Enhancing Hypoglycemia Prediction in Type 1 Diabetes through Semantic Knowledge Integration and Machine Learning Optimization*

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Abstract. Managing type 1 diabetes (T1D) is challenging due to unpredictable hypoglycemia episodes that can lead to serious health risks. To address this issue, a novel hybrid artificial intelligence (AI) model is being developed that aims to improve the prediction of hypoglycemia in patients with T1D by leveraging deep semantic knowledge of hypoglycemia and T1D integrated into a machine learning (ML) framework. This model incorporates comprehensive knowledge graphs derived from patient-specific data and evidence-based information. These graphs enable ML models that incorporate knowledge graph embeddings (KGEs) and advanced analytic techniques to improve early detection and proactive treatment of hypoglycemia. The expected result is a significant increase in prediction accuracy, sensitivity, and specificity compared to existing models, with a possible reduction in prediction error rates inferred from lower root-mean-square error (RMSE) values. Preliminary findings indicate that integrating semantic knowledge with machine learning in T1D care can identify complex patterns and patient-specific factors, improving the predictive accuracy of hypoglycemia and enabling more personalized, effective management strategies. Future work will focus on developing the hybrid model and implementing real-world validation in personalized medicine and hypoglycemia management, as well as evaluating its scalability and generalizability across diverse populations and healthcare settings.

Keywords: Semantic Integration · Machine Learning · Hypoglycemia · Type 1 Diabetes · Predictive Models

1 Introduction/Motivation

Hypoglycemia is a serious medical condition characterized by an abnormal drop in blood glucose levels, usually equal to or less than 70 mg/dL or 3.9 mmol/L [6]. The consequences of hypoglycemia can be life-threatening, potentially leading to seizures, loss of consciousness, and even death [9]. This risk is particularly more

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prevalent among patients receiving insulin treatment for diabetes and is three times more likely to occur in patients with type 1 diabetes (T1D) compared to those with type 2 diabetes (T2D) [18]. The varied frequencies of hypoglycemic episodes among patients emphasize the critical need for personalized management strategies that focus on predictions [35,6].

Predicting hypoglycemic events is challenging due to individual variations influenced by factors such as age, type of diabetes, and lifestyle. Symptoms like tremors, sweating, headaches, anxiety, and hunger serve as warning signals for an impending episode [3]. However, the onset and occurrence of these symptoms can differ among individuals and change over time [1]. This means that these symptoms can occur at different glycemic thresholds and can be absent in some cases, making it harder to anticipate hypoglycemia [18]. Additionally, hypoglycemic events can occur at different times of the day (daytime, postprandial, nocturnal). Circumstances like physical activities, food intake, and medication use influence when hypoglycemic events may occur or be most impactful - emphasizing the need for tailored approaches to preventing and predicting hypoglycemia in patients with T1D [18].

Given these complexities, various machine learning (ML) techniques like Random Forest [28], Support Vector Regressors [11], and Multi-Layer Perceptron Neural Networks [28] have been tested for hypoglycemia detection and prediction, using different input parameters and training algorithms [25,26]. However, these models have variable performance due to reliance on generalized data and lack of well-defined methods for personalization [10]. In addition to known factors such as long-term diabetes, recurrent hypoglycemia, and poor glycemic control [22], there are other potential predictors not routinely measured in clinical settings. Wearable and mobile sensing devices, automated insulin delivery systems, and continuous glucose monitors have accumulated extensive data for monitoring hypoglycemic events in real-world contexts for individual patients susceptible to hypoglycemia [14,16]. Studies have shown non-invasive detection of hypoglycemia by analyzing continuous sensor data including electrocardiogram, heart rate, respiratory rate, and lifestyle activity data from wearable devices [21]. However, a comprehensive method to analyze these variables and estimate the effects of manually entered and largely unquantified variables like stress, carbohydrate intake, physical activity, and infections on hypoglycemia is still lacking.

In addition, traditional ML methods struggle with feature selection, model portability, and interpretability, leading to inter- and intra-patient variability, time lag between sensor monitoring data and actual blood glucose values, and handling multifaceted healthcare data [32]. Customized data collection is needed to enable sophisticated analytical frameworks and semantic analysis. Moreover, medical repositories offer valuable information for understanding patients' conditions and developing personalized treatment plans [17]. In this context, ontologies and knowledge graphs (KGs) emerge as promising tools to address these limitations, enabling the integration of data from various sources — including clinical records, psychosocial databases, and wearable/mobile technologies. These tools extract, manage, interpret, and use semantically nuanced information associated with complex health conditions like diabetes. By integrating data semantics, more relevant features can be generated, handling noisy and ambiguous data, and optimizing ML models to interpret better context, patterns, relationships, and data meaning [34]. This synthesis provides a comprehensive view of a patient's health status, significantly improving the complexity, performance, and accuracy of prediction models [13,31].

This research focuses on developing advanced predictive models for hypoglycemia events in T1D patients by harnessing the synergistic potential of advanced semantic technologies and ML optimizations. Ontologies enrich KGs by providing structured data representation [4]. Knowledge graph embeddings (KGEs) preserve semantic relationships within these graphs, converting complex graph data into vector representations for ML algorithms. These embeddings integrate KGs with ML frameworks, broadening the predictive scope and fostering tailored hypoglycemia prediction and management. Techniques such as TransE and Graph Convolutional Networks (GCNs) generate these embeddings, facilitating feature selection and enhancing ML predictive algorithms' accuracy [33,5]. This research aims to uncover latent connections crucial to revolutionizing personalized health management by leveraging semantically enhanced ML models to parse T1D data and identify patterns beyond human expertise [13,31,5]. This approach promises to improve interoperability, advance personalized diabetes management, and enhance ML's application in predicting health outcomes. The implications extend beyond diabetes management, offering transformative prospects in e-health, personalized medicine, and health delivery systems. This paper presents the problem statement, contributions, research methodology, approach, and evaluation plan for the developed hybrid AI model.

2 State of the Art

Despite advances in prediction model optimization, the integration of ML models with semantic knowledge from diverse sources remains underexplored. This section reviews the extraction and representation of semantic knowledge within medical AI, focusing on technologies like KGs and ontologies. These studies bridge biological knowledge with medical histories and health outcomes of individual patients [29] [19]. Research has aimed to enhance disease information management, improve disease assessments, and support decision-making, potentially reducing errors in disease treatment and patient care by analyzing semantic knowledge from medical literature [26]. For example, Wang *et al.* (2022) [29] investigated personalized disease-specific KGs in cardiology and cardiovascular medicine, highlighting how KGs encapsulate critical patient information, including clinical symptoms, activities, diagnostic results, medical history, medications, and potential surgeries. This review also elucidates how KGs identify common risk factors among patients, thereby facilitating the discovery, sharing, and application of new knowledge by health professionals in diagnosis, treatment, and disease management [29].

Furthermore, a study explored the link between Kawasaki disease - a cardiac condition of unknown etiology primarily affecting children under five years of age - and two frequently mentioned viruses using semantically enabled searches and medical KGs. Another contribution reviewed the link between dietary factors and cardiovascular outcomes such as acute myocardial infarction and fatal coronary heart disease, using data from the Nurses' Health Study to build KGs. The KGs served as decision support tools in clinical settings [29].

Although limited research on KGs and their implications in diabetes management and treatment has been done, one study [30] successfully combined expert-reviewed clinical evidence to construct a KG encompassing diabetes complications such as retinopathy, diabetic nephropathy, foot issues, and depression. The data used for constructing the graph included T2D information such as lifestyle risk factors, clinical test results, medications, and their associated complications. The strength of relationships between these entities was determined through systematic evaluations and meta-analyses, providing insights into odds ratios, correlations, and relative risks.

3 Problem Statement and Contributions

This research contributes to semantic web research, ML, and the medical domain by developing a personalized, predictive solution for hypoglycemia in individuals with T1D that captures the effects of lifestyle factors like diet, physical activity, stress, and infections on blood glucose levels. The contributions of this work are manifold and innovative, including:

1. Construction of comprehensive knowledge graphs from patient-specific and evidence-based medical data, leveraging varied data sizes, types, velocities, and sources such as publications, databases, repositories, and evolving knowledge bases, captures patient-specific data inferring glucose variability and hypoglycemia in T1D individuals [2]. This research employs knowledge discovery techniques to mine bio-text corpora, uncover concepts and attributes, and establish correlations between data concepts organized within an interpretable and structured knowledge graph. These graphs serve as the backbone for ML algorithms, providing structured and semantically rich data to enhance predictive performance.
2. Developing a hybrid AI model that integrates deep semantic knowledge of hypoglycemia and T1D into a custom ML framework. While feature engineering and deep learning enable the extraction of predictive features and pattern identification within datasets, they often overlook semantic meanings, and the contextual information is incomplete, ambiguous, and messy [19]. This work incorporates a personalized approach to identify, characterize, and integrate high-quality, multidimensional data, leading to the identification of patterns and correlations across vital parameters derived from multiple sensors, paving the way for more accurate hypoglycemia prediction models. This research promises a more individualized and context-aware prediction capability by acknowledging each patient's intricacies.

3. Application of graph embeddings and advanced analytics to improve early detection and proactive management strategies for hypoglycemia. Knowledge graphs are gaining popularity for information storage and retrieval as the field shifts toward systems biology [15]. This work can be used as a reference for developing hypotheses and responding to inquiries about hypoglycemia, elevating the clinical utility of the predictive models.
4. Enhanced Predictive Performance through a substantial reduction in prediction error rates and increased accuracy, sensitivity, and specificity of hypoglycemia predictions. These improvements are critical for real-world clinical applications due to the potential costs of inaccuracies.
5. Integration of this work into clinical settings offers the opportunity to enhance day-to-day clinical practices by developing more accurate preventive measures and personalized treatment options for improved patient outcomes. Additionally, it creates a dynamic model that benefits from continuous improvement through real-world application [2]. The hybrid AI model and knowledge graphs in clinical scenarios contribute to an evolving knowledge base. Feedback from healthcare professionals and patient outcomes refines the AI algorithms and knowledge graph accuracies, ensuring sensitivity to the changing patient health data, reducing prediction errors, and increasing reliability [19][15]. Implementing machine learning models in the clinical environment, along with ongoing assessment and adaptation, strengthens the bridge between computational innovation and medical praxis, signifying a progressive step towards an adaptive, learning healthcare system.

These contributions address a critical need in diabetic care and represent a significant step in adopting AI and semantic analysis in precision medicine.

3.1 Aim and Research Questions

This research aims **to develop and evaluate a hybrid AI model that integrates semantic knowledge and optimizes ML models to improve the prediction of hypoglycemia in patients with T1D**. The goal is to address the limitations of current prediction models by integrating a comprehensive KG and advanced embedding techniques for personalized predictions, leading to proactive hypoglycemia management. To achieve this aim, several sub-research questions will be addressed:

RQ1 ***Insights from the Knowledge Graph***: What novel insights can KGs uncover regarding the factors contributing to hypoglycemia in patients with T1D? To what extent do these findings improve our understanding beyond traditional databases towards a more interconnected representation of patient data and biomedical knowledge?

RQ2 ***Role of Knowledge Graph Embeddings***: What role do KGEs play in improving the semantic representation and usability of patient data for predicting hypoglycemia in patients with T1D?

RQ3 ***Comparison with State-of-the-Art Approaches***: How does the semantic-based ML model compare with existing state-of-the-art approaches, particularly in terms of model performance—accuracy, sensitivity, specificity, and interpretability?

RQ4 ***Personalization and Subgroup Analysis***: How can KGs facilitate identifying and analyzing patient subgroups within T1D to personalize hypoglycemia prediction models?

4 Research Methodology and Approach

This section elaborates on the research plan depicted in Figure 1 and the systematic approach to leveraging KGs for hypoglycemia prediction in patients with T1D, as shown in Figure 2.

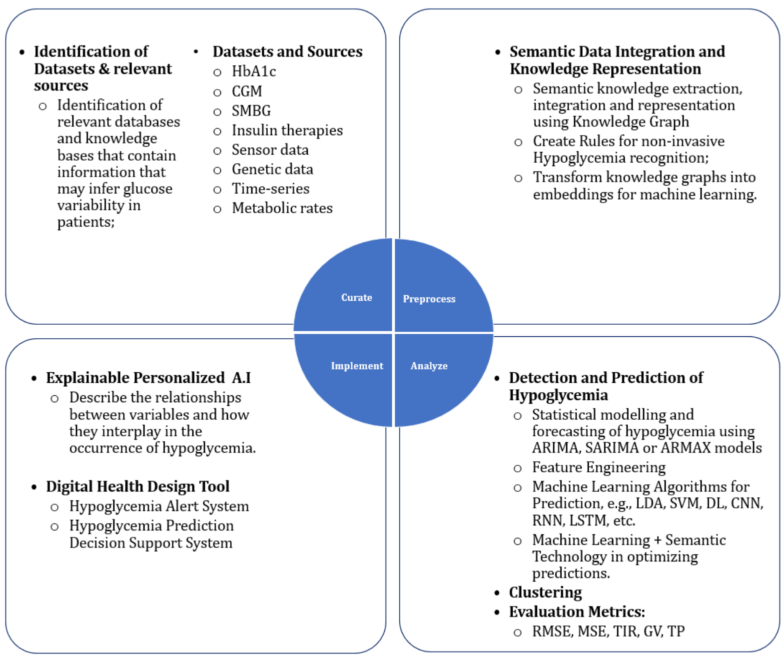

Fig. 1. Research Plan and Activities

4.1 Data Collection and Preparation

Structured and Unstructured Patient Data: To enrich our understanding of hypoglycemia in T1D, electronic health records (EHRs), patient databases, such as MIMIC-III database [12,23], the OhioT1DM Dataset, and the D1NAMO

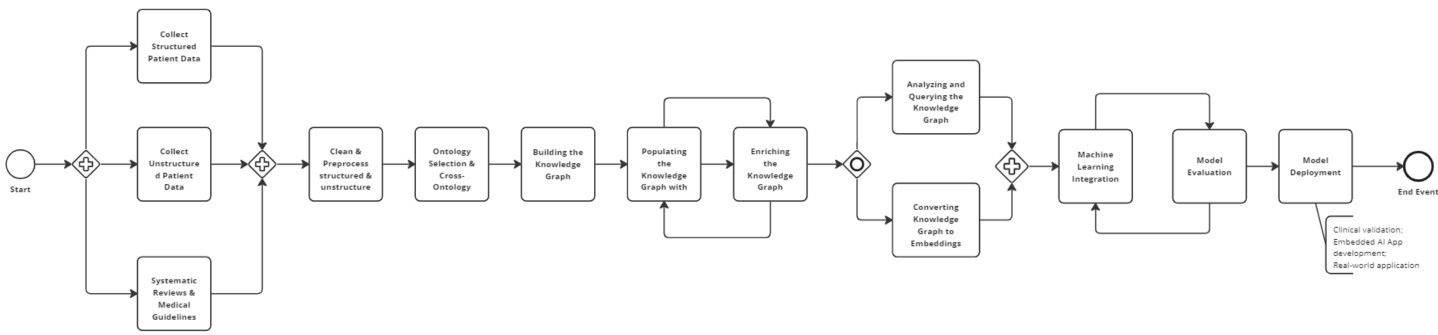

Fig. 2. A Process Map for Semantic Knowledge Integration and Machine Learning Optimization

Dataset [8] are accessed. These sources provide a wealth of structured clinical records alongside unstructured data captured from doctor's consultation notes and discharge summaries using natural language processing (NLP) techniques.

Systematic Reviews and Medical Guidelines: It is pertinent to ensure that the ontology's definitions align with the latest scientific findings. Hence, evidence-based recommendations gathered from medical journals, healthcare organizations, and clinical trial repositories across various articles including systematic reviews [7,20,27] - are essential for providing valuable insights into understanding the disease mechanisms and treatment outcomes and guiding clinical decisions.

4.2 Ontology Development and Knowledge Graph Construction

Ontology Selection: A variety of related ontologies such as the Diabetes Mellitus Ontology (DMO), Symptom Ontology (SYMP), Human Phenotype Ontology (HPO), SNOMED-CT, LOINC, RxNorm, and the Semantic Sensor Network Ontology (SSN) are meticulously curated to construct an extensive KG. The integration of these ontologies captures diabetes-related data, clinical symptoms and phenotypes, detailed classifications of symptoms and treatments, standardized laboratory test results and measurements, medication information, wearables and sensor data integration. Additionally, the TimeML ontology is utilized to capture temporal dynamics related to T1D events.

Building the Knowledge Graph: The selected ontologies are harmonized into a unified framework that serves as the schema for standardizing and mapping data from diverse sources onto the KG. This ensures semantic consistency through consistent representation of concepts and relationships, while synthesizing overlapping ontology elements to maintain the integrity within the semantic model.

Populating and Enriching the Knowledge Graph: Structured patient records are imported to populate the KG, and each element is aligned with defined entities and relationships from the ontology. Moreover, additional details from unstructured data such as patient-specific clinical notes and medical literature help fill in missing connections between entities. This process allows for integrating global medical knowledge along with personalized insights derived from patient records.

4.3 Leveraging Knowledge Graph Embeddings

In addition to identifying hypoglycemia mechanisms and understanding unique patient-specific care patterns, various embedding techniques such as TransE, DistMult or graph convolutional networks (GCNs) transform entities within graphs into numerical vectors while preserving their contextual meaning. These vector embeddings are then fed into ML models, aiding in predicting hypoglycemia risk factors alongside key features and patterns associated with hypoglycemia events.

4.4 Model Evaluation, Refinement, and Deployment

The KG and models are continuously assessed and enhanced, utilizing specified evaluation metrics, feedback from healthcare professionals, and new data to fine-tune the predictions and insights. This iterative process of model evaluation and refinement involves ongoing feedback loops aimed at boosting accuracy and reliability. Ultimately, validated models are implemented in clinical settings where they are monitored and adjusted based on real-world performance, as well as evolving healthcare developments.

5 Research Evaluation/Evaluation Plan

The effectiveness and quality of the proposed hybrid hypoglycemia prediction model are evaluated comprehensively. This involves delving into various aspects of the research questions to ensure thorough analysis and high-quality results.

RQ1 In order to comprehensively assess the model's capability to uncover new insights about hypoglycemia in patients with T1D, this study utilizes feature importance techniques such as decision tree-based algorithms or Pearson's correlation coefficient. These methods rank the importance of each feature or determine the statistical relationship between numerical features and blood glucose levels. Furthermore, integrating SHapley Additive exPlanations (SHAP) values enhances interpretability and insight derivation from individual features on predictions.

RQ2 The evaluation goes beyond simple assessment by considering how KGEs impact the performance of prediction models. Metrics like accuracy, completeness, disambiguation, semantic validity, and consistency are examined to evaluate the quality of the embeddings thoroughly. In addition, visualization techniques like t-Distributed Stochastic Neighbor Embedding (t-SNE) and Principal Component Analysis (PCA) qualitatively assess the capacity of the embeddings to meaningfully represent patient data and biomedical knowledge for semantic integration into the ML pipeline.

RQ3 A rigorous comparative analysis would involve benchmarking against existing predictive models, such as the baseline Auto-Regressive Integrated Moving Average (ARIMA) model [24] and traditional ML models. Statistical tests, including measures like accuracy, mean squared error (MSE), and root-mean-square error (RMSE), are computed and comparing different models, aiding optimal algorithm selection for hypoglycemia prediction.

RQ4 The personalization aspect is evaluated using advanced clustering algorithms optimized for high-dimensional and temporal data, like dynamic time warping (DTW). These methods help in identifying patient profiles or glucose variability patterns efficiently - for instance, using clustering distance metrics, visualizing patterns, or inspecting anomalies - thus further enhancing customization possibilities within subgroups.

6 Results

Preliminary findings from analyzing structured data in the MIMIC-III dataset are presented. The research utilized a combination of the ARIMA model and selected ML algorithms to predict blood glucose levels in T1D patients. Table 1 presents a detailed comparison of the performance of the models compared to the lagged model which predicts glucose values from previous ones, showing promising results.

Table 1. Blood Glucose Prediction Model Performance Evaluation Metrics of a MIMIC-III patient with participant ID-96232

Metric	Naive (Lagged) Model	ARIMA	XGBOOST	LSTM
MSE	5.1763	4.3032	0.0030	0.0006
RMSE	2.2751	0.0066	0.0547	0.0238

Furthermore, this research provides a comprehensive semantic representation of hypoglycemic events from the integration of various relevant data sources including blood glucose levels, insulin regimens, patient-specific wearable and sensor data, as well as multiple variables like time of day (e.g., during sleep), physical activity, and diet. A summary of concepts and attributes extracted from the MIMIC-III dataset can be found in Table 2.

Table 2. Sample Semantic Concepts identified in the MIMIC-III Curated Dataset

Semantic Concept	Details/Examples
Enumerate Terms	subject_ID, hospital_admission_ID, ICU_stay_ID, LOS_ICU_days, first_ICU_stay, timer, start_time, GLC_timer, end_time, input, input_hours, GLC_level, GLC_source, insulin_type, event, infusion_stop
Define Classes	Patient, Hospital, Intensive Care Unit, Glucose, Insulin
Define Properties	Time, ID, GLC_Source, Insulin_Type, Insulin_Regimen
Create Constraints	Boolean, String, Integer
Create Instances	Fingerstick/Blood Glucose Test, Short-Acting/Long-Acting Insulin, Bolus Injection/Infusion/Bolus Push Insulin Regimen

7 Conclusions/Lessons Learned

This research is still in its early stages and focuses on developing a personalized, predictive solution for hypoglycemia in T1D patients through the integration of semantic knowledge and optimization of ML models. The research methodology implies the extension of state-of-the-art ML algorithms, including constructing and refining KGs by integrating, representing, and storing diverse information that can infer hypoglycemia, incorporating graph embeddings, and evaluating the models. The results of this research have the potential to improve the prediction accuracy and personalized management strategies for hypoglycemia in T1D patients. This research also indicates the need for semantic domain knowledge to improve the performance of ML models for hypoglycemia detection and prediction in T1D. Although hypoglycemia is a complex condition influenced by several factors, the ability to predict its occurrence can help prevent dangerous and potentially life-threatening situations and ultimately improve the quality of life of patients with T1D.

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