1] Advantages and Disadvantages of Using LLMs: Although there are multiple significant downsides, LLMs can be used in clinical pharmacy due to their benefits. For instance, LLMs allow simplifying documentation preparation, patient education, and summarizing of the data retrieved from different sources. Nevertheless, besides AI hallucinations, the use of LLMs raises concerns about biases, breaches of patient privacy rights, and generative AI.^[12,15,7]

12.2] CONCLUSION

In conclusion, LLMs can be employed as helpers in document creation and management, although they should be controlled when used in clinical practice.

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