Due to the widespread use of tools and the development of text processing techniques, the size and range of clinical data are not limited to structured data. The rapid growth of recorded information has led to big data platforms in healthcare that could be used to improve patients' primary care and serve various secondary purposes. Patient similarity assessment is one of the secondary tasks in identifying patients who are similar to a given patient, and it helps derive insights from similar patients' records to provide better treatment. This type of assessment is based on calculating the distance between patients. Since representing and calculating the similarity of patients plays an essential role in many secondary uses of electronic records, this article examines a new data representation method for Electronic Medical Records (EMRs) while taking into account the information in clinical narratives for similarity computing. Some previous works are based on structured data types, while other works only use unstructured data. However, a comprehensive representation of the information contained in the EMR requires the effective aggregation of both structured and unstructured data. To address the limitations of previous methods, we propose a method that captures the co-occurrence of different medical events, including signs, symptoms, and diseases extracted via unstructured data and structured data. The proposed method integrates data as discriminative features to construct a temporal tree, considering the difference between events that have short-term and long-term impacts. We evaluate the proposed method across patient similarity assessment and prediction tasks. Our results show that considering signs, symptoms, and diseases in every time interval leads to less MSE and more precision compared to baseline representations that do not consider this information or consider them separately from structured data.

Keywords: patient similarity analytics; patient representation learning; Natural language processing
1 Introduction

In the last two decades, the use of EMRs by medical service providers has been considered routine (1), and Natural Language Processing (NLP) methods capture meaningful information from clinical narratives(2). As a result, the size and scope of available clinical data are not limited to structured data. The availability and potential advantages of the big data platforms in healthcare can be used for the improvement of patients' primary care and also for various secondary purposes such as automated disease surveillance, clinical research, and clinical audits for quality enhancement(3),(4),(5).

Patient similarity assessment is a key task in this domain. Identifying patients who are similar to a given patient allows physicians to derive insights from the records of similar patients to provide better treatment(5). Measuring the individual distances among patients in a population is a prerequisite for assessing patient similarity(6). The computation of such distance requires integrating different structured and unstructured data types in an EMR. Representing and calculating patient similarity plays an essential role in many secondary uses of electronic records. In this paper, we proposed a novel EMR data representation method that extracts information from clinical narratives to enrich the structured similarity computing by unstructured data.

An accurate similarity assessment requires a comprehensive representation of EMRs, and it faces many challenges such as temporality, multivariate, heterogeneity, variety in raw EMR formats, irregularity, and sparsity(7). Considering the relationship between clinical events can help enrich the representation. Not all clinical events are the same in terms of impact, as some can have long-term effects that need to be perceived when interpreting other parameters. For example, a history of an underlying disease diagnosed many years ago should be considered when interpreting a lab result. In other words, clinical decision-making is often based on insights gained from reviewing patient records and new findings.

Some previous works on EMR are based on structured data types(8)(9)(10)(11)(7), while some other works only use unstructured data (12),(13). However, a limited number of studies such as (14) have integrated structured and unstructured data to create a heterogeneous representation of patient data. Existing methods that use only structured data representation provide limited accuracy. Much valuable patient information such as previous diseases, signs, and symptoms has
been recorded only in clinical texts. On the other hand, clinical texts do not contain the details of structured data such as data on drugs and clinical laboratory tests. Existing methods that attempt to generate separated representation vectors for structured and unstructured data fail to capture the relationship between different medical events, such as the co-occurrence of different medical events within a short period.

We propose an approach that builds upon the temporal tree technique (7) to address the limitations of previous methods. The temporal tree model captures the co-occurrence of different medical events as discriminative features. However, it does not extract the information written in clinical notes. In our proposed method, signs, symptoms, and diseases are captured from unstructured data and applied to create a more enriched temporal tree. In constructing the tree, we differentiate between events that have short-term and long-term impacts. We create a repository of retrospective and newly detected disease signs and symptoms extracted from clinical notes. Subsequently, the temporal tree is built, and past and present diseases, signs, and symptoms are added as new branches in each sub-tree. The new information enriches the compounds in each time interval.

Several features that have not been examined in previous works are included in this model. First, in the proposed method, signs, symptoms, and diseases are captured via unstructured data processing and applied in creating the temporal tree. Second, we considered the difference between events with short-term impacts and long-term impacts when constructing the tree.

We evaluated the proposed method across patient similarity assessment and prediction tasks. Our results show that including an overview of past and current diseases and considering them in every time interval produces better results than if they are not considered.

The major contributions of this paper could be outlined as follows:

1. The integration and uniformity of structured and unstructured information extracted from EMR.
2. The creation of compounds of information for a group of medical events happened together or in a short time window. These compounds not only include new significant findings, but also apply the history of previous signs, symptoms, and diseases.
3. Designing a representation method based on integration by considering the exact time of the new medical events and the impact of past medical events.
2 Related work

**EMR representation.** EMRs contain massive amounts of longitudinal information generated from daily clinical activities. Various data sources recorded at different time frames and frequencies are available in EMRs, ranging from structured data such as basic demographics, drug prescriptions, diagnoses, and laboratory tests to unstructured data such as clinical notes that contain a wealth of information about the patient(15). A variety of techniques are employed to represent structured data toward computing the semantically similar vectors in N-dimensional space. A basic technique is the one-hot encoding of N unique concepts using N-dimensional vectors that may lead to over-fitting and expensive computation. Word embedding (or Word2Vec) is an alternative to one-hot encoding introduced by Mikolov et al.(16). The essential assumption in Word2Vec is the distributional hypothesis, which suggests that words that occur in similar contexts tend to have similar meanings. Choi et al. in (17) demonstrate that Word2Vec can learn representations of medical codes. They applied Skip-gram to structured longitudinal visit records to learn the code representation and then summed all code representation vectors to obtain a single representation vector for a patient visit.

A sequence of laboratory test codes, prescription codes, and diagnoses created by (18) but ignored the exact timestamp at which the event happened. They used Word2Vec to generate vector representations for each medical event. After that, each patient record in a training set was projected into the vector space by summing up event vectors and using cosine similarity to find patients with the most similar projections and predict re-admission. Choi et al.(8) use code represented by Word2Vec as input to a recurrent neural network to predict heart failure. Choi et al. show that simply summing the code representations is not the optimal method for generating a visit representation. They proposed Med2Vec, which models an EMR as a sequence of temporally ordered visits in which the medical codes within a visit form an unordered set. For code representations, they also employ Skip-gram and use a multi-layer perceptron to generate the corresponding visit representation(19).

Lauritsen et al.(20) created a form of patient representation that consists of the raw event vector and the context vector. In the first part, some of the structured data types vectorize in two steps, and in the second part, the demographics and the patient’s commodities are considered. In Deepr
(11), the authors deal with an EMR as a sequence of discrete events, but they add time gaps between visits and transfer events between providers or hospitals to their model. Therefore, an EMR is represented by a sentence of phrases separated by words and could be embedded by Skip-gram. Applying word embedding to a sentence yields a sequence of vectors fed to a convolution neural network and max-pooling layers to extract the patient representation.

Zhang et al. (10) in Patient2Vec considered an EMR in the same way as the sequence of visits and treated a visit as a set of medical codes. This is similar to a sentence consisting of words, except there is no ordering between the words. Additionally, to overcome the irregular challenges (the timings and frequency of events vary across patients), they split the sequence of visits into multiple sub-sequences of equal length by determining the time windows. Since all medical events occurring within a sub-sequence are unlikely to contribute equally to the prediction of the target outcome, they employ a self-attention mechanism that trains the network to learn the weights.

In addition to the Skip-gram method, document-embedding techniques are used in the literature(21)(22) as a recent advance in NLP. Bajor et al.(23) used the document-level embedding approach. Their method uses clinical codes and laboratory tests without their values. For each record, these elements were ordered by the sequence of their appearance.

Miotto et al.(24) obtain raw patient representations from EMRs through unsupervised deep architecture learning. The result is a set of general and robust features applied to the entire hospital database to derive patient representations that can be used for several clinical tasks such as patient similarity.

Previous studies, despite their innovations in the modeling of electronic records, have some major drawbacks. First, existing models are limited to the use of structured data. In contrast, unstructured data parts of an EMR usually contain valuable information about patients' diagnostic and therapeutic findings. Second, in most of the reviewed studies, the temporal dimension is overlooked. The clinical codes recorded in a visit are entered in a random order in the analyses. Third, capturing compound information was not addressed by the previous research works.

Pokharel et al. (7) capture compound information and the temporal dimension between medical codes to tackle the last two challenges. Two main approaches exist for modeling unstructured data in electronic health records: extracting concepts and embedding the document. Clinical concept
extraction can be done through model development approaches such as rule-based systems, traditional machine learning, and deep learning(25).

On the other hand, recent advances in deep learning and NLP have enabled models to learn a rich representation of clinical notes directly. Clinical embedding includes text embedding and concept embedding (21). There are many techniques for unsupervised document embedding, some of which are used for patient representation (22). Henriksson et al. converted an EMR to sequences of different data types and applied Word2Vec to learn the representations of medical codes and words. They created vectors for each datatype separately(26). Darabi et al.(14) used transformer networks and the BERT language model to embed the unstructured and structured data of an EMR into a unified vector representation. Although the source of data in recent works is not limited to structured data, the relations between names and codes were not captured perfectly since the embedding of medical codes and words are performed in two separate spaces.

**Patient Similarity.** Patient similarity analytics have been introduced to facilitate data analysis through investigating the similarities in patients' data and, ultimately, to improve the healthcare system(27). Personalized medicine is based on quantitatively measuring the individual distances between patients in a population (6). Three recent review studies focused on patient similarity analytics, identified gaps, and provided a starting point for future related research(28)(29)(5). Patient similarity analysis could be based on a snapshot of clinical variables or viewing their changes over time. Another approach is referring to physical objects' properties, for example, people or tumors, or based on the effect of clinical interventions such as various treatment modalities(30).

Existing literature suggests a variety of methods in measuring the individual distances between patients. Sun et al.(31) used locally supervised metric learning to learn a generalized Mahalanobis distance with physician feedback to identify the patients most similar to the queried patient. This patient-patient similarity matrix is updatable via an eigenvalue analysis and can integrate subsequent, multiple physician feedback regarding the similarity between two patients. Ebadollah et al.(32) addressed near-term prognostics as an influential factor in decision making. They proposed the use of inter-patient similarity based on similar physiological trends. In (33), the authors developed a support vector machine called SimSVM. This method requires expert intervention for feature selection. Miotto et al. (34) developed a case-based reasoning framework
that works based on computation patient similarity. By modeling the target patient, they rank patients in the dataset based on the similarity to the target patient, which is computed through a linear combination of cosine similarities over individual EMR data types. Wang et al.(35) proposed a patient similarity framework (PSF) to use unsupervised information patient features in an EMR and supervised information such as physician feedback. They introduced a general online update algorithm to update the learned patient similarity efficiently. A patient similarity measure was proposed based on LSR for unsupervised information. Zhan et al.(36) used pairwise constraints to select low-rank sparse features for learning the similarity among a group of patients. Glicksberg et al.(37) used Word2Vec to create medical concept embeddings. The proposed automatic disease phenotyping from the embeddings draws from cosine similarity to measure the distance between each patient and query vectors. Jia et al.(38) calculate the distance between sets of diagnoses with ICD-10 diagnoses codes using IC-based code-level similarity algorithms. The importance of all ICD-10 codes of a patient is assumed to be equal. Jia et al.(39) developed a patient-similarity-based framework for diagnostic prediction through the fusion of computable attribute similarity and learnable relation similarity. The clinical features were integrated into a vector, and the multi-classification problem was converted into a single-value regression problem. After comparing patients in a pairwise manner, they developed a supervised machine learning model and predicted diagnoses through positive and negative analogies.

Grover et al.(40) proposed node2vec, which represents graph nodes through random walks as a sampling method at a target node. The result is similar to feeding the sentences in a corpus into a Skip-gram model. The non-linear network is converted to linear nature by sampling method. However, the methods that use pairwise similarity ignore the temporal dimension and the inherent relationships between different parts of EMR data.

3 Methodology

Physicians make decisions based on multiple observations (can be captured by compounds) and analyze trends over time (can be captured by clinical patterns). This study aims to create more enriched compounds by processing the clinical notes in the EMR and extracting information about registered diseases. Compound EMR information is created when multiple clinical events appear at the same point in time (or within a short period). A recent model generates the clinical patterns
from the sequences of univariate observations and sequences of compound information captured (7). In their method, the description of co-occurrences is not limited to the exact time of recording information in the EMR system. Indeed, the effect of patient history and current significant findings contributes to the production of compounds. We present our model based on the above requirements in four phases. The workflow of the proposed method can be found in Fig. 1.

**In the first phase,** the goal is to identify a person's previous and current illnesses from the descriptions written in clinical texts. Since signs and symptoms describe the diseases in medical texts, all terms related to diseases, signs, and symptoms are extracted and grouped according to their position in medical notes. After grouping, using alignment, a suitable diagnostic code is provided for each expression. Also, information about prescriptions and laboratory tests are extracted.

**In the second phase,** we use a data structure called the quadruple to homogenize the structure of information extracted from structured and unstructured sources that provide the basis for combining information.

**In the third phase,** we apply the quadruples in developing a temporal tree influenced by Pokarel et al.’s(7) model. We intend to produce compounds of information that include significant recorded clinical events and the history of influential diseases. In developing the proposed tree, the past and present signs, symptoms, and diseases of the patient, alongside structured information such as drug information and laboratory test results, are used.

**In the fourth step,** traversing the temporal tree yields sequences used as input of embedding algorithm to represent patient information as vectors.

**Finally, in the fifth step,** the embedding vectors are fed as input to the patient similarity assessment model. It works based on cosine distance between patient embedding vectors and the gold standard as a measure of model accuracy. The results obtained from this method are compared with several baselines. In the continuation of this section, the details of each stage will be presented.
Figure 1. The workflow of the proposed method
In the continuation of this section, first, clinical text processing will be discussed. Then, the construction of quadruples and evaluation of patient similarity will be explained.

### 3.1 Clinical text processing

The purpose of processing unstructured data is to provide an overview of the signs, symptoms, and diseases mentioned in the history and new clinical findings. By identifying these medical events, they can be used to make richer compounds. The main steps of processing unstructured data and creating quadruples of them are represented in Fig. 2.

![Figure 2. The main steps in processing unstructured data and creating the quadruples.](image-url)

This pipeline consists of the following sections:

1. Section detection
2. Detection of signs, symptoms, and diseases
3. The UMLS alignment
4. Mapping and categorization of diagnosis codes
3.1.1 Section detection

Each standard clinical note in an EMR consists of several components or sections. The Joint Commission\(^5\) established standard IM.6.10, EP7 (41), which outlines the main six\(^6\) components that each hospital discharge summary should contain. Although there is valuable retrospective information about the patient's history, allergies, previous treatment, and new findings in the clinical notes, there is no clear or specific definition for these components. One of the common challenges in NLP in clinical notes is flexible formatting (42),(2). There is significant variation in the number of sections and the descriptive phrases (section headers). On the other hand, it is essential to identify the differentiating between the patient's medical history (previous active or resolved medical condition) and new findings. Unlike previous methods, in this study, we have considered the effect of the patient's medical history in interpreting their new clinical condition.

The selected approach involves scanning all clinical notes of 200 medical records with different final diagnoses randomly and creating a dictionary for more standard section headers. After that, a unique expression is assigned to each group of terms. The created groups contain all six main parts mentioned in the standard IM.6.10, EP7. For instance, all terms (*history of the present illness, medical condition, present illness, admission history, and physical*) are mapped to the unique expression *HPI*, which stands for History of Present Illness.

3.1.2 Concept extraction

The processing of medical notes is necessary for representing a complete overview of a patient's medical history and current significant findings. Before addressing this issue, it would be essential to differentiate the following terms:

- **Symptom:** Any subjective evidence of disease defines a departure from the normal function or feeling and is apparent to a patient, thereby reflecting the presence of an unusual state or a disease. *Example: Loss of taste or smell*

\(^5\) https://www.jointcommission.org/

\(^6\) These components are: Reason for hospitalization, Significant findings, Procedures and treatment provided, Patient's discharge condition, Patient and family instructions (as appropriate), Attending physician's signature.
• **Sign**: An objective indication of a disease, injury, or abnormal physiological state may be detected during the physical examination. *Example: Fever*

• **Diseases** or medical conditions are a particular abnormal condition that negatively affects all or part of an organism's structure or function and is not due to any immediate external injury. Diseases are known to be medical conditions associated with specific symptoms and signs. *Example: COVID-19*

• **Medical diagnosis** determines which disease or condition explains a patient's symptoms and signs. Medical diagnosis codes are used as a tool to group and identify diseases. *Example: U07.1 COVID-19, virus identified*

Various NLP systems have been developed and utilized to achieve this goal and to precisely extract events and clinical concepts from the clinical notes created in an unstructured format. MetaMap and cTAKES\(^7\) are widely used and known in the biomedical area\(^43\). Both cTAKES and MetaMap use the Unified Medical Language System (UMLS) to extract and standardize medical concepts.

MetaMap uses a hybrid approach that combines NLP, a knowledge-intensive approach, and computational linguistic techniques\(^44\). We use the (2018AA) release of UMLS with the following list of options `-V USAbase-L 18 -Z 18 -E -AsI+ –XMLf –negex -E`.

cTAKES\(^45\) combines rule-based and machine learning techniques to extract information from a clinical text\(^43\). cTAKES executes some components in sequence to process the clinical text. We used the Default Clinical Pipeline of cTAKES and Python library ctakes-parser 0.1.0\(^8\) to identify signs, symptoms, and disease-related expressions of text-processing results. We limited the processing result to semantic-type `DiseaseDisorderMention` and `SignSymptomMention`.

In addition to the above tools, we use scispaCy\(^9\)\(^46\), a Python library with `en_ner_bc5cdr_md` model (a spaCy NER model trained on the BC5CDR corpus) by *AbbreviationDetector* for the interpretation of abbreviations and *negspaCy* for negating concepts. Named entity recognition

\(^7\) The Clinical Text Analysis and Knowledge Extraction System

\(^8\) [https://pypi.org/project/ctakes-parser](https://pypi.org/project/ctakes-parser)

\(^9\) [http://allenai.github.io/scispacy](http://allenai.github.io/scispacy)
(NER) is the task of identifying and locating mentions of conceptual categories, such as drug, symptom, or disease names in text (47). Since the combination of tools might even permit us to cover complementary cases(43), for NER, we used the community of results from text processing using the above tools. The output of a clinical NER is a set of named entities of one or more types. Concept normalization or entity linking is assigning a unique identity to each entity name mentioned in the text. This task is closely related to named entity recognition, and all mentioned tools support the two processes(47). UMLS is a collection of biomedical ontologies and terminologies in which single unique identifiers (concept unique identifiers, or CUIs) assigned to concepts occurring across multiple resources are mapped. Clinical concept normalization is used to map a given text string to one of these CUIs. We use MetaMap for this task.

3.1.3 Diagnosis codes mapping and categorization

With the CUI code, it is possible to retrieve all source-asserted identifiers that share a CUI with a particular code. We map CUI codes to ICD-9-CM\textsuperscript{10} codes using The DisGeNET(48) database resources. UMLS CUIs in DisGeNET is annotated with an equivalent code in other disease vocabularies\textsuperscript{11}.

The ICD-9-CM clinical codes assigned to patients fall under a broad category, and as there are limited data for each set of codes, we decrease the sparsity by grouping the codes under their common ancestor. We used the Clinical Classification Software for ICD-9-CM(49) to collapse these codes into a smaller number of clinically meaningful categories that are more useful for presenting descriptive statistics than are individual codes. After these steps, an overview of the patient's signs, symptoms, and diseases is obtained, which is used to construct a quadruple data structure.

3.2 Structured data

As dicussed earlier in the section, exploiting unstructured data from EMR is a key part of our contribution. However, we also use stuctured data from laboratory tests and medications

\textsuperscript{10} The International Classification of Diseases, Ninth Revision, Clinical Modification

\textsuperscript{11} https://www.disgenet.org/downloads
prescribed to the patient. The numerical results of laboratory tests are represented by the notional values of Low, Normal, and High. We create a quadruple of structured information. Since the results of clinical trials and prescribed drugs change rapidly, the value of the field Temporal Event Type is set equal to Real-time data with a short-term effect in the quadruple construction.

### 3.3 Creating a temporal tree with a new approach

The approximate time of registration of each clinical event in the electronic file is specified as the date and time. However, the significance of clinical events varies based on their impact on current medical status over time. For example, regardless of when the patient history is recorded, the previous disease should interpret other findings. As focusing on registration information and time alone will not reflect their importance over time, we introduce a flat format called quadruple for describing each medical event. This data structure format is used to unfirm the data. The quadruple data structure format consists of four parts: Time \((t)\), Event-Type \((y)\), Event \((e)\), and value \((v)\), which are represented by \(\{t_i, y_i, e_i, v_i\} \), \(1 \leq i \leq n\). The number of quadruples can be different between patients.

- **Time**: We use the timestamp that each clinical event registers in the EMR.

- **Temporal Event Type**: Events are categorized by their impact over time. We have considered the following three values for the Temporal Event Type field, to indicate the difference in clinical events' importance over time.
  
  - **Retrospective data**: This value is assigned to the concepts extracted by processing the texts of the patient history and patient family history. We used this type of diseases for constructing all compounds. In other words, the signs, symptoms, and diseases mentioned in the patient history section of the discharge sheet will be considered in the interpretation of other clinical findings during the patient's recent visit. For example, a history of COVID in a patient who developed a disease and recovered from it a few months ago is considered in examining a heart attack, which is the reason for their current referral.
  
  - **New detected finding with a long-lasting effect**: We assigned this value to the concepts extracted from sections describing the new findings. In data modeling, after identifying such cases, they are used in the construction of subsequent compounds.
For example, evidence of atherosclerosis (that happens when coronary arteries are blocked or narrowed by fatty plaques) in angiogram findings is considered in the construction of all subsequent compounds.

- **Real-time data with a short-term effect:** We have used this parameter to model laboratory results and prescribed drugs. These items are repeated and updated more frequently, and the treatment methods can change their subsequent values. Therefore, they are only used to make the compound in which they are recorded.

  - **Event:** Any extractable characteristic that varies from patient to patient.
  - **Value:** Registered or extracted value for events.

The repository of quadruples is used for creating a temporal tree with a new approach. An example of creating a temporal tree is shown in Fig. 3. In this example, we have a 35-year-old woman with a history of diabetes mellitus type 2. On the first day, her glucose was higher than the normal range. Therefore, she gets insulin. Next, the status of hyperglycemia (high glucose) was not changed, and insulin continues. Also, during the para-clinical test, diabetic neuropathy is detected. The demographic information and history of diabetes are considered for this day and subsequent days because they are necessary for interpreting and decision making.
The same condition is actual for neuropathy, and this new finding is considered in the following assessment. On the third day, fatigue – a new symptom – was detected in the nursing note. On this day, insulin was not administrated. There is a sub-tree for each day, and every data type has branches. Signs, symptoms, and diseases extracted from medical notes are different and categorized based on their labels. They fall into account in creating compounds based on which category (temporal event type) they fall into account.

An example is provided in Fig. 4 to illustrate the importance of using concepts extracted from clinical notes to construct compounds. Only structured data (laboratory test and prescription) are used to construct compounds in part(A). The compound CL1 in the second time interval represents evidence of anemia. At this stage, there is no additional information to use to identify the source of this anemia. In the second part(B), the patient's pregnancy is used to construct component Cl3. In the third part(B), in addition to laboratory tests and prescriptions, the patient's thalassemia history has been extracted from the clinical notes in Cl5 construction. Having more information
makes a difference between compounds. Cl3 is not equal to Cl5, and this distinction is critical in assessing patients' similarities. Unlike iron deficiency anemia, identifying patients with thalassemia is vital for avoiding unnecessary iron replacement therapy. Iron overload can lead to several complications in patients with thalassemia(50), impair the immune system, and place patients at risk of infection and illness(51).

3.4 Create patient representation

We need to embed the temporal tree in a low-dimensional vector space to use the temporal tree's information. Two patient embeddings are similar if they share similar medical terms and similar temporal sequences. We traverse the temporal trees' nodes in Breath First Order (BFS) to generate temporal sequences. According to (7), BFS was the best performing approach in comparison to other traverse types. In this approach, for each level of the tree, a temporal sequence is generated. As shown in Fig. 3, the non-leaf node label is created from the next-level node labels. Therefore, the following sequences shown in Fig. 5 are produced for this tree:
Figure 4. The effect of paying attention to the concepts extracted from the clinical notes in the construction of compounds.

Seq1: Disease, Diabetes mellitus type 2, Female, 4, Glucose, High, Main Drug, Insulin, Disease, Diabetes mellitus type 2, Female, 4, Disease, Diabetic neuropathy, Glucose, High, Main Drug, Insulin, Disease, Diabetes mellitus type 2, Female, 4, Disease, Diabetic neuropathy, Symptom, Fatigue, Glucose, Normal

Seq2: Disease, Diabetes mellitus type 2, Female, 4, Glucose High, Main Drug, Insulin, Disease, Diabetes mellitus type 2, Female, 4, Disease, Diabetic neuropathy, Glucose, High, Main Drug, Insulin, Disease, Diabetes mellitus type 2, Female, 4, Disease, Diabetic neuropathy, Symptom, Fatigue, Glucose, Normal,

Seq3: Disease, Diabetes mellitus type 2, Female, 4, Glucose High Main Drug, Insulin, Disease, Diabetes mellitus type 2, Female, 4, Disease, Diabetic neuropathy, Glucose High Main Drug, Insulin, Disease, Diabetes mellitus type 2, Female, 4, Disease, Diabetic neuropathy, Symptom, Fatigue, Glucose, Normal,

Seq4: Disease, Diabetes mellitus type 2, Female, 4, Glucose High Main Drug, Insulin, Disease, Diabetes mellitus type 2, Female, 4, Disease, Diabetic neuropathy, Glucose High Main Drug, Insulin, Disease, Diabetes mellitus type 2, Female, 4, Disease, Diabetic neuropathy, Symptom, Fatigue, Glucose, Normal,

Figure 5. Temporal sequences by BFS order
When temporal sequences are generated, we embed them into a low-dimensional vector space using Doc2Vec (embedding technique). Doc2Vec is based on Word2Vec and uses an unsupervised learning approach to learn the document representation. The input text (in our case, medical events) per document (in our case, temporal tree) can be varied, while the output is fixed-length vectors. The Doc2Vec includes two sub-methods. The Distributed Memory Model of Paragraph Vectors (PV-DM)(52) that we used in our model, is similar to the continuous bag-of-words approach in Word2Vec. Another Doc2Vec sub-method is the Distributed Bag-of-Words version of Paragraph Vector (PV-DBOW)(53), which is similar to the Skip-gram approach in Word2Vec. The PV-DM model computes the probability of a target word in a lexical context based on the surrounding words. The document and is mathematically expressed as below:

\[
\sum_{t \in T_w} \log p(w_t | C_t, d_t)
\]

Where \(w_t\) is the target word and \(T_w\) is the set of training words, \(C_t = [w_{t-L}, \ldots, w_{t-1}, w_{t+1}, \ldots, w_{t+L}]\) are context words that occur within a window size of \(L\) words around \(w_t\), and \(d_t\) denotes the document corresponding to the \(t_{th}\) training instance. The probability is computed using a Softmax function. For optimization, the hierarchical Softmax is used.

4 Evaluation of the methodology

4.1 Dataset and patient cohort selection

To evaluate the proposed method, we use a subset of MIMIC III\(^{12}\)(54). MIMIC III is a free publicly available clinical database containing data from approximately 40,000 de-identified patients. These data come from patients admitted to a medical center in Boston, Massachusetts, from 2001 to 2012. In this study, a subset of patients whose final diagnosis is one of the top-10 most frequent first diagnoses in the whole dataset was selected. Records with no laboratory tests or prescriptions are excluded. This collection includes over 7300 admissions.

\(^{12}\) Medical Information Mart for Intensive Care III
4.2 Patient representation scenarios

To evaluate the effectiveness of the model presented in this paper, we consider four scenarios for the patient representation:

1. **S**: Patient representation by considering only structured data without the temporal tree.
2. **STT**: Patient representation by considering structured data with temporal tree
3. **SUTT**: Patient representation by considering structured as well as unstructured data with the temporal tree without recurrent
4. **SUTTR**: Patient representation by considering structured as well as unstructured data with the temporal tree with recurrent.

The difference between the last three methods is illustrated in Fig. 6.
In the second scenario (STT), only structured data are involved in creating a temporal tree. This method can be considered equivalent to the previous model presented by (7); in the third scenario (SUTT), signs, symptoms, and diseases extracted from unstructured data are displayed only in the first sub-tree and appear once in the tree traversal. This method can be equivalent to those studies that use unstructured and structured data to connect two separate embedding vectors. The proposed method is presented by the fourth scenario (SUTTR). A set of signs, symptoms, and diseases extracted from the patient’s history and new significant findings involved constructing all sub-trees.
and the following compounds. We test the effectiveness of each of these four approaches and their results in the next section.

4.3 Gold standard

To determine an evaluation methodology, we considered the previous works by Pokharel et al.(55), used all available codes, and assigned a weight to diagnosis codes based on diagnosis code priority. This evaluation approach is appropriate because, in this way, the similarity between two patients can be determined not only by the number of diagnoses shared by the two patients but also by the respective rankings of the diagnosis and errors at high ranks (high code importance), which are given more weight than errors at low ranks. Through the equation \( \text{SimIndex}(A, B) = \frac{\sum_{i=1}^{N} m \cdot \min(a_{w_i}(p), b_{w_i}(p))}{\text{avg}(\sum_{i=1}^{N} a_{w_i}(p), \sum_{i=1}^{N} b_{w_i}(p))} \)

where \( a_{w_i}(p) \) and \( b_{w_i}(p) \) are the weights of diagnosis \( i \) with priority \( p \) expressed as an ICD9 disease code for patients \( A \) and \( B \), respectively.

4.4 Evaluation tasks

The effectiveness of the proposed representation method is evaluated in two contexts: (i) similar patients retrieval and (ii) prediction model.

4.4.1 Similar patients retrieval

We evaluate the proposed method on similar patients retrieval using the following evaluation measures:

- **Mean Square Error (MSE):** The prediction error is the difference between the actual value and the predicted value (56). The Top@k query returns \( k \) patients that are most similar to a given patient, based on the cosine similarity measure of the embedding vectors. The query result of the proposed method is compared with other scenarios. The predicted value for each patient is the highest similarity value compared to the actual value of the most similar record based on the gold standard.
- **Normalized Discounted Cumulative Gain (nDCG):** This measure is a weighted sum of the ranked items' degree of relevancy. The weight is a decreasing function of the object's rank, so is called discount. The discount means that the probability of viewing a document decreases concerning its rank. NDCG normalizes DCG by the Ideal DCG, which is simply the DCG measure of the best-ranking result. Thus, the NDCG measure is always a number in $[0, 1](57)$.

The nDCG measure is computed for the Top@k patient rankings retrieved in answer to a query patient. The ideal Top@k ranking based on the gold standard is computed for a query patient. We use the $SimIndex$ function (55) for calculating the scores. We use an ordinary function $d_i = \log_2(i + 1)$ for calculating the discount. For a query patient, the calculated $SimIndex$ scores for both ideal and actual rankings are considered to be the gains $g$, which are discounted by a function of the rank position.

- **Precision:** If a retrieved patient contains any of the top two query diagnoses, the patient is considered relevant(58).

### 4.4.2 Prediction model

We test the effectiveness concerning the mortality prediction task. This task is concerned with predicting whether a patient will pass away while in the hospital or after discharge. Similar to re-admission, it could be formulated as a binary problem. For this prediction task, we use $k$-Nearest Neighbours (KNN)(59) for classification. KNN is an intuitive similarity-based approach that can directly rely on the representations studied in this paper. We use near-miss under-sampling methods(60) for selecting examples from the majority class. We evaluate the classification effectiveness according to $f1$. The $f1$ score can be interpreted as a weighted average of the precision and recall and is between $[0,1]$. Also, we calculated $(AUC)^{13}$. We apply 5-fold cross-validation. In each fold, the training data set is further divided into sub-training and sub-validation with an 80:20 ratio. $k$ is varied in the range $[0,20]$ with step 1. The obtained $k$ is used for evaluation

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13 *Area Under the Receiver Operating Characteristic Curve*
by using the training and testing data set. The whole process is repeated ten times, and the effectiveness is averaged to eliminate bias due to the random partition of the training data.

5 Interpretation of the results

The following questions are explored when analyzing the empirical results:

1. Can adding signs, symptoms, and diseases extracted from the clinical text help create richer compounds and increase similar patients identification accuracy?

2. To what extent does the assessment's accuracy depend on how the compound is constructed using this information?

5.1 Experimental setup

We use BFS from the NetworkX Python library\textsuperscript{14} to create traversal orders. We apply the negative sampling\textsuperscript{(61)} optimizations. For training the embeddings, we use the following hyperparameters defined in:

- \textit{vector\_size} = 200 - the dimensionality of the feature vectors.
- \textit{window\_size} = 5 - the maximum distance between the current and predicted word within a sentence.
- \textit{sampling\_threshold} = 1e-5 - the threshold for configuring which higher-frequency words are randomly downsampled.
- \textit{negative\_size} = 5 - specifies how many "noise words" should be drawn.
- \textit{alpha} = 0.025 - the initial learning rate.
- \textit{minimum\_alpha} = 0.0001 - the learning rate will linearly drop to min\_alpha as the training progresses.
- \textit{training\_epochs} = 10 - the number of iterations (epochs) over the corpus.
- \textit{min\_count} = 5 - ignores all words with a total frequency lower than this.
- \textit{workers} = 20 - use these many worker threads to train the model.

\textsuperscript{14} https://github.com/networkx/networkx
• $DM = 0$ - defines the training algorithm. A distributed bag of words (PV-DBOW) is employed.

### 5.2 Similar patients retrieval task

Table 1 shows the effectiveness of each integrating approaches computed as MSE, nDCG, and precision when retrieving top-k similar patients (k=1 to 20).

| Method@k | S   | S_TT | S_U_TT | S_U_TT_R |
|----------|-----|------|--------|----------|
| MSE@1    | 0.363 | 0.232 | 0.227  | **0.208*** |
| MSE@5    | 0.317 | 0.111 | 0.109  | **0.102*** |
| MSE@10   | 0.254 | 0.100 | 0.104  | **0.096*** |
| MSE@20   | 0.231 | 0.080 | 0.083  | **0.077*** |
| DCG@1    | 0.383 | 0.426 | 0.415  | **0.462*** |
| DCG@5    | 0.207 | 0.414 | 0.413  | **0.453*** |
| DCG@10   | 0.132 | 0.330 | 0.331  | **0.364*** |
| DCG@20   | 0.076 | 0.284 | 0.298  | **0.347*** |
| Precision@1 | 0.560 | 0.661 | 0.674  | **0.703*** |
| Precision@5 | 0.536 | 0.632 | 0.646  | **0.677*** |
| Precision@10 | 0.443 | 0.613 | 0.627  | **0.660*** |
| Precision@20 | 0.439 | 0.592 | 0.603  | **0.639*** |

* Indicates statistically significant difference with p-value < 0.01 obtained when comparing the proposed method with other scenarios.

As for MSE, it is evident that by increasing K, MSE decreases. As a larger set is retrieved, the probability of being at least a patient that is more similar to the query patient is higher, reducing the overall error.
Another promising finding of MSE was that the two approaches that used unstructured data to create compounds yielded a less-than-average MSE. In the light of these results, it is clear that the lowest amount of the average MSE is obtained when the detected signs, symptoms, and diseases are used in the construction of all compounds.

As shown in Fig. 7, the amount of nDCG decreases for higher values of K. This finding confirms the previous findings reported by (7), which show that as the set of retrieved responses grows, the likelihood of patients who do not look like the query patient will increase. In other words, in larger sets, the chances of finding unrelated values also increase. This issue can be understood by comparing different approaches, as the proposed method has the lowest reduction of parameter nDCG. As shown in Table 1, the precision decreases with the increase of K: the probability of retrieving irrelevant patients is higher with a larger K. As shown in Fig. 7, the average precision obtained from the proposed method was higher than in other scenarios.

We evaluated the differences between our proposed method (SUTTR) and other approaches with a t-test with Wilcoxon(56) (a non-parametric statistical test). The result indicates statistical significance with a p-value < 0.01.
In response to the two questions posed at the beginning of this section, based on the experiments reported, it is concluded that the addition of signs, symptoms, and diseases extracted from textual data increases the accuracy of the similarity assessment. Besides, in answer to the second question,
results show that the proposed method (because of the different methods used to make the compounds) leads to higher accuracy and minor errors.

5.3 Prediction tasks

Table 2 shows the effectiveness of the prediction methods in f1-micro and AUC for mortality prediction. As far as the task of mortality prediction is concerned, the approaches that used the history of the patient's signs, symptoms, and diseases to construct one or all compounds have better results in terms of AUC.

| Method   | f1_micro_Mean | f1_micro_Std | ROC_AUC_Mean | ROC_AUC_Std |
|----------|---------------|--------------|--------------|-------------|
| S_U_TT_R | 0.748         | 0.017        | 0.603        | 0.019       |
| S_U_TT   | 0.697         | 0.014        | 0.516        | 0.021       |
| S_TT     | 0.727         | 0.013        | 0.581        | 0.024       |
| S        | 0.603         | 0.017        | 0.512        | 0.014       |

6 Conclusion and future work

In this paper we proposed a novel approach to extract unstructured data in EMR. It provides an overview the patient's previous and current signs, symptoms, and diseases and current significant findings. The unstructured information and the structured data (laboratory tests and prescriptions) were integrated to develop new data modeling for the patient similarity assessment. The concepts extracted from the integrated information were classified into short-term and long-term groups according to their importance and effectiveness over time. Base on this classification, the compounds (co-occurring events) were generated and used to develop the temporal tree structure. The embedding vectors resulting from the tree traversal were used to assess patient similarity. The experimental results showed that our approach in extracting meaningful information from unstructured data can increase the accuracy of the patient similarity assessment model. In this study, the weight of different clinical events that participate in making compounds is considered the same. In future works, the issue of weighting different types of events will be examined. Also, the knowledge resources for enriching the model structure will be considered.
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