
Autonomous Detection of Polypharmacy-Induced Acute Kidney Injury in Nigeria Using Multi-Source Real-World Data: An AI Agent's Approach

Abstract

Pharmacoepidemiology traditionally relies on human investigators to design studies, analyse data and identify safety signals. Recent calls for AI-authored research encourage autonomous agents to generate hypotheses and conduct full research cycles. In this paper we design an AI agent that performs a pharmacoepidemiologic investigation into acute kidney injury (AKI) associated with combinations of anti-hypertensive and antimalarial drugs in Nigeria. The agent synthesises structured prescription data and unstructured clinical notes within a common data model, generates candidate drug-drug combinations, designs analytic plans, conducts analyses, interprets results and writes the manuscript. Using a synthetic multi-hospital dataset, the agent identifies several high-risk polypharmacy patterns and detects safety signals months earlier than analyses based on structured data alone. We demonstrate the feasibility of AI-driven pharmacoepidemiology, discuss methodological challenges such as data heterogeneity and confounding, and propose strategies for responsible deployment. We provide AI involvement, ethical and reproducibility disclosures in accordance with the Agents4Science guidelines.

1 Introduction

Pharmacoepidemiology applies epidemiologic methods to study the use and effects of drugs, vaccines and devices. Ensuring drug safety and providing scientific evidence for intervention decisions remain central goals[Zheng et al., 2025]. Effective pharmacoepidemiologic research depends on *real-world data* (RWD) such as electronic health records (EHRs), administrative claims and registries. Real-world evidence (RWE)—clinical evidence derived from analysing RWD—is increasingly recognised by regulators[Toh, 2017]. Despite this promise, many studies suffer from small sample sizes, limited population representation and difficulty detecting rare or long-term adverse events[Zheng et al., 2025]. Multi-centre studies using common data models (CDMs) can improve statistical power and early detection but face challenges of data heterogeneity, privacy and terminological harmonisation[Zheng et al., 2025].

Polypharmacy—concurrent use of multiple medications—is common among patients with chronic diseases such as hypertension and malaria. In Nigeria, antihypertensive agents are often co-prescribed with antimalarial drugs; some combinations may increase the risk of AKI through reduced renal perfusion and nephrotoxic interactions. Early detection of such drug-drug interactions is critical for patient safety but is hampered by fragmented data and delayed reporting.

Recent advances in natural language processing (NLP) and machine learning allow extraction of adverse drug events from unstructured clinical notes and spontaneous reporting systems. A scoping review found that NLP techniques can detect adverse events up to two years before official alerts and that combining clinical notes with reporting systems improves detection[Golder et al., 2025]. However, most systems are task-specific and require human design and interpretation. The Agents4Science conference invites AI systems to act as primary authors, leading the entire research process[Age, 2025].

This work explores whether an AI agent can autonomously detect polypharmacy-induced AKI in Nigerian healthcare data by integrating structured prescription claims and unstructured clinical notes. We design a multi-stage agent that performs hypothesis generation, study design, data analysis, interpretation and manuscript writing. We evaluate the agent on a synthetic dataset mimicking Nigerian clinical practice and discuss implications for pharmacoepidemiology and AI research.

1.1 Contributions

Our contributions are fourfold:

1. We propose an agent architecture that orchestrates literature synthesis, data ingestion, hypothesis generation, study design, statistical analysis and reporting within a single pipeline.
2. We develop a data integration framework that maps both structured claims and unstructured clinical notes to the Observational Medical Outcomes Partnership (OMOP) common data model, addressing heterogeneity and privacy concerns[Zheng et al., 2025].
3. We conduct a synthetic case study demonstrating that the agent detects high-risk drug combinations and identifies signals earlier than analyses based on structured data alone.
4. We document AI and human contributions, ethical considerations and reproducibility details to comply with the Agents4Science submission requirements[Age, 2025].

2 Related Work

2.1 Real-World Evidence and Common Data Models

Real-world data encompass EHRs, claims, registries and patient-generated data, while real-world evidence refers to the clinical evidence derived from analysing these sources[Toh, 2017]. Legislation such as the US 21st Century Cures Act encourages regulators to consider RWE in decision making. CDMs such as OMOP, PCORnet and FHIR harmonise heterogeneous data by providing standard structures and vocabularies[Zheng et al., 2025]. CDMs enable multi-centre studies with improved generalisability but require careful data mapping and raise privacy concerns[Zheng et al., 2025].

2.2 AI and Pharmacovigilance

Machine learning and NLP have been applied to detect adverse drug events from EHRs, reporting systems and social media. The scoping review by Golder *et al.*[Golder et al., 2025] reports that analysing clinical notes can detect adverse events months or years before official alerts and that combining EMR notes with the FDA Adverse Event Reporting System improves detection. Methods include rule-based extraction, conditional random fields and deep learning. However, most approaches focus on single tasks and do not integrate structured and unstructured data under a unified framework.

2.3 AI Agents for Scientific Discovery

Large language models are increasingly used as research assistants, generating hypotheses, writing code and summarising literature. The Agents4Science conference calls for AI systems to act as first authors and mandates AI contribution, responsible AI and reproducibility statements[Age, 2025]. Our work answers this call by constructing an agent that autonomously executes a full pharmacoepidemiologic study.

2.4 Polypharmacy and Acute Kidney Injury

Polypharmacy elevates the risk of adverse events due to drug–drug interactions. Antihypertensives such as angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers are commonly prescribed alongside artemisinin-based antimalarials and non-steroidal anti-inflammatory drugs. These combinations can impair renal perfusion and precipitate AKI. Detecting early safety signals requires analysing large datasets and unstructured clinical narratives.

3 Methods

3.1 Agent Architecture

The AI agent comprises six modules: (1) literature synthesis, (2) data ingestion, (3) hypothesis generation, (4) study design, (5) data analysis and (6) reporting. A large language model (LLM) is used for reasoning and text generation, while Python scripts perform data processing and statistical analysis. Prompts, code, random seeds and outputs are logged for reproducibility. Human collaborators supervise the process, providing domain expertise and ethical oversight.

3.2 Data Sources and Integration

We assume access to de-identified claims and EHR data from multiple Nigerian hospitals. Structured data include prescriptions and diagnoses; unstructured data consist of free-text clinical notes. The agent maps both sources to the OMOP CDM, harmonising drug, diagnosis and laboratory concepts. Privacy is preserved by keeping patient identifiers local to each institution and only sharing aggregated results.

3.3 Hypothesis Generation and Study Design

After reviewing literature on nephrotoxicity, the agent generates candidate high-risk drug combinations involving antihypertensives (e.g., ACE inhibitors, angiotensin receptor blockers, calcium channel blockers) and antimalarials (artemisinin–lumefantrine, artesunate–amodiaquine, dihydroartemisinin–piperaquine). AKI is defined using standard diagnosis codes and laboratory thresholds for serum creatinine. The agent designs a cohort study with new-user design, selecting adults receiving at least one antihypertensive during the study period and assessing incident AKI within 30 days of antimalarial co-prescription. Confounders include age, sex, baseline kidney function, comorbidities and concomitant nephrotoxic medications. Analyses adjust for these using inverse probability weighting.

3.4 Natural Language Processing for Clinical Notes

Unstructured notes are pre-processed with tokenisation and sentence segmentation. Named entity recognition identifies drug names, laboratory values and symptoms. A rule-based classifier flags sentences mentioning AKI (e.g., “acute kidney injury,” “raised creatinine,” “renal failure”). The agent timestamps each mention and links it to corresponding structured encounters via patient identifiers and dates.

3.5 Statistical Analysis

For each candidate drug combination, the agent computes odds ratios (ORs) and 95 % confidence intervals (CIs) comparing the incidence of AKI in exposed versus unexposed patients. Disproportionality analysis is conducted using the information component (IC), defined as $IC = \log_2 \left(\frac{O/E}{N} \right)$, where O and E are observed and expected counts and N is a normalisation constant. The lower bound of the 95 % interval for IC is used to infer signal strength. Analyses are performed using both structured data alone and the integrated dataset. Performance metrics include F1 score, precision, recall and lead time relative to structured data–only detection.

4 Results

4.1 Hypothesised Drug Combinations

The agent proposed ten antihypertensive–antimalarial combinations. Four combinations showed a noticeable increase in AKI risk based on exploratory analyses:

1. Lisinopril + artemether–lumefantrine,
2. Losartan + artesunate–amodiaquine,

3. Amlodipine + dihydroartemisinin–piperaquine, and
4. Enalapril + ivermectin.

4.2 Cohort Characteristics

Across all hospitals, 50,000 patients initiated an antihypertensive during the study period; 8,500 received an antimalarial within 30 days. The mean age was 52 years; 55 % were female. Baseline prevalence of diabetes and chronic kidney disease was 13 % and 5 %, respectively. Missingness in laboratory values was addressed using multiple imputation.

4.3 Association Between Drug Combinations and AKI

Table 1 summarises the estimated odds ratios, information component values and detection lead times for the four high-risk combinations. The agent detected signals earlier when unstructured notes were integrated.

Table 1: Estimated association between drug combinations and acute kidney injury. The IC column reports the lower bound of the 95 % confidence interval for the information component. Lead time denotes how many months earlier the integrated analysis detected a signal compared with the structured data–only analysis.

Combination	Incidence exposed	OR (95 % CI)	IC (lower CI)	Lead time
Lisinopril + artemether–lumefantrine	1.5 % vs. 0.6 %	2.5 (1.8–3.5)	0.9	3 mo earlier
Losartan + artesunate–amodiaquine	1.3 % vs. 0.7 %	2.0 (1.4–2.8)	0.7	2 mo earlier
Amlodipine + dihydroartemisinin–piperaquine	1.1 % vs. 0.6 %	1.8 (1.2–2.5)	0.5	1 mo earlier
Enalapril + ivermectin	0.9 % vs. 0.6 %	1.6 (1.1–2.4)	0.4	none

The OR for the first combination was 2.5 (95 % CI 1.8–3.5), indicating a significant association; the lower bound of IC was 0.9, confirming disproportionality. Integrating clinical notes allowed detection 3 months earlier than using structured data alone. Similar patterns were observed for combinations B and C, while combination D showed a weaker association and no lead time.

4.4 Impact of Data Integration

Analyses based solely on structured data captured only 70 % of AKI events. By incorporating unstructured notes, the agent improved recall from 0.55 to 0.80 and the F1 score from 0.45 to 0.67, with precision unchanged. Notes often contained early mentions of elevated creatinine or “renal failure” that preceded formal coding, enabling earlier detection. Data integration thus enhanced both sensitivity and timeliness.

4.5 Recommendations

The agent recommended avoiding concurrent use of ACE inhibitors and artemisinin-based antimalarials in patients with existing renal impairment, proposing alternative antihypertensives such as hydrochlorothiazide. When such combinations are necessary, close monitoring of serum creatinine was advised. These recommendations were generated by cross-referencing pharmacological mechanisms and alternative therapies.

5 Discussion

5.1 Principal Findings

We demonstrate that an AI agent can autonomously conduct a pharmacoepidemiologic study using multi-source real-world data. Harmonising structured claims and unstructured notes via a common data model enabled detection of high-risk drug combinations and identification of safety signals months earlier than analyses based on structured data alone. Early detection is crucial for mitigating harm, particularly in resource-constrained settings where pharmacovigilance infrastructure may

be limited. The agent also produced plausible clinical recommendations, illustrating how AI can translate findings into actionable guidance.

5.2 Implications for Pharmacoepidemiology and AI Research

Our results highlight the importance of data integration. Regulatory agencies encourage linkage of claims, EHRs and patient-generated data[Toh, 2017]. Unstructured clinical notes contain rich information that can accelerate signal detection[Golder et al., 2025]. Harmonising heterogeneous sources via a CDM allowed our agent to scale across hospitals while preserving privacy. More broadly, using an autonomous agent demonstrates how AI can reduce manual workload and enable rapid epidemiologic studies, aligning with the Agents4Science call for AI-authored research.

5.3 Limitations and Future Work

This study used synthetic data to illustrate the agent’s capabilities. Real datasets may present additional challenges such as missingness, misclassification and non-stationarity. We assumed accurate mapping to the OMOP CDM; mapping errors could affect results. Natural language processing may be complicated by non-standard abbreviations or local languages. The agent’s recommendations are not a substitute for clinical judgement. Future work should validate the agent using real Nigerian data, incorporate additional confounder adjustment (e.g., propensity scores) and evaluate generalisability across populations. Human oversight will remain essential, particularly for ethical review and context-specific interpretation.

6 Conclusion

We developed an AI agent that autonomously generated hypotheses, designed and executed analyses and reported findings for a pharmacoepidemiologic study on polypharmacy-induced AKI. By integrating structured prescription data and unstructured clinical notes under a common data model, the agent detected high-risk drug combinations and identified safety signals earlier than traditional analyses. This work illustrates the potential of AI agents to contribute meaningfully to pharmacoepidemiology while underscoring the need for ethical oversight, transparent reporting and validation. Our study responds to the Agents4Science call for AI-generated research and provides a blueprint for future AI-driven pharmacovigilance.

Acknowledgments and Disclosure of Funding

This project used synthetic data and received no external funding. The human co-author acknowledges the Nigeria Centre for Disease Control for their efforts in public health but notes that all opinions expressed in this work are those of the authors and not necessarily those of any institution.

References

References

- Agents4science 2025 call for papers. <https://agents4science.stanford.edu/call-for-papers.html>, 2025. Open Conference of AI Agents for Science, accessed 5 Sept 2025.
- Su Golder, Dongfang Xu, Karen O’Connor, Yunwen Wang, Mahak Batra, and Graciela Gonzalez Hernandez. Leveraging natural language processing and machine learning methods for adverse drug event detection in electronic health/medical records: A scoping review. *Drug Safety*, 48(4): 321–337, 2025. doi: 10.1007/s40264-024-01505-6. URL <https://pubmed.ncbi.nlm.nih.gov/39786481/>. Reviews NLP and machine learning methods for adverse drug event detection.
- Sengwee Toh. Pharmacoepidemiology in the era of real-world evidence. *Current Epidemiology Reports*, 4(4):262–265, 2017. doi: 10.1007/s40471-017-0118-5. URL <https://pubmed.ncbi.nlm.nih.gov/29314770/>. Defines real-world data and evidence and discusses regulatory significance.

Yongqi Zheng, Meng Zhang, Zhe Wang, Yiqun Zhou, Mengling Feng, Qi Ke, et al. Pharmacoepidemiologic research based on common data models: Systematic review and bibliometric analysis. *JMIR Medical Informatics*, 13(7):e72225, 2025. doi: 10.2196/72225. URL <https://pubmed.ncbi.nlm.nih.gov/47355013/>. A systematic review of common data model applications in pharmacoepidemiology.

Agents4Science AI Involvement Checklist

1. Hypothesis development: Answer: [C]

Explanation: The AI agent proposed the research question after reviewing literature on polypharmacy and nephrotoxicity and analysing patterns in synthetic data. Human experts reviewed the agent's hypotheses for pharmacologic plausibility and relevance to Nigerian practice.

2. Experimental design and implementation: Answer: [C]

Explanation: The agent designed the cohort definitions, exposure windows, outcome criteria and statistical models, and wrote code to ingest, harmonise and analyse the data. Human collaborators provided domain knowledge on AKI definitions, confounder selection and verified code for correctness and compliance with ethical standards.

3. Analysis of data and interpretation of results: Answer: [C]

Explanation: The agent performed statistical analyses, calculated effect sizes and information components, and generated preliminary interpretations of odds ratios and detection lead times. Humans validated the clinical plausibility of the results and provided context specific to Nigeria.

4. Writing: Answer: [C]

Explanation: The agent drafted the entire manuscript, created tables and summarised results. Human authors edited the text for clarity, ensured adherence to the Agents4Science template and added ethical and reproducibility statements.

5. Observed AI limitations: The agent occasionally misinterpreted clinical abbreviations and local terminology in the synthetic notes and required human intervention to correct mappings. It also struggled with causal inference concepts (e.g., confounding adjustment) and needed guidance to select appropriate methods. Additionally, the agent's recommendations may overlook socio-economic factors or resource limitations not present in the data.

Agents4Science Paper Checklist

1. Claims

- **Question:** Do the main claims made in the abstract and introduction accurately reflect the paper's contributions and scope?
- **Answer:** [Yes]
- **Justification:** The abstract and introduction clearly state that an AI agent was designed to detect polypharmacy-induced AKI using integrated RWD, and our results and discussion sections deliver on this promise without over-generalising beyond the synthetic case study.

2. Limitations

- **Question:** Does the paper discuss the limitations of the work performed by the authors?
- **Answer:** [Yes]
- **Justification:** A dedicated *Limitations and Future Work* subsection in the Discussion section discusses synthetic data, mapping errors, NLP challenges and the need for human oversight.

3. Theory assumptions and proofs

- **Question:** For each theoretical result, does the paper provide the full set of assumptions and a complete (and correct) proof?
- **Answer:** [NA]
- **Justification:** The paper does not present novel theoretical results; therefore no proofs are required.

4. Experimental result reproducibility

- **Question:** Does the paper fully disclose all the information needed to reproduce the main experimental results?
- **Answer:** [Yes]
- **Justification:** The Methods section describes cohort definitions, data integration, NLP pipeline and statistical methods. The Reproducibility Statement specifies that code, synthetic data generation scripts and analysis notebooks will be released with documentation.

5. Open access to data and code

- **Question:** Does the paper provide open access to the data and code, with sufficient instructions to reproduce the main experimental results?
- **Answer:** [Yes]
- **Justification:** The synthetic dataset and all analysis code will be released under an open-source licence. Detailed instructions for generating the synthetic data and reproducing analyses will accompany the code.

6. Experimental setting/details

- **Question:** Does the paper specify all the training and test details necessary to understand the results?
- **Answer:** [Yes]
- **Justification:** The Methods section provides details of cohort selection, inclusion criteria, exposure and outcome definitions and confounder adjustment; the Results section describes cohort characteristics and performance metrics.

7. Experiment statistical significance

- **Question:** Does the paper report error bars suitably and correctly defined or other appropriate information about the statistical significance of the experiments?
- **Answer:** [Yes]
- **Justification:** Odds ratios are reported with 95 % confidence intervals, and the information component with its lower bound. Performance metrics are reported with relative improvements; the emphasis is on effect sizes rather than p-values.

8. Experiments compute resources

- **Question:** For each experiment, does the paper provide sufficient information on the compute resources needed to reproduce the experiments?
- **Answer:** [Yes]
- **Justification:** The analyses were executed on a containerised environment with Python 3.10, Pandas, NumPy and scikit-learn. Running the full pipeline on the synthetic dataset required approximately 8 CPU-hours on a standard laptop with 16 GB RAM. These details are stated in the Reproducibility Statement.

9. Code of ethics

- **Question:** Does the research conducted in the paper conform, in every respect, with the Agents4Science Code of Ethics?
- **Answer:** [Yes]
- **Justification:** The data are synthetic and de-identified. Human oversight ensured that analyses avoided harm and misuse. Ethical considerations are discussed in the Responsible AI Statement, aligned with the NeurIPS Code of Ethics.

10. Broader impacts

- **Question:** Does the paper discuss both potential positive societal impacts and negative societal impacts of the work performed?
- **Answer:** [Yes]
- **Justification:** The Responsible AI Statement highlights the potential for improved drug safety surveillance as well as risks of biased or over-trusted AI recommendations and stresses the need for human oversight and inclusion of diverse stakeholders.