

Comparative Analysis of Automated and Manual Ontology Engineering for Modeling Clinical Trial Outcomes in Diabetes

Marin Marian

Vrije University, 1081 HV Amsterdam, Netherlands

Abstract. Diabetes is a prevalent global health issue, which necessitates thorough research and evaluation of treatment methods. Clinical trials play a crucial role in determining the effectiveness and safety of new diabetic treatments. However, the variability in outcome measures used in these trials poses challenges in comparing and interpreting results. Ontologies are valuable instruments in effectively analyzing a wide range of outcome measures across various studies and trials. This research investigates the effectiveness of automated techniques in ontology engineering compared to manual approaches for modelling clinical trial outcomes related to diabetes.

Keywords: Ontology engineering · Automated approaches · Outcome measures · Diabetes clinical trials

1 Introduction

Diabetes is a major health issue that affects a large number of people around the world. Approximately 9.3% of the worldwide population suffers from diabetes [1]. It ranks among the top ten causes of death in adults, with an estimated four million deaths around the world in 2017 [1]. Researchers have explored numerous treatments to reduce the risk of diabetes. However, these treatments do not always guarantee the most qualitative results. Thorough research is necessary to test the safety and effectiveness of new medications and approaches that aim to prevent, diagnose, treat, and manage diabetes before implementing them on a large scale. These concerns are investigated in diabetes clinical trials [2]. Clinical trials are essential for determining the efficacy and safety of new diabetic treatment methods. However, the variability of outcome measures utilised in these trials makes it challenging to compare and interpret the results.

In the context of computer science and information science, an ontology is a set of representational elements used to model a specific domain, such as e-commerce, social networks, or geography. These elements include classes (concepts), attributes (properties), individuals (instances), and relationships between class members [3]. Ontology engineering is one of the most critical components of knowledge representation, which aims to capture and formalise concepts and

relationships within a particular domain. The use of ontologies is becoming increasingly popular in various fields, including medicine and healthcare. In large-scale research studies, such as those focused on diabetes, ontologies serve as a valuable tool for efficiently analysing numerous outcome measures across trials.

Modelling an ontology for clinical trial outcomes in diabetes requires a rigorous and methodical approach. Ontology engineering is a time-consuming and laborious process that requires a deep understanding of the domain and the ability to organise knowledge in a structured manner [4]. As a result, this meticulous and systematic approach leads to greater accuracy and a better representation of the domain. It also allows for greater control over the modelling process. In contrast, employing computational techniques to assist in the ontology engineering process offers a comparative advantage by saving time and effort [5]. Furthermore, automated approaches excel at managing large amounts of data and ensure consistency since they follow strict guidelines. However, they also have limitations like constrained domain expertise and difficulties with ambiguity. Nevertheless, the performance of automated techniques in comparison to manually constructed ontologies remains an open question. It is important to address this issue because it can provide insights into the benefits and limitations of each approach, and help researchers determine the most efficient and effective way to model ontologies for clinical trial data.

This paper aims to address the following research question: Do automated steps, specifically concept identification and classification, in ontology engineering outperform manual ontology modelling in the context of clinical trial outcomes for diabetes? The study's objective is to examine the effectiveness of computational techniques in ontology engineering in comparison to traditional ontology development methods, with a specific focus on modelling clinical trial outcomes related to diabetes. The automated techniques include several approaches, such as named-entity recognition (NER) and support vector machines (SVM), to identify and classify a multitude of clinical trial outcome measures. It is important to note that the automation part implemented in this research project only covers the concept identification and categorization aspects of ontology engineering, rather than generating a complete ontology. However, this is sufficient to evaluate the performance of an automated approach for ontology development. Nonetheless, this study involved the manual construction of an outcome measure ontology that meets all the necessary criteria. Subsequently, a thorough evaluation was conducted using competency questions and the Ontology Pitfall Scanner! (OOPS) methodology to assess the quality of the ontology [6]. This investigation provides a comprehensive understanding of the performance and correctness of an automated and a manually modelled ontology for clinical trial outcomes in diabetes. The findings of this evaluation contribute to the continuing debate over the usefulness and efficiency of automated versus manual ontology engineering approaches in healthcare and clinical research.

This thesis will analyse the research question by first addressing related works, which provide an overview of the existing literature and research in the field of ontology engineering. The following section describes the methods and

techniques used for both the manually modelled outcome measures ontology and the automated steps implemented for ontology engineering. Next, I present the evaluation methodology used to assess the quality and effectiveness of both parts described in the "Approach". The "Results" section presents the findings of the evaluation. The discussion introduces possible reasons behind the obtained results. In the "Limitations and Future Work" section, I acknowledge the constraints of the study and suggest directions for future research. Finally, the paper summarizes the main findings of the study and presents the overall conclusions.

2 Related Work

The field of ontology engineering has seen a substantial increase in interest because of the rapidly growing use of semantic web technologies [7]. Researchers have conducted numerous studies to explore ontology developing methods and improve the quality and effectiveness of ontologies.

Zouaq and Nkambou [7] provide a survey of domain ontology engineering, with a focus on automatic methods for ontology learning. The article discusses the state of the art in natural language processing (NLP) and statistical and machine learning techniques for ontology extraction. Similarly, this study also utilises NLP and machine learning approaches for concept extraction, however, it also focuses on classification. Moreover, it evaluates the performance and effectiveness of these methods by comparing them to a manually designed ontology.

In another study, Gangemi et al. [8] presented a method for ontology engineering based on a hybrid approach. They proposed using machine learning techniques to extract concepts and relations from a set of source ontologies and then using these extracted concepts and relations to generate a new ontology for a specific domain. The results showed that automatic techniques can achieve high performance and that their approach produced ontologies that were comparable in quality to manually modelled ontologies. In a similar vein, this paper also focuses on concept extraction and compares the performance of computational techniques for ontology engineering with a manually constructed ontology. However, in contrast to Gangemi et al.'s [8] approach of reusing ontologies, this research utilizes clinical trials as the data source for ontology development.

Similarly, Elnagar et al. [4] propose in their article a new framework for automatically generating ontologies from unstructured text data. Their framework is designed to be domain-independent and can generate knowledge graphs from unstructured text data, which can then be refined and corrected to be consistent with domain ontologies. However, it is important to note that the effectiveness of this automatic approach in various domains still needs to be evaluated. Therefore, while their work presents promising potential, it does not directly address my research question at this stage, as the validity of the system remains to be assessed.

Kiritchenko et al. [9] focus on the development of an automatic information extraction system called ExaCT, which assists in locating and extracting key clinical trial characteristics (e.g., eligibility criteria, sample size, drug dosage,

primary outcomes). My paper investigates the performance of automated approaches for identification and classification only for outcome measures. While both papers use different methods, they share a common goal of leveraging automated techniques to improve efficiency and effectiveness in the field of medical research, specifically analyzing clinical trial data.

3 Approach

The methodology section of this thesis serves as a detailed guide that outlines the systematic approach used to conduct the research and achieve the study’s objectives. It includes a full description of the research design, data collection and methods applied.

3.1 Manual modelling of an outcome measures ontology

The first task was to manually model an outcome measures ontology (Fig. 1). This part was conducted in a group of three people. Each group member was responsible for searching and selecting a subset of clinical trials for diabetes. The selected clinical trials were carefully examined to identify the outcome measures used in each trial. We identified the measures by reviewing the primary and secondary endpoints defined in the trial protocols.



Fig. 1: High-level diagram for the modelling process

Based on the identified outcome measures, we defined classes and properties in the ontology. Classes represent distinct categories of outcome measures. Additionally, every single outcome measure is also modelled as a separate class within the ontology schema, not as an individual. This was a requirement from the domain experts consulted. Also, by focusing solely on classes, our ontology provides a high-level representation of the domain.

Five main classes were established to organize and classify the outcome measures based on their characteristics and attributes. Each class was given a descriptive label to clearly represent its meaning and scope: Biomarker, DiabeticDisease, EndpointScore, OutcomeMeasurementTool and Questionnaire. By defining these classes, we aimed to provide a comprehensive categorization framework that can accommodate various types of outcome measures encountered in clinical trials.

Furthermore, our team identified the properties necessary to capture the characteristics of the outcome measures. Object properties were defined to establish relationships between classes, such as "measures" to link an outcome

measurement tool with the biomarker it quantifies (Fig. 2). We also defined annotation properties to attach additional descriptive information to the classes, such as "hasExactSynonym" or "definition" (Fig. 2). Since our ontology does not utilize any instances, data properties were unnecessary.



Fig. 2: GlucoseMeter class

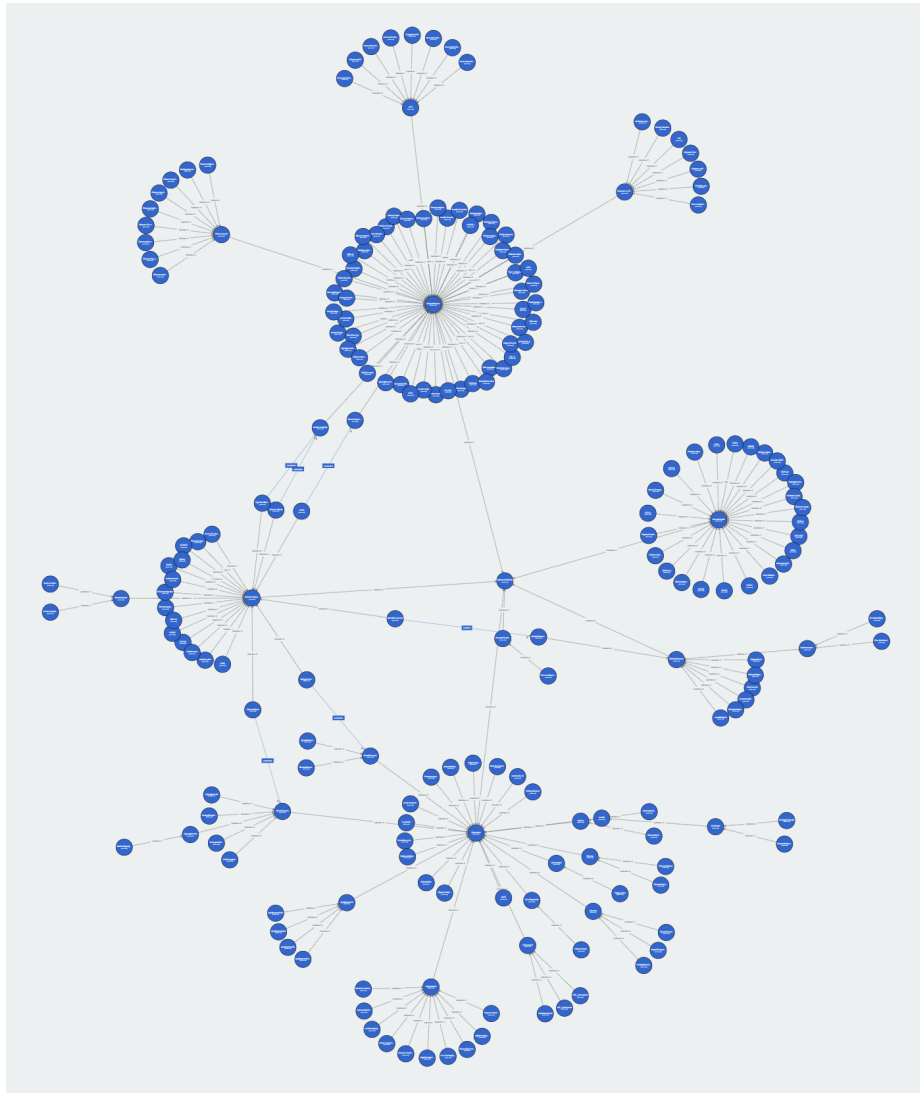
To create the outcome measures ontology and define the classes and properties, we used the ontology development platform Protégé. As highlighted by Mizoguchi and Kozaki [10] in their comparative study of ontology engineering tools, Protégé is an ontology editor and knowledge management system that offers a customizable output file format to adapt to any formal language and a customizable user interface, making it a versatile tool for knowledge acquisition, merging of existing ontologies, and ontology building.

Additionally, we present an ontology visualization (Fig. 3) utilizing The Visual Notation for OWL Ontologies (VOWL) [11].

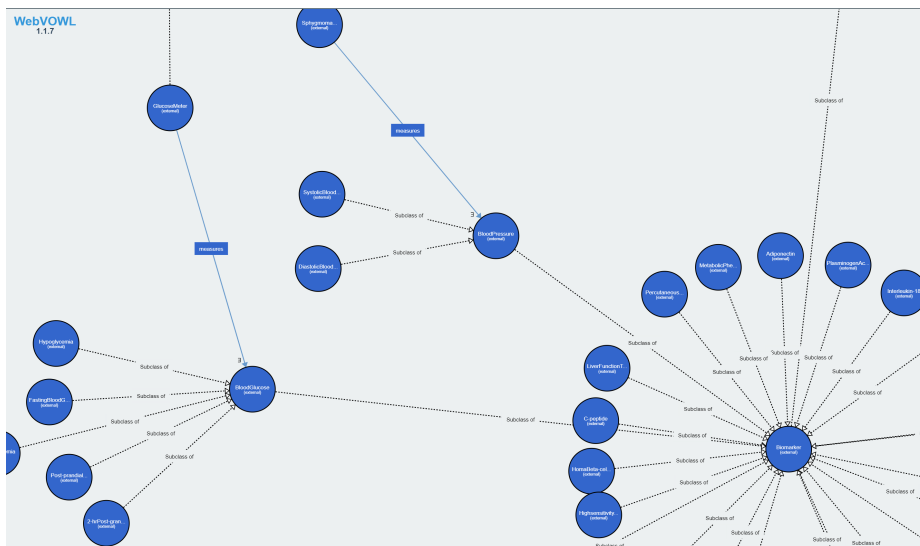
3.2 Automated steps for ontology engineering

The second part of the research project, involved utilizing automated procedures to assist in the development of an outcome measures ontology. This process involved various steps, including concept extraction and classification (Fig. 4). The initial stage was to collect data from a large corpus of clinical trials. The obtained dataset consists of a wide range of outcome measures (Fig.5) from 10,000 trials. For both ontologies was used an extensive database of privately and publicly funded clinical studies conducted around the world, ClinicalTrials.gov [12].

3.2.1 Concept extraction To carry out the concept extraction step, two approaches were implemented: Named Entity Recognition (NER) and a filtering



(a) Modelled ontology (the 5 main classes can be observed)



(b) Closer look at the Biomarker class and its subclasses

Fig. 3: Ontology visualization

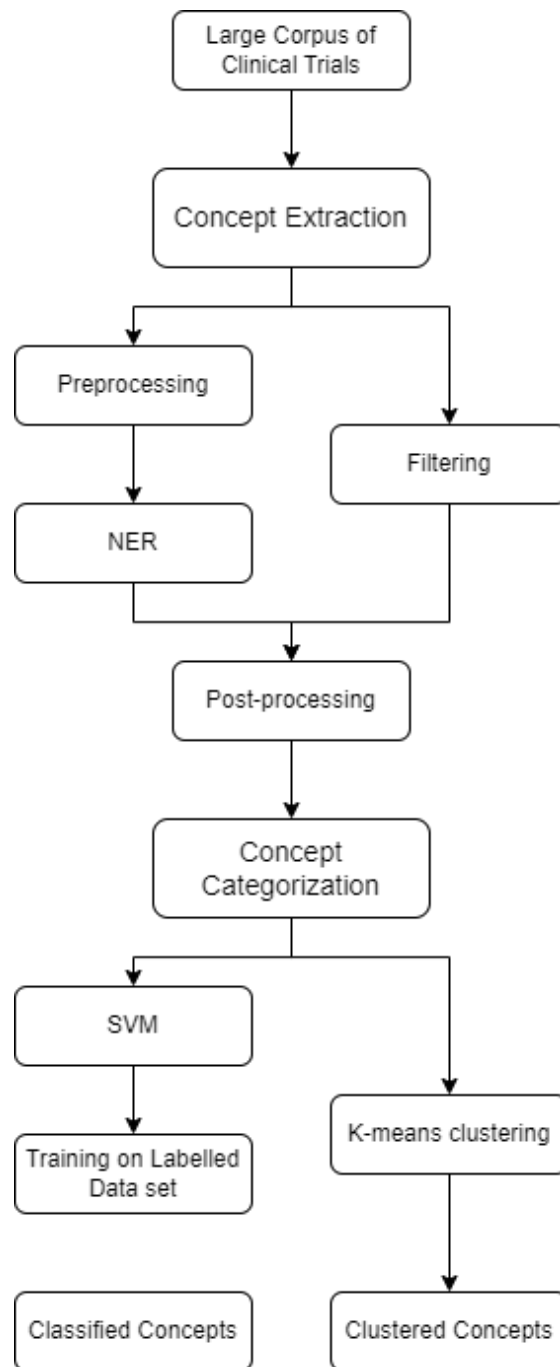


Fig. 4: High-level diagram for the automated steps

Outcome Measures	Outcome Measures
<ul style="list-style-type: none"> • Changes From Baseline in the Standard Deviation (SD) of 24-hour Blood Glucose Values • Change From Baseline in AUC for Blood Glucose When Specific Blood Glucose Levels (180 mg/dL) Are Observed During the 3 Hour Time Period After Breakfast, Lunch and Evening Meal • Change From Baseline in AUC for Blood Glucose When Specific Blood Glucose Levels (110 mg/dL) Are Observed During the 3 Hour Time Period After Breakfast, Lunch and Evening Meal • (and 21 more...) 	<ul style="list-style-type: none"> • Glycaemic control • Fasting blood glucose (FBG) • Weight

(a)
(b)

Fig. 5: Outcome measures representation in clinical trials (this section of the trial protocols was used for both ontologies)

method. Additionally, I compared the performance of both approaches. First, the NER technique was employed. After creating the dataset, several preprocessing steps were performed to prepare the collected data for further analysis. First, I tokenized the text into individual words, allowing processing the data at a granular level. Next, I removed common stopwords, such as articles and prepositions, as they do not carry significant semantic information. After that, I applied lemmatization to reduce words to their root forms, for improved contextual analysis. To perform NER and identify the concepts from the preprocessed clinical trial data, I used the Natural Language Toolkit (NLTK) library in Python. After the entity recognition step, additional post-processing was performed, such as removing the duplicates.

I have also developed a filtering function specifically designed to refine the outcome measures extracted from clinical trials. This function effectively removes lengthy and excessively wordy measures, as depicted in Figure 5a, which previously posed challenges for NER. Instead, it selectively chooses outcome measures that are concise and clearly stated (Fig. 5b), eliminating the need for named entity recognition altogether. This way, the function ensures that only the most relevant and easily understandable outcome measures are retained for further analysis. This approach simplifies the overall process and improves the efficiency of extracting meaningful data from clinical trials.

3.2.2 Concept categorization After extracting the relevant concepts from the clinical trial data, the next step was classifying these concepts into distinct categories. Two methods were implemented for concept categorization: Support Vector Machines (SVM) and K-means clustering. Both approaches utilized the Python libraries spaCy and scikit-learn (sklearn).

For the semi-supervised learning technique, SVM, a small dataset was manually labelled to serve as the training set. The labelled dataset consisted of representative examples from different concept categories. In order to ensure easier comparison with the manually modelled ontology, the same five main classes used in the first ontology were employed as the categories for the SVM model. The model was then trained using this dataset to learn the patterns and characteristics of each concept category. Once trained, the SVM model was able to

classify new concepts into the appropriate categories based on their features and similarities to the labelled examples.

On the other hand, K-means clustering was employed as an unsupervised learning technique. The K-means algorithm divides the concepts into a predetermined number of clusters, which in this case was set to five for consistency.

3.3 Evaluation protocol

The evaluation focuses on assessing the quality and effectiveness of the manually modelled ontology and the automated techniques used for ontology engineering.

To evaluate the coverage of the modelled ontology, I used competency questions that test the ontology’s ability to answer specific queries and provide relevant information. Another approach utilized to evaluate the quality and identify potential pitfalls in the ontology was the Ontology Pitfall Scanner (OOPS) [6].

Next, to evaluate more easily the performance of the implemented automated techniques for ontology engineering, a subset of outcome measures from 100 clinical trials was randomly selected from the main dataset. This subset was then hand-labelled to obtain gold labels, which served as the ground truth for comparison with the predicted labels generated by the classification models. The labels defined were Biomarker, Endpoint score, Measurement tool, Questionnaire, and Complications, similarly to the main classes from the modelled ontology. However, to enable the evaluation of the concept extraction methods as well, besides these five main categories used in the modelled ontology, an additional category, Misidentified, was included to capture concepts that were wrongly identified and extracted by NER.

The computational techniques for concept extraction (NER and the filtering function) and classification (SVM and K-means clustering) were applied to the selected subset. The predicted labels generated by these methods were compared against the gold labels to evaluate their correctness. A confusion matrix was created to provide a more detailed analysis and a visual representation. Additionally, evaluation metrics were calculated. These included accuracy, precision, recall, and F1 score.

4 Results

In this section, I present the results obtained following the evaluation process detailed above.

4.1 Evaluation of the manually modelled ontology

An example of a competency question used in the process of evaluation is listing all the endpoint subtypes for diabetes, which are a score (Fig. 6). The ontology was able to accurately identify and provide a comprehensive list of endpoint subtypes.

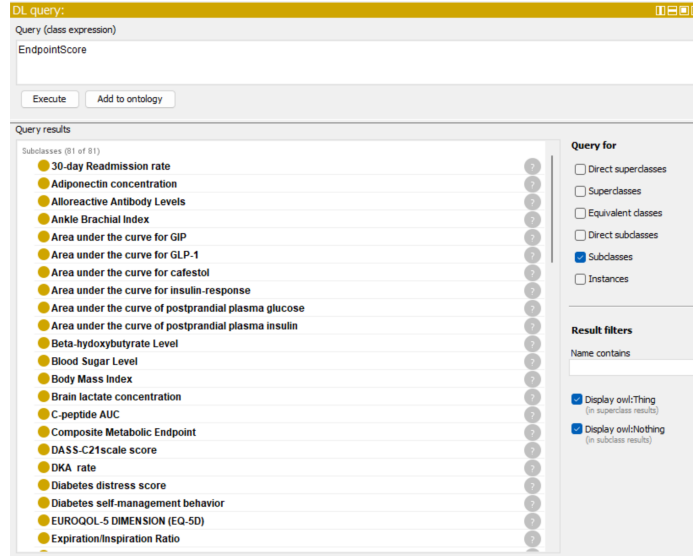


Fig. 6: DL Query that finds all subclasses of EndpointScore

The next part of the ontology evaluation using OOPS revealed several findings. First, the pitfall labelled P04 [6] indicated the presence of unconnected ontology elements. While this issue was considered minor, it could impact the overall coherence and comprehensiveness of the ontology. The evaluation also identified the pitfall labelled P10 [6], which pointed out missing disjointness axioms. This finding highlights the need to establish proper disjointness relationships within the ontology to enhance its logical consistency and accuracy. Another relevant pitfall, P13, highlighted the absence of explicitly declared inverse relationships for certain non-symmetric properties within the ontology. Inverse relationships play a crucial role in establishing bidirectional associations between entities, and their absence may hinder the ontology's expressiveness and interpretability. The identified pitfalls were thoroughly addressed and resolved in the ontology to enhance its quality and ensure its effectiveness.

The ontology underwent significant improvements, addressing the identified pitfalls. By rectifying these issues, the ontology became more robust, coherent, and aligned with best practices in ontology development. These enhancements contribute to its reliability and usefulness in supporting clinical trial research and facilitating the representation and analysis of outcome measures.

4.2 Evaluation of the automated steps

The SVM method, which incorporated, first, Named Entity Recognition (NER) and then the filtering function, was evaluated using various metrics such as accuracy, precision, recall, and F1 score (Fig. 7). The first approach, which relied

solely on NER, achieved a lower accuracy of 49%. Out of the 63 entities extracted, 18 were not actual outcome measures and were labelled Misidentified. In contrast, the second approach achieved a higher accuracy of 78%.

Classification Report:					Classification Report:				
	precision	recall	f1-score	support		precision	recall	f1-score	support
Biomarker	0.44	1.00	0.61	23	Biomarker	0.62	0.96	0.75	27
Complications	0.50	0.50	0.50	2	Complications	1.00	1.00	1.00	1
Endpoint score	1.00	0.50	0.67	4	Endpoint score	0.96	0.96	0.96	23
Measurement tool	1.00	0.20	0.33	10	Measurement tool	1.00	0.18	0.30	17
Misidentified	0.00	0.00	0.00	18	Questionnaire	0.88	0.83	0.86	18
Questionnaire	0.60	0.50	0.55	6					
accuracy			0.49	63	accuracy			0.78	86
macro avg	0.59	0.45	0.44	63	macro avg	0.89	0.79	0.77	86
weighted avg	0.46	0.49	0.39	63	weighted avg	0.84	0.78	0.74	86

(a) using NER

(b) using filtering

Fig. 7: Evaluation metrics for SVM

It was apparent, even without conducting an extensive analysis, that the k-means clustering algorithm was unsuitable for this particular task. The resulting clusters did not resemble the expected classes of measures at all, suggesting that this implementation of k-means clustering was not able to effectively categorize the concepts in a meaningful way for this specific domain.

The evaluation results underscore the superior performance of the filtering function over NER for concept extraction. Additionally, the SVM method outperformed the k-means clustering approach in the classification task for automatic ontology engineering. These findings demonstrate the effectiveness of the SVM method coupled with the filtering function in accurately categorizing concepts, making it a more suitable choice for this particular task compared to NER and k-means clustering.

5 Discussion

This section introduces possible reasons behind the obtained results. Firstly, the underperformance of the Named Entity Recognition method can be attributed to the use of clinical trial data that contains domain-specific terminology and abbreviations. The NER model was not specifically trained and fine-tuned for the diabetes domain, resulting in its struggle to accurately identify and extract relevant concepts. Regarding the implemented filtering method, although it does not encounter the same issues as NER, it is not flawless. It deletes a significant portion of the outcome measures, which can impact the completeness of the results.

In addition, the underperformance of the K-means algorithm could be due to the inappropriate choice of features. Selecting the right set of features is crucial for clustering algorithms like K-means to accurately group and differentiate the

data points. Despite SVM showing significantly better results compared to K-means, its performance was affected by the limited size of the trained dataset, struggling to capture the full complexity of the data.

Furthermore, comparing the manually modelled ontology with the automated approach for ontology engineering has proved to be challenging due to the fact that an automated ontology has not been generated. The evaluation process for the automation focuses on concept extraction and classification, assessing the correctness of predicted labels compared to the hand-labelled gold labels. While evaluation metrics such as accuracy, precision, recall, and F1 score were calculated, direct comparison with the coverage and quality evaluation of the manually modelled ontology is not feasible at this stage. It is important to note that the automated techniques have the potential to streamline ontology engineering tasks and improve efficiency, but further evaluation is required once the automated ontology is generated to comprehensively assess its coverage, quality, and effectiveness in supporting clinical trials research in diabetes.

6 Limitations and Future Work

In this passage, I will further discuss the limitations, shortcomings, and potential improvements for further research related to the tasks at hand.

One limitation is the reliance on a general-purpose Named Entity Recognition model that was not specifically trained for the diabetes domain. This results in lower accuracy in identifying and extracting the outcome measures concepts. To address this, future work can involve training and fine-tuning the NER model on a larger dataset specifically focused on diabetes or clinical trials.

The implemented filtering function, while effective in reducing noise and improving accuracy, also leads to the deletion of relevant outcome measures. This impacts the completeness of the extracted concepts and potentially may result in missing important information. Future studies can explore combining multiple techniques to strike a balance between accuracy and completeness.

Secondly, the limited size of the trained dataset affects the performance of the SVM classification method. With a larger and more diverse dataset, the SVM model could capture the full complexity of the data and potentially improve its accuracy. One possible area for future research can involve expanding the training dataset by including a broader range of outcome measures.

The k-means clustering algorithm showed unsatisfactory results in categorizing the outcome measures. It would be beneficial to explore alternative clustering algorithms that are better suited for this specific task. However, clustering might not be the most appropriate choice for such large datasets specifically focused on medical measures.

One limitation of the evaluation process is the challenge of gathering feedback from domain experts to enhance the modelled ontology. Expert input is crucial for identifying potential shortcomings such as missing or inaccurately represented concepts, relationships, or attributes within the ontology. Reviewing the outcomes measures extracted by automatic procedures also presents difficulties

in terms of validation and verification, as experts may encounter complexities in assessing the accuracy and completeness of these results. Incorporating specialist feedback becomes essential to address these limitations and ensure a more refined and reliable ontology.

By addressing these limitations and exploring the suggested areas for future work, the ontology and the automated techniques can be refined and improved to enhance their applicability, accuracy, and usability in supporting clinical trials research and knowledge representation.

As stated in the discussions point, a fully generated ontology has not been developed. While the evaluation section covered the assessment of the manually modelled ontology and the automated techniques employed in ontology engineering, a definitive and conclusive comparison between the two approaches is yet to be conducted. Given the significance of ontology development in both the AI field and the medical domain, further studies should explore the comparison between manual and automated engineering approaches. These studies can focus on generating a complete ontology using both approaches and assessing their respective strengths and weaknesses in terms of coverage, accuracy, efficiency, and usability.

7 Conclusions

This research paper investigates the performance of automated techniques in ontology engineering for clinical trial outcomes in diabetes compared to manual ontology modelling. The process of creating an ontology for outcome measures was explained, discussing both the manual modelling approach and the automated method involving concept extraction (using NER and the filtering function) and classification (using SVM and K-means clustering). The evaluation process assessed the quality of the manual ontology and identified potential pitfalls using competency questions and the OOPS methodology. The performance of the automated techniques was evaluated by comparing the predicted labels with the manually annotated gold labels. The evaluation of the automated techniques showed that the SVM method, coupled with the filtering function, outperformed other approaches in concept extraction and classification tasks. This study's findings contribute to the understanding of the benefits and limitations of automated ontology engineering approaches and provide insights into the efficiency and effectiveness of modelling ontologies for clinical trial data in diabetes.

It is also important to acknowledge the limitations of this study. The reliance on a general-purpose NER model not specifically trained for the diabetes domain resulted in lower accuracy in concept extraction. Moreover, the limited size of the trained dataset affected the performance of the SVM method. Furthermore, the evaluation process faced challenges in gathering feedback from domain experts and validating the accuracy and completeness of both the modelled ontology and the automated results.

In summary, this research paper lays the foundation for further advancements in automated ontology engineering for clinical trial outcomes in diabetes. By addressing the limitations and building upon the findings, researchers can continue to improve the efficiency and effectiveness of modelling ontologies, ultimately enhancing our understanding and management of diabetes through clinical trial data analysis.

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