Deep learning architectures for vector representations of patients and exploring predictors of 30-day hospital readmissions in patients with multiple chronic conditions

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Abstract. This empirical study of a complex group of patients with multiple chronic concurrent conditions (diabetes, cardiovascular and kidney diseases) explores the use of deep learning architectures to identify patient segments and contributing factors to 30-day hospital readmissions. We implemented Convolutional Neural Network (CNN) and Recurrent Neural Network (RNN) on sequential Electronic Health Records data at the Danderyd Hospital in Stockholm, Sweden. Three distinct sub-types of patient groups were identified: chronic obstructive pulmonary disease, kidney transplant, and paroxysmal ventricular tachycardia. The CNN learned about vector representations of patients, but the RNN was better able to identify and quantify key contributors to readmission such as myocardial infarction and echocardiography. We suggest that vector representations of patients with deep learning should precede predictive modeling of complex patients. The approach also has potential implications for supporting care delivery, care design and clinical decision-making.

Keywords: 30-day hospital readmissions, Multiple Chronic Conditions, Deep Learning

1 Introduction

Machine learning (ML) algorithms, particularly deep neural networks for sequential Electronic Health Records (EHR) data, have been extensively applied in the past decade to inform clinical decision making. However, the unstructured nature of EHR poses a challenge in its implementation, even more so if implemented for complex patients such as patients with multiple chronic conditions (MCCs). One such group of patients with

MCCs is patients with concurrent diagnoses of cardiovascular and chronic kidney diseases and diabetes, hereinafter referred to as MCC patients. This triad of diseases constitutes a huge burden of disease around the world [1] due to high health care utilization [2]. MCC patients are complex due to the underlying pathophysiological mechanisms, conflicting treatment guidelines for each individual disease, and lack of studies [3,4]. This makes it challenging for physicians to treat MCC patients optimally.

Clinicians have been using deep neural networks such as Convolutional Neural Networks (CNN) and Recurrent Neural Networks (RNN) together with patients' medical histories and demographics (e.g. age and gender) to gain insights into the EHR data and tailor treatments according to individual patient needs. Sequential and time-dependency features in patients' journeys such as diagnoses and clinical procedures are increasingly being utilized in ML algorithm development to ensure accuracy and generalizability [5]. However, interpretation of the results obtained from deep neural networks is difficult. Practitioners tend to use simpler models as they have better interpretability, even though they are less accurate than modern ML algorithms [6]. This tradeoff between accuracy and interpretability of the model is not an optimal solution and researchers are developing modern ML algorithms that have both better accuracy and interpretability [7].

The aim of this study is to demonstrate how diagnosis and procedure codes contribute towards predicting 30-day hospital readmissions for MCC patients, and to explore MCC patients' subtypes through vector representations.

Our contribution through this study is three-fold: Firstly, based on the data obtained from one of the busiest tertiary hospitals in the Nordic countries, we demonstrate the effectiveness of deep learning architectures in the exploration of descriptive analytics for MCC patients. More specifically, we explore patterns in vector representations of patients and identify the contributors to 30-day hospital readmissions in terms of diagnoses and procedures. Secondly, the use of the Word2Vec model in conjunction with CNN places the MCC patients' records in EHR in sequential order for the entire care episode. This output can be fed into any type of deep neural architecture and used for making exploratory analysis and predictions. Thirdly, by applying the deep neural network architectures of CNN and RNN on real patient data set we demonstrate how these algorithms developed in one setting can be generalized and implemented in another setting.

2 Related work

Hospital readmissions prediction, a key measure to assess quality of health care delivery, has increasingly become the focus of ML applications. Traditionally, demographics are used to predict hospital readmissions, but the use of other EHR variables is increasing with ML applications. A recent systematic review of models predicting hospital readmissions found that among the twenty-eight types of predictive risk variables, mostly comorbidity, demographics, and social variables were used [8]. Of the seventy-three unique predictive models, forty-five used socio-demographic variables, and only fourteen and sixteen used diagnoses and procedures respectively. Among the twenty-two models related to cardiovascular diseases, only four used diagnoses together with the socio-demographic variables, seven used procedures with the socio-demographics variables, and none of them used diagnoses and procedures simultaneously. Two models used diagnoses and procedures simultaneously, but they were used to predict all-cause hospital readmissions [8].

Most of the existing models for hospital readmissions prediction make use of the conventional ML algorithms such as logistic regression, support vector machines, and k-nearest neighbors [8,9]. One potential limitation of the conventional approaches is that they don't take time duration and temporality into account. RNNs have been recently implemented in health care to address issues of unequal time duration and temporality [5]. Convolutional and recurrent neural networks have been used to predict mortality [10], clinical events [11], diagnoses [12,13], and clinical intervention[14]. CNN, a variant of RNN among others that are well known for capturing underlying structures in sequential data, have been applied in many fields such as speech recognition [15], natural language processing [16] and text classification [17]. Deep neural networks have also been recently implemented to predict hospital readmissions [9,18]. However, only a few studies have implemented deep neural networks for exploratory and descriptive analysis of complex patients with MCCs [19].

3 Methods

3.1 Study design

In this empirical study, we implemented two different types of RNNs to learn about vector representations of patients and factors contributing to 30-day hospital readmissions for MCC patients.

Experiment 1

In experiment 1, we implemented a CNN model complemented with the Word2Vec feature embedding in an unsupervised way, i.e. MCC patients readmitted within 30 days were not labelled and the algorithm learned the inherent structure from the EHR data. The study follows the approach developed by Zhao et al. [20].

We implemented the Word2Vec model that takes the patients' diagnoses (ICD codes) and procedure codes as input (in the form of a text corpus) and produced words in the form of output vectors. The Word2Vec model placed the ICD codes and procedures in their respective clusters. For MCC patients, the ICD codes and procedures were observed in a temporal order and they were organized into sequences. The Word2Vec model was trained on these sequences, and arrays of sequences were produced that were later fed into the CNN model in the form of a stacked matrix. The same hyper-parameters from Zhao et al [20] were used.

The CNN model was trained on the learned sequences for MCC patients in the Word2Vec model. Inputs for MCC patients (*p*) were developed as an embedding matrix ($X_p \in R^{np*d}$), where *np* is the number of records for MCC patients and *d* is the embedding dimension for MCC patients' diagnosis and procedure codes. A 1D convolution was applied over sequential dimension of the matrix. K filters were used in varying lengths of 2 to 5 to capture sequential variations. The filters looked for the presence of a specific pattern in the MCC patients' data. Max pooling layers were used that transformed user outputs from each filter to real numbers [20].

After the model was trained on MCC patients, a predominant single representation of MCC patients' sequential encounters was obtained which was further used to cluster MCC patients' vector representations. Various clustering algorithms were explored to group MCC patients' vector representations after learning the powerful sequential representation from the CNN model. Both feature based clustering (K-Means) and t-Distributed Stochastic Neighbor Embedding (tSNE) were used to cluster the MCC patients' vector representations.

Experiment 2

In experiment 2, we implemented the REverse Time AttentIoN (RETAIN) model, a variant of RNN, to identify the contributors of 30-day hospital readmissions for MCC patients. The study follows the approach developed by Choi et al. [11].

Using the RETAIN model we identified the predictors among diagnosis and procedure codes by assigning a significant portion of prediction to the attention weight generation process. EHR data is stored in such a way that every visit is recorded for each patient at a particular time and all the events that occur are recorded as multiple variables for each visit. The RETAIN model uses weights both for visits and for all the events occurring at a single visit, i.e. visit-level and variable-level weights. The visit level attention weights tackle the effect of each patient's visit embedding and variable level attention weights tackle each activity/event at a visit. For this purpose, RETAIN uses a model with two RNNs, i.e. RNNα and RNNβ, in a backwards direction to generate attention vectors. We used different hyper-parameters compared to Choi et al. [11], as shown in Table 1.

Table 1. Comparison of hyper-parameters used in RETAIN and Experiment 2

Hyper-parameter	REATIN	Experiment 2
Size of visit embeddings, hidden layer for RNNα and RNNβ	128	4
Regularization for final classifier weight, input embedding weight, α generating weights, and β generating weights	0.0001	0.00001
Number of epochs	10	500
Training, validation and test split ratio	0.75:0.1:0.15	0.6:0.2:0.2

3.2 Data collection

The study was conducted at an Integrated Multidisciplinary Clinic (HND-centrum) at a tertiary academic medical hospital, Danderyd University Hospital (DSAB), in Stockholm, Sweden. DSAB is one of the largest Emergency Hospitals (approximately 500 beds) in northern part of Stockholm, Sweden, and provides health services for approximately 650,000 people.

EHR data were obtained for all patients (n = 610) who were registered at the HND-centrum at DSAB between November 2010 and January 2017, and included personal identification numbers, visit dates, visit types, ICD diagnoses codes, clinical procedures codes, mortality dates, DRG codes, hospital admission dates and hospital discharge dates. The majority of MCC patients were between 70 and 80 years old. In total, 3,200 hospital admissions were observed in the selected period, the majority (87.5 %) of which were acute hospital admissions (n=2,801). A total of 76 diagnoses and 59 procedures were fed into the model to develop the sequence vector.

4 Results

4.1 Experiment 1: CNN for vector representations of MCC patients with 30-day hospital readmissions

A total of 268 MCC patients with 30-day hospital readmissions were selected. The most significant ICD codes and procedures that contributed to the 30-day hospital readmissions were identified as shown in Table 2.

Table 2. Salient contributors (diagnoses and procedures) of 30-day hospital readmissions for MCC patients

No	ICD code (diagnoses)	Procedures
1	I109 (Essential Hypertension)	Patient Conference
2	E118 (Diabetes Mellitus type2)	Control and reprogramming of pacemaker
3	N183 (Chronic Kidney Disease stage 3)	Information and teaching directed at patients
4	I259 (Chronic Ischemic Heart Disease)	Transthoracic Doppler echocardiography
5	I509 (Heart Failure)	Telemetry monitoring
6	N184 (Chronic Kidney Disease stage 4)	Unplanned admission for end of life care
7	E119 (Diabetes mellitus without complications)	Information and teaching directed at patients
8	E117 (Non-insulin-dependent Diabetes Mellitus)	Coronary angiography
9	Z921 (Long term use of anticoagulants)	Use of interpreter
10	E785 (Hyperlipidemia, unspecified)	Distant consultation

Table 2 shows that MCC patients readmitted to hospital within 30 days mostly had essential hypertension, diabetes mellitus type 2, and chronic kidney diseases stage 3 and 4 as the key contributors. Similarly, the most significant procedures that MCC patients experienced were patient conferences, echocardiography, coronary angiography, telemetry monitoring, and distant consultations. Since MCC patients are a niche group selected through very strict inclusion and exclusion criteria, it is not surprising that the model identified the contributors shown in Table 2, because these are the most frequent ICD codes and procedures among the selected MCC patients. However, the order of the contributions is noteworthy as they are ordered from most relevant to the least relevant.

Based on MCC patients' vector representations learned by the model, further exploration of the readmitted MCC patients was conducted. Distinct sub-groups were identified by t-SNE clustering as shown in Figure 1. Patients in cluster 1 appear to diverge most from the others.

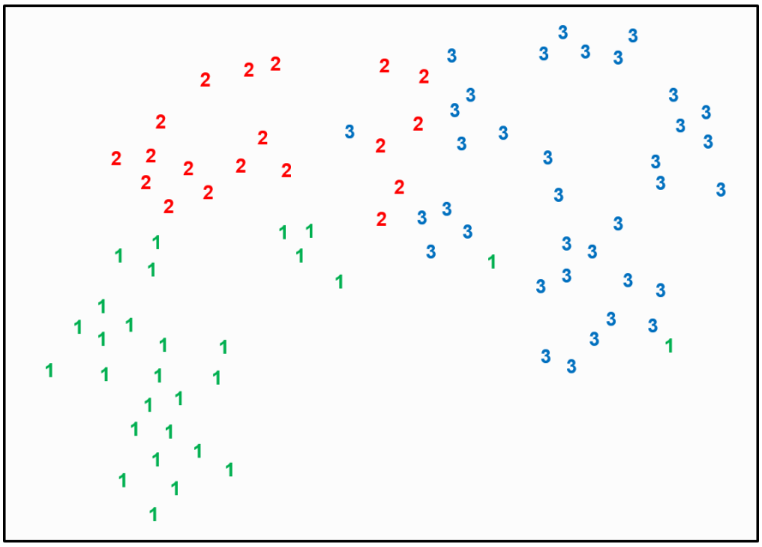

Fig. 1. t-SNE visualization of MCC patients' clusters. Each cluster represents sub-groups within MCC patients who were readmitted within 30 days of their previous hospital admission.

In order to study what differentiates the three clusters from each other, we identified events most common to each cluster. Table 3 presents the key features for each cluster in terms of diagnoses and procedures that the MCC patients experienced (direct output from the model).

As shown in Table 3, Cluster 1 is distinct from Cluster 2 and 3. It was found that MCC patients in cluster 1 had Chronic Obstructive Pulmonary Disease (COPD), labelled with the ICD code R060 (Dyspnea), and required bronchodilation and spirometry more frequently. This indicates that MCC patients with concomitant COPD are more likely to be readmitted within 30 days.

MCC Patients in Cluster 2 have had a kidney transplant (ICD code Z940) and went through several team visits and team conferences, illustrating the complex nature of their conditions.

Lastly, patients in Clusters 3 had paroxysmal ventricular tachycardia (ICD code I472) and repeatedly required control and reprogramming of their pacemaker or defibrillator, and hence were more likely to be readmitted within 30 days.

As we can see from the results in experiment 1, the model identified the most relevant contributing factors to 30-day hospital readmission among MCC patients, and the salient features of the clusters. However, the interpretation of the results can be very tricky because the contributing factors were not quantified or labelled as positive or negative. Thus, we aimed for a more explanatory model in experiment 2.

Table 3. Salient features of clusters of MCC patients with 30-day hospital readmissions

Cluster 1	Cluster 2	Cluster 3
E117, N185, I350, I259, I109, E119, Cystoscopy, Information and teaching directed at patients, sampling (non-specific), R060, Arterial puncture, N409, Arterial puncture, Spirometry before and after bronchodilation, Exercise ECG standard, Spirometry before and after bronchodilation	N183, E107, Distant consultation, Z940, L979, N184, E117, I350, Patient Conference, Team visit, Z940, Patient Conference, E107, L979, Team visit, Z921, E117, L979, Patient Conference	N183, E117, N184, Control and reprogramming of the pacemaker or defibrillator (AICD), E119, I109, N185, I509, Patient Conference, Information and teaching directed at patients, N183, I472, Control and reprogramming of the pacemaker or defibrillator (AICD, Control and reprogramming of the pacemaker or defibrillator (AICD)

E117 = type 2 diabetes mellitus with multiple complications, N185 = chronic kidney disease stage 5, I350 = non-rheumatic aortic valve stenosis, I259 = nonspecific chronic ischemic heart disease, I109 = type 1 diabetes mellitus without complications, R060 = dyspnea, N409 = benign prostatic hyperplasia, N183 = chronic kidney disease stage 3, E107 = type 1 diabetes mellitus with multiple complications, Z940 = kidney transplant, L979 = non-pressure chronic ulcer of unspecified part of lower leg, N184 = chronic kidney disease stage 4, Z921 = long term use of blood thinning agents, E119 = type 2 diabetes mellitus without complications, I509 = unspecified heart failure, I472 = ventricular tachycardia

4.2 Experiment 2: RETAIN for MCC patients with 30-day hospital readmissions

Given the temporal sequences of MCC patients' diagnoses and procedures, we attempted to identify factors that contributed to 30-day hospital readmission. The same number of patients with 30-day hospital readmissions (n=268) were included. We were able to attain Validation and Test accuracy of 0.900 and 0.794 respectively with RETAIN, which was better than the AUC of 0.8705 obtained by Choi et al [11].

Table 4 shows results obtained from the RETAIN model in terms of contributions of the diagnoses and procedures to 30-day hospital readmissions and overall risk of readmission for MCC patients (direct output from the model). The contribution scores range between the lowest and highest values of -0.5 and 1.5 respectively. The overall risk score is calculated between 0 (no risk) and 1 (absolute risk). Table 4 shows readmission risk scores for three MCC patients and the contribution scores, either positive or negative, of each ICD code and procedure. The contribution scores show how each diagnosis and procedure contributed to the final prediction score (the contribution scores are added and put through the sigmoid function in the model).

Table 4. Contributions of the diagnosis and procedure codes in predicting 30-day hospital readmissions for MCC patients at each successive patient visit.

Visit No	MCC patient 1	MCC patient 2	MCC patient 3
1	I489B: 0.353787	E107: -0.055551	E119: 0.651345
2	Z950: 1.018832	Allogenic red cell transfusion: 0.104865	Patient Conference: 0.846334
3	I472: 0.638967	G473: 2.641692	Information and teaching directed at patients: 1.341413
4	Control and reprogramming of the pacemaker or defibrillator: -0.009479	Z921: 1.971326	Z921: 0.978889
5	Preoperative assessment: 0.073104	I489B: 0.557335	Patient Conference: 0.196036
6	E785: 1.050597	I219: 0.019547	Distant consultation: 0.082917
7	I489B: 0.294173	I501: 0.006919	E119: 0.604113
8	G473: -0.223236	Telemetry monitoring: 0.004798	E669: 0.070579
9	Telemetry monitoring : -0.030263	Transthoracic Doppler echocardiography: -0.087382	N183: 0.365141
10	-	Coronary angiography: - 0.042835	Orthostatic test: -0.021256
11	-	-	Distant consultation: 0.014503
12	-	-	I109: -0.029082
	Overall Risk score: 0.952125	Overall Risk score: 0.992927	Overall Risk score: 0.992786

I489B = unspecified atrial fibrillation and atrial flutter, Z950 = presence of cardiac pacemaker, I472 = ventricular tachycardia, E785 = unspecified hyperlipidemia, G473 = sleep apnea, E107 =

type 1 diabetes mellitus with multiple complications, Z921 = long term use of blood thinning agents, I219 = unspecified acute myocardial infarction, I501 = left ventricular failure, E119 = type 2 diabetes without complications, E669 = unspecified obesity, N183 = chronic kidney disease stage 3, I109 = essential hypertension

As we can see in Table 4, RETAIN determined the 30-day hospital readmission risk score for each individual MCC patient based on the diagnoses and procedures in their respective past medical encounters. In contrast to the results obtained from experiment 1, RETAIN assigned each diagnosis and procedure its specific contribution score and determined the overall risk of 30-day hospital readmission. Each contribution can either negatively or positively affect the overall risk of readmission.

MCC patient 1 in Table 4, likely belonging to Cluster 3 in experiment 1 because the patient had paroxysmal ventricular tachycardia (ICD I472), required reprogramming and controlling of the pacemaker or defibrillator, and preoperative assessment among other procedures. We can see that paroxysmal ventricular tachycardia diagnosis increased the risk of readmission (0.638967) while the procedure for control and programming of the pacemaker reduced the risk of readmission (- 0.009479). Other notable contributions for MCC patient 1 were preoperative assessment and telemetry monitoring which increased (0.073104) and decreased (- 0.030263) the risk for 30-day hospital readmission respectively.

MCC patient 2 had coagulation disorder (ICD code Z921) and acute myocardial infarction (ICD I219) in the past, and also required a blood transfusion among other things. We can see in Table 4 that a myocardial infarction and blood transfusion contributed positively to the readmission score (0.019547 and 0.104865 respectively), whereas echocardiography and coronary angiography reduced the risk of readmission (- 0.087382 and - 0.042835 respectively). Similarly, we can see the contributing factors and scores for MCC patient 3. For example, other than the three common diagnoses underlying the MCC condition, the patient had obesity (ICD code E669), which positively contributed to 30-day hospital readmission (0.070579).

5 Discussion

Both the CNN and RNN used in this study identified the most salient predictors for 30-day hospital readmissions among MCC patients. Experiment 1 demonstrated that various distinct sub-types exist among MCC patients readmitted within 30 days, and MCC patients with COPD, kidney transplant and paroxysmal ventricular tachycardia are at higher risk of readmission within 30 days. Experiment 2 demonstrated that the model was able to identify contribution scores for diagnoses and procedures such as myocardial infarction and echocardiography, and overall 30-day hospital readmission risks for individual MCC patients.

Experiment 1 also demonstrated that patient conferences preceded 30-day hospital readmissions among MCC patients. Control and reprogramming of pacemakers, telemetry monitoring and distant consultations were also associated with the 30-day hospital readmissions. But, experiment 1 was not able to demonstrate the quantitative contribution, either positive or negative, of the diagnoses and procedures to 30-day hospital readmissions. However, this challenge associated with interpretation of results obtained from deep neural networks is common, and some models have been applied in health care to address this issue [11,21].

In experiment 2, we demonstrated that RETAIN was better able to quantify the individual contributions of diagnoses and procedures to 30-day hospital readmissions, both in terms of either causing (positive contribution) or preventing (negative contribution) readmissions. These contributions were determined for individual patients considering the sequence and timing of the previous MCC patients' visits as shown in Table 4. In coming studies we aim to explore how the RETAIN model is affected by adding more variables to the MCC patients' sequential records, such as demographics, medications, laboratory values, number of visits, and length of stay.

This study suggests that vector representations of patients and sub-typing among complex patients, such as MCC patients, by the type of health care encounters, like hospital readmissions, is as important as sub-typing patients by age and gender. Vector representations of patients are a road map in disease progression [22–24] that can identify key disease patterns among complex chronic patients. Sub-grouping patients, and hence identifying specific medical journeys for complex patients may enhance clinicians' ability to make optimal care decisions. As demonstrated in this study, robust deep learning algorithms such as CNN and RNN have been proposed to learn typical vector representations of complex patients, and stratify them into suitable sub-groups that can help clinicians in their day-to-day decision making process during disease and operational management.

The CNN and RNN used in this study have the potential to positively influence practical decisions around MCC patients and optimize resource utilization. The models can be used to inform physicians about high consumers of care, and develop process maps and clinical pathways for unique clusters. They also have predictive potential and can be used to identify MCC patients' sub-types for which prediction models can be developed. These models can predict both clinical and healthcare operations management outcomes such as mortality, cardiovascular events, length-of-stay, and hospital readmissions. For instance, if physicians are able to classify patients into a particular cluster that follows a specific sequence of treatment events, they would be able to stream patients into a sequential care process, or if not, into a more customized process [25]. Predictive models can also be incorporated into interactive analytics tools for patients with MCCs where physicians could review individual MCC patient's risk scores for selected outcomes. The tool could also provide a visualized overview of a patient's past medical history and encounters.

6 Limitations/Methodological considerations

This study reports the findings based on ICD codes and procedures only for a relatively small sample size of MCC patients. Therefore, prediction score accuracy might be low. We aim to increase the sample size and refine the models' parameters in order to increase accuracy, and include more variables for the development of a predictive decision support model for MCC patients. Some ICD codes and procedures are also inherently associated with certain already-made clinical decisions. In the future, we will carefully select diagnosis and procedure codes relevant for specified research questions, for instance using directed acyclic graphs.

7 Conclusion

Temporal data on ICD codes and procedures appears to be valuable for personalized disease management strategies for MCC patients. In this study, three distinct sub-types of MCC patients with increased risk for readmission were identified. We suggest that temporal vector representations of patients and sub-typing with deep neural networks such as CNN and RNN are useful in the development of predictive analytics tools for patients with MCCs.

In the future, we plan to explore the application of deep neural networks in the development of prediction models for MCC patients that can be used to predict both clinical and operations management outcomes, and aim to make the results easily accessible for clinicians and other health care professionals.

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9 Ethical considerations

The study has been approved by the Regional Ethics Committee (Diary Numbers: 2014/384-31/1 and 2017/999-31/2).

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