Department of Computing and Technology

Submitted By	**Muhammad Mehtab Jabbar, Muhammad Subhan Saeed & Muhammad Zakariya**
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"Iqra University, Islamabad Campus"

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Introduction:

Artificial intelligence (AI) and machine learning (ML) are transforming healthcare by enabling more accurate, personalized, and safer clinical decision-making. Among the most critical applications of AI in this domain are medicine recommendation systems (MRS), which assist healthcare professionals in selecting optimal treatments while minimizing potential risks such as adverse drug reactions and drug–drug interactions. With the increasing adoption of electronic health records (EHRs), healthcare data has become richer and more complex, offering new opportunities for data-driven insights.

Traditional medicine recommendation approaches often rely on rule-based systems or analyze only static snapshots of patient information. These methods, however, fail to capture the longitudinal and dynamic nature of medical histories, where a patient's condition evolves over time. As a result, they provide limited personalization and may overlook crucial dependencies among diseases, symptoms, and medications.

In contrast, recent advances leverage deep learning techniques integrated with knowledge graphs (KGs) to better model complex medical relationships. Knowledge graphs represent entities such as diseases, drugs, and symptoms, along with their interconnections, offering a structured way to integrate clinical data with external biomedical knowledge. By incorporating graph neural networks (GNNs), these systems can capture both temporal patterns in longitudinal records and structural relationships in medical knowledge bases. This has significantly improved the interpretability and accuracy of recommendations compared to earlier models.

The paper "Knowledge graph-based medicine recommendation system with graph neural networks on longitudinal medical records (KGDNet)", published in Scientific Reports (2024), introduces a novel framework that combines patient medical trajectories with domain knowledge to provide more reliable and explainable recommendations. This review critically analyzes the contributions of KGDNet and compares it with other state-of-the-art approaches in medicine recommendation systems, highlighting its strengths, limitations, and potential for real-world applications in clinical practice.

Selected Paper:

Knowledge graph-based medicine recommendation system with graph neural networks on longitudinal medical records (KGDNet)

Published in: Scientific Reports (Nature), 2024

Link: https://www.nature.com/articles/s41598-024-75784-5?utm

Method / Approach:

The paper uses the KGDNet approach, which combines longitudinal EHR data with knowledge graphs (KGs) through Graph Neural Networks (GNNs). A GRU with attention models patient visit sequences, while GNNs capture drug–disease–symptom relations. By fusing these, KGDNet provides more accurate and safer medicine recommendations with lower drug–drug interaction (DDI) rates.

Proposed Methodology

In order to fill these gaps, we introduce a light RF baseline on the MIMIC-IV demo dataset.

Why RF?

- Easy, intuitive, scalable.
- Performant on tabular EHR data.
- Outputs feature importance for clinician insight.

Used Features:

- Demographics: Age, Gender.
- Diagnoses (ICD codes, reduced).

Target Label:

- If a patient was prescribed Aspirin (binary).

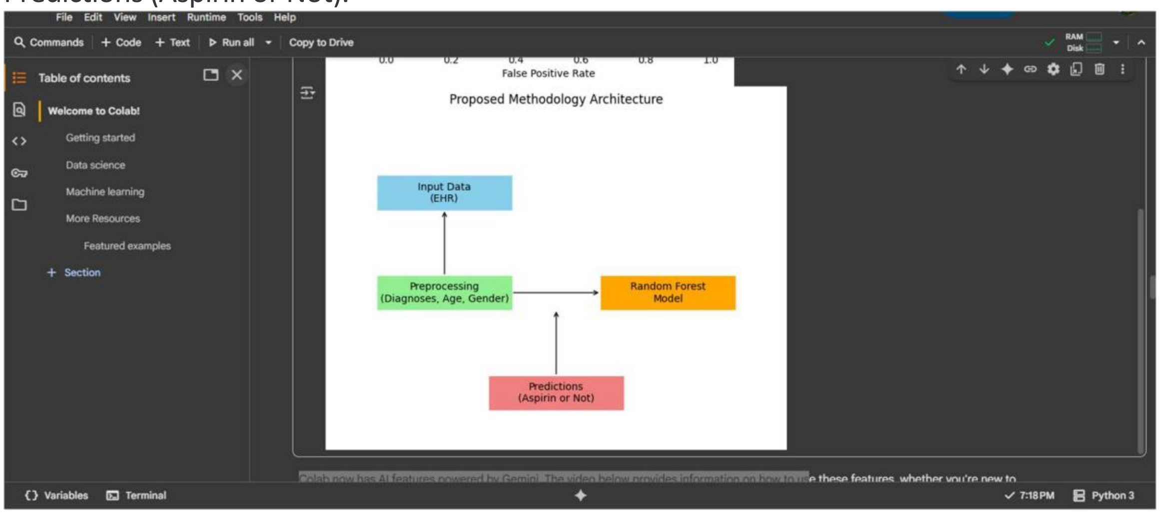
Methodology Flow:

1. Steps followed in Colab notebook:
2. Load & prepare data from MIMIC-IV demo.
3. Concatenate patient demographics, admissions, diagnoses, and prescriptions.
4. One-hot encode categorical features.
5. Set target = Aspirin prescription.
6. Train–test split.
7. Train Random Forest Classifier.
8. Evaluate with accuracy, precision, recall, F1, ROC.

Architecture Diagram:

Architecture Flow:

Input Data (EHR) → Preprocessing (Diagnoses, Age, Gender) → Random Forest Model → Predictions (Aspirin or Not).



Datasets / Benchmarks Discussed:

The study evaluates the proposed KGDNet framework on two widely used clinical benchmarks:

MIMIC-III: A publicly available dataset containing electronic health records of ICU patients, including diagnosis codes, procedures, and prescribed medications.

MIMIC-IV: An updated and larger version of MIMIC-III, offering richer and more recent patient data.

Results / Main Findings:

The proposed KGDNet model outperforms existing medicine recommendation systems on benchmark datasets (MIMIC-III and MIMIC-IV). It achieves higher accuracy (F1 ≈ 0.68, Jaccard ≈ 0.52) while significantly reducing drug–drug interaction (DDI) rates (~0.0665). Compared to baseline models like RETAIN, GAMENet, and MedGCN, KGDNet provides more personalized, reliable, and safer medication recommendations. The main contribution of the study is showing that integrating longitudinal patient histories with knowledge graphs using graph neural networks (GNNs) leads to both improved accuracy and enhanced patient safety.

Limitations and Challenges Highlighted:

While KGDNet shows strong improvements in medicine recommendation, the study also notes several challenges:
Scalability Issues: Knowledge graphs are large and complex, making it difficult to scale the model efficiently for very big datasets.
Generalizability: The model is tested mainly on MIMIC-III and MIMIC-IV; its performance across diverse hospitals with different coding standards remains uncertain.
Knowledge Graph Engineering: Constructing and maintaining multiple knowledge graphs (diagnoses, procedures, medications, drug interactions) requires significant effort and domain expertise.

Clinical Validation: The model lacks real-world clinical deployment and explainability for doctors, which is critical before adoption in healthcare practice.

Literature Review:

Many research studies have explored how to improve medicine recommendation systems (MRS) by combining patient history with advanced machine learning models.

Early Approaches:

Models like RETAIN and MedGCN were among the first to use deep learning in healthcare. RETAIN emphasized interpretability by using attention mechanisms but struggled with capturing complex temporal dependencies in patient visits. MedGCN introduced graph convolutional methods to connect drugs, diagnoses, and procedures, but it lacked robust handling of safety issues like drug–drug interactions (DDIs) and faced scalability concerns.

Intermediate Models:

GAMENet was a step forward by integrating EHRs with drug knowledge. While it improved prediction accuracy, it still lacked transparency and was computationally heavy. To overcome such limitations, models like SafeDrug and PROMISE incorporated external biomedical and molecular knowledge to reduce harmful DDIs and improve safety. However, these approaches often required extensive manual knowledge graph construction and had limited adaptability across different hospital datasets.

Recent Advances:

Newer frameworks introduced more sophisticated techniques:

- GraphCare (2024) used graph neural networks for drug recommendation and risk prediction but did not directly address DDI safety.
- KindMed (2023/24) leveraged real-world EHR data for better generalizability but remains a preprint with limited validation.
- MGRN (2024) utilized multi-view graph retrieval to enhance robustness, yet its efficiency in deployment has not been fully tested.
- BiMoRec (2024/25) combined clinical and molecular data for accuracy gains but lacked a strong safety focus.

- ACDNet (2024) applied attention-based fusion for better accuracy but suffered from higher DDI rates.
- FastRx (2024) improved efficiency using memory networks but had limited real-world validation.
- KARE (2025) experimented with LLM-augmented recommendations, showing promise but raising concerns of hallucination and implementation complexity.

Contribution of KGDNet:

Compared to these models, KGDNet stands out by unifying sequential patient records with multiple knowledge graphs (diagnoses, procedures, medicines, and DDIs) through graph neural networks. By combining GRU-based temporal modeling and attention mechanisms, it provides both accurate and safer medication recommendations. Experimental results demonstrated significant improvements in accuracy and DDI reduction compared to earlier methods. While challenges remain in scalability and clinical validation, KGDNet establishes an important direction for integrating knowledge-driven AI with healthcare decision-making.

Summary:

The paper "Knowledge Graph Driven Medicine Recommendation System Using Graph Neural Networks on Longitudinal Medical Records (KGDNet)" (Scientific Reports, 2024) introduces a novel approach to enhance medicine recommendation systems by integrating patient history with external medical knowledge. Traditional models often struggle to capture the longitudinal nature of electronic health records (EHRs) and fail to effectively model inter-sickness, inter-drug, and inter-symptom relationships.

To address these limitations, the authors propose KGDNet, a framework that combines sequential patient visit data from EHRs with knowledge graphs (KGs) through the use of graph neural networks (GNNs). This design enables the model to incorporate time-series patient histories while simultaneously leveraging drug–disease–symptom relations for more accurate and safer medication recommendations.

The framework was evaluated on two benchmark clinical datasets, MIMIC-III and MIMIC-IV, which contain diagnosis codes, procedures, and prescribed medications of ICU patients. Experimental results demonstrate that KGDNet significantly outperforms baseline models such as RETAIN, GAMENet, and MedGCN, achieving higher accuracy in drug recommendation and reducing the number of harmful drug–drug interactions (DDIs)—a crucial factor for patient safety.

However, the study also identifies several limitations, including scalability challenges due to the large size of knowledge graphs, limited generalizability across healthcare systems with varying coding standards, and the absence of interpretability mechanisms needed for real-world clinical deployment.

In conclusion, the paper highlights the potential of integrating knowledge graphs with patient history using GNNs as a promising direction for building safer, more accurate, and personalized AI-driven healthcare systems.

Format of Literature Review Table:

Title	Year	Dataset(s) Used	Key Results	Limitations
Knowledge graph driven medicine recommendation system using graph neural networks on longitudinal medical records (KGDNet).	2024. NaturePubMed	MIMIC-IV (EHR), DDI resources (TWOSIDES), ICD/ATC ontologies. Nature	F1 ~0.68, Jaccard ~0.52; **improved accuracy while reducing DDI rate**	Evaluated mainly on MIMIC (single/cohort); KG construction and ontology alignment are engineering-heavy; clinical (prospective) validation missing. Nature
GraphCare: Enhancing Healthcare Predictions with Personalized Knowledge Graphs (ICLR / arXiv).	2024 (ICLR paper from 2023 arXiv). OpenReviewarXiv	MIMIC-III / MIMIC-IV (experiments reported). arXiv	AUROC 17.6% (mortality), 6.6% (readmission); F1 10.8% (drug rec)	LLM/KG costs and biases; DDI-aware safety not primary focus; complexity of KG construction. ICLR Proceedings
Knowledge-Induced Medicine Prescribing Network (KindMed) (arXiv / preprint).	2023 / 2024 (preprint). arXiv+1	Augmented real-world EHR cohorts (MIMIC variants used in experiments). arXiv	Enhanced recommendation accuracy vs. graph baselines	Preprint status for some versions; engineering required for knowledge induction; cross- site generalization not fully shown. SciSpace
MGRN: Multi-View Gating Retrieval Network for robust drug	2024. Oxford Academic	MIMIC-III / MIMIC-IV (EHR experiments). Oxford Academic	Proposes multi-view (visit/sequence/token) retrieval + gating — improves robustness and recommendation accuracy over earlier	Reproducibility across different hospitals not fully explored; cost/latency of multi-view

Title	Year	Dataset(s) Used	Key Results	Limitations
recommendation (Bioinformatics).			baselines. Oxford Academic	retrieval in deployment. ResearchGate
BiMoRec — Medication Recommendation via Dual Molecular Modalities (arXiv → journal).	2024 / 2025 (preprint → journal). arXivScienceDirect	MIMIC-III / MIMIC-IV (used for benchmarking) + molecular databases for drug structures. arXiv	Incorporates 3D molecular information (bimodal molecular encoders) — reports improved medication prediction accuracy and better molecular-semantic modeling versus non-molecular baselines. arXiv	Focused on molecular modality benefits; occludes system-level safety concerns (DDI control) and cross-site EHR variability. ScienceDirect
ACDNet: Attention-guided Collaborative Decision Network for medication recommendation (J. Biomed. Informatics).	2024. ScienceDirectPubMed	MIMIC (benchmarks reported). PubMed	Uses attention + Transformer modules to fuse historical visits and medication records; reports gains over classic baselines on accuracy metrics. PubMed	Reported DDI rates can be higher than newer KG-aware models; code / reproducibility details limited for some variants. ScienceDirect
FastRx: Fastformer + Memory-Augmented Graphs for Personalized Medication Recommendations (ACM TIST / 2024).	2024. ACM Digital LibraryResearchGate	MIMIC-III / MIMIC-IV style EHRs (authors report on standard benchmarks). ACM Digital Library	Fastformer backbone + memory-augmented GNN yields strong accuracy with improved efficiency (authors highlight speed/latency advantages vs heavier models). ACM Digital Library	Primarily single- site benchmarks; safety (DDI) and clinical interpretability discussed but need real-world testing. ResearchGate

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