Label-dependent and event-guided interpretable disease risk prediction using EHRs

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Abstract-Electronic health records (EHRs) contain patients' heterogeneous data that are collected from medical providers involved in the patient's care, including medical notes, clinical events, laboratory test results, symptoms, and diagnoses. In the field of modern healthcare, predicting whether patients would experience any risks based on their EHRs has emerged as a promising research area, in which artificial intelligence (AI) plays a key role. To make AI models practically applicable, it is required that the prediction results should be both accurate and interpretable. To achieve this goal, this paper proposed a label-dependent and event-guided risk prediction model (LERP) to predict the presence of multiple disease risks by mainly extracting information from unstructured medical notes. Our model is featured in the following aspects. First, we adopt a label-dependent mechanism that gives greater attention to words from medical notes that are semantically similar to the names of risk labels. Secondly, as the clinical events (e.g., treatments and drugs) can also indicate the health status of patients, our model utilizes the information from events and uses them to generate an event-guided representation of medical notes. Thirdly, both label-dependent and event-guided representations are integrated to make a robust prediction, in which the interpretability is enabled by the attention weights over words from medical notes. To demonstrate the applicability of the proposed method, we apply it to the MIMIC-III dataset, which contains real-world EHRs collected from hospitals. Our method is evaluated in both quantitative and qualitative ways.

Index Terms-Label-dependent prediction, Event-guided prediction, Cross-attention mechanism, Disease risk prediction.

I. INTRODUCTION

Artificial intelligence (AI) is being increasingly applied to extract information from electronic health records (EHRs) for implementing various prediction tasks, such as ICU staying time estimation [13], disease diagnosis [4], [8], statistical phenotype prediction [4], and etc. EHRs collect heterogeneous information about the patients from medical providers involved in the patients' care, including medical notes, laboratory observations, treatments, clinical events, electrocardiogram waveforms (ECG), and medication.

With rapid advances in deep learning, many methods like attention-based RNN [13] and convolutional neural networks (CNN) [2] are being developed to predict disease risks using EHRs. To make these models practically useful, the predictive model is required to generate interpretable results while still

retaining predictive power. However, for rare diseases, aforementioned approaches would not be applicable due to the lack of prior knowledge.

This paper aims to develop an AI model to fulfil the disease risk prediction task, and we are interested in utilizing attentionbased methods to achieve interpretability for the task of risk prediction using medical notes. Our approach is different from self-attention-based methods [11] which did not use any external information to learn the important weights of words in medical notes. We propose a label-dependent and event-guided risk prediction (LERP) model that both names of disease risk labels and clinical events would be used to determine the importance of different words from medical notes. Apart from using the names of disease risk labels, we also use clinical events to set the attention weights of words from medical notes. Clinical events are treatments received from clinicians, and thus can be very informative in reflecting the patient health status. Our contributions can be summarized as follows:

- We propose a cross-attention mechanism to learn the attention weights of words in medical notes by measuring their semantic similarities with names of disease risk labels and clinical events.
- To encode textual information, we apply a pre-trained biomedical language model, Clinical-BERT [1], for jointly embedding names of disease risk labels, clinical events, and medical notes such that information learned from a large biomedical corpus can naturally be incorporated into the model. Label names, clinical events, and words in medical notes with similar meanings will be assigned with similar embedding vectors by Clinical-BERT.

II. RELATED WORK

A. Label-dependent Predictive Modelling

Label-dependent predictive models are being developed in various domains, such as computer vision (CV) (e.g., object detection [7]) and modern healthcare (e.g., disease codes prediction [8]). In the medical healthcare domain, [8] first proposed the convolutional attention for a multi-label classification model (CAML) and deep CAML to predict multiple diseases by introducing the label information via a attention layer. Following the work of CAML, [12] proposed

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the label-embedding attentive model (LEAM) to jointly learn the embeddings of medical notes and label names in the same latent space.

B. Using Clinical Events for Disease Prediction

Clinical events recorded in EHRs indicate treatments that were given to patients based on their own clinical conditions. Many researchers attempted to use clinical events for predictive model construction. [13] treated clinical events as interventions and also adopted the attention mechanism to generate the weighted embedding of electrocardiogram (ECG) for patients' mortality prediction. [3] adopted the gated recurrent units (GRUs) to detect relationships among various time-stamped events for the heart failure prediction.

III. METHODS

A. Problem Definition and Notations

In this work, we focus on using medical notes and clinical events to predict whether patients would experience some disease risks. Let us first define the vocabulary of words that occurred across all EHRs as V, whose size is represented as |V|. The information from each EHR used for the risk prediction is defined as $X = \{M, \mathcal{L}_E, \mathcal{L}_Y\}$. Here, M = $\{m{m}_1,...,m{m}_{N_M}\}$ contains a sequence of words from a medical note; $\mathcal{L}_E = \{ \boldsymbol{l}_1, ..., \boldsymbol{l}_{N_E} \}$ refers to a set of clinical events; and $\mathcal{L}_Y = \{ \boldsymbol{l}_1, ..., \boldsymbol{l}_{N_Y} \}$ represents the names of disease risk labels. Each element from M, \mathcal{L}_E , \mathcal{L}_Y is a |V|-dimensional one-hot vector for representing a word, an event and the name of a risk label, respectively. Please note that for each EHR, M and \mathcal{L}_E are different but \mathcal{L}_Y is identical. This is because \mathcal{L}_Y just encodes names of disease risk labels and does not indicate their presence. A sample from the training dataset is represented as (\mathbf{X}, \mathbf{y}) , where $\mathbf{y} \in \mathcal{Y}$ is a N_Y -dimensional vector with elements equal to 1 or 0 indicating the presence of different disease risks. The goal for disease risk prediction is to learn a mapping function $f: \mathcal{X} \to \mathcal{Y}$ by minimizing the prediction loss.

B. Model Overview

Fig. 1 shows the details of our proposed model, LERP. The text encoder based on Clinical-BERT first converts the medical note M, the sequence of clinical events \mathcal{L}_E , and the names of disease risk labels \mathcal{L}_Y into embedding matrices \mathbf{E}^M , \mathbf{E}^E , and \mathbf{E}^Y , respectively. Then the cross-attention mechanism is introduced to generate attention matrices α^E and α^Y . α^E measures the similarities between elements from \mathbf{E}^M and \mathbf{E}^E , while α^Y is similarly calculated for \mathbf{E}^Y and \mathbf{E}^M . With these two attention matrices, the model obtains two weighted representations of the medical note, denoted as \mathbf{z}^E and \mathbf{z}^Y . Our model uses the information encoded in \mathbf{z}^E and \mathbf{z}^Y to predict the presence of N_Y different disease risks.

C. Embedding Layer

First, M, \mathcal{L}_E , and \mathcal{L}_Y are passed through an embedding layer f_0 to get $\mathbf{E}^M \in \mathbb{R}^{D \times N_M}$, $\mathbf{E}^E \in \mathbb{R}^{D \times N_E}$ and $\mathbf{E}^Y \in \mathbb{R}^{D \times N_Y}$, where D is the embedding size. In our model,



Fig. 1. The structure of the LERP Model. It takes the information from medical notes, clinical events and names of disease risk labels as the inputs. LERP is composed of embedding layers for textual information embedding, cross-attention layer for learning weighted representations of the medical note, and the fusion layer together with the output layer to predict the presence of different disease risks.

 f_0 is implemented by Clinical-BERT [6]. To get embedding matrices E^Y and E^E , we use the averaged embeddings of input tokens to represent the overall embedding of an event or the name of a disease risk label. To generate E^M , Clinical-BERT encodes medical notes and returns N_M embedding vectors for all N_M words.

D. Cross-attention Layer

The cross-attention layer is illustrated in the middle part of Fig. 1, where E^M , E^E , and E^Y are the inputs. We first apply a fully connected layer f_1 to reduce the embedding dimension of E^M , E^E , and E^Y from D to F. The outputs of f_1 are then used to compute the scaled-dot similarity matrices $G^E \in \mathbb{R}^{N_M \times N_E}$ and $G^Y \in \mathbb{R}^{N_M \times N_Y}$:

$$\boldsymbol{G}^{E} = ScaledDot(f_{1}(\boldsymbol{E}^{M}), f_{1}(\boldsymbol{E}^{E})) = \frac{(f_{1}(\boldsymbol{E}^{M}))^{T} * f_{1}(\boldsymbol{E}^{E})}{\sqrt{F}}$$
(1)

where the $(.)^T$ is the transpose operator and * is the matrix product operator. We use the same equation to calculate G^Y with the input of E^Y and E^M .

We use a one-dimensional (1-D) CNN with a max-pooling (MP) layer to better capture the relative spatial information of successive words and to increase the ability of implicit information extraction:

$$\boldsymbol{u}^{E} = MaxPool(ReLU(Conv(\boldsymbol{G}^{E}, k_{1}, q)), k_{2})$$
(2)

where ReLU is the nonlinear activation layer, k_1 is the kernel width (N-Gram) of CNN, q is the padding size of CNN (set to

'same padding' in our implementation), and k_2 is the kernel width of MP. The u^Y is generated by the same formula as u^E with input of G^Y .

The outputs $u^E \in \mathbb{R}^{N_M}$ and $u^Y \in \mathbb{R}^{N_Y}$ are then normalized by a SoftMax function to generate α^E and α^Y . With α^E and α^Y , we can obtain the two weighted representations of the medical note as follows:

$$\boldsymbol{z}^{E}, \boldsymbol{z}^{Y} = \sum_{n=1}^{N_{M}} \alpha_{n}^{E} \boldsymbol{E}_{n}^{M}, \sum_{n=1}^{N_{M}} \alpha_{n}^{Y} \boldsymbol{E}_{n}^{M}$$
(3)

where $E_n^M \in \mathbb{R}^D$ is the *n*th column of E^M , α_n^E and α_n^Y are the *n*th elements from α^E and α^Y respectively.

E. Fusion and output Layers

After we have obtained z^E and z^Y , we combine them into one vector via fully connected layers f_1 , f_2 , and f_3 :

$$\hat{\boldsymbol{y}} = Sigmoid(f_3(f_1(f_2(\boldsymbol{z}^E \oplus \boldsymbol{z}^Y)))), \qquad (4)$$

where \oplus is the concatenation operator and $\hat{\boldsymbol{y}} \in \mathbb{N}^{Y}$.

F. Model Training

To train our model, the loss for each EHR is defined as follows:

$$Loss = -\frac{1}{N_Y} \sum_{j=1}^{N_Y} (y_j \cdot \log(\hat{y}_j)) + (1 - y_j) \cdot \log(1 - \hat{y}_j)),$$
(5)

where $y_j \in \{0, 1\}$ indicates the presence of the *j*th disease risk.

IV. EXPERIMENTS

A. Experimental Dataset

We evaluate the performance of our proposed LERP model on a public EHR dataset, MIMIC-III [6]. In this paper, for disease risk prediction we only focus on using the information from medical notes of the discharge summary and clinical events. We choose 25 types of disease risks (defined in [4]) as our prediction tasks, where some of them are clinically different. Across all EHRs, there are 1,152 distinct clinical events. The MIMIC-III dataset contains 58,976 EHRs from 46,520 patients. We select 31,484 unique EHRs with no missing information. The data pre-processing approach used in CAML is adopted to analyze the unstructured medical notes. For performance evaluation, we follow the data splitting strategy as used in [4] to get 25,190 training and 6,294 testing samples (80% for training and 20% for validation).

B. Comparative Methods and Implementation Details

In order to make a comprehensive comparison, we compare our model with other comparative methods as described below:

• LEAM: LEAM is a cutting-edge deep learning model that was created specifically for ICD-9 code prediction by utilizing textual information of medical notes. We select the default setting of LEAM as implemented in ¹ for comparison.

¹https://github.com/guoyinwang/LEAM

- **TS**: This baseline model applies Clinical-BERT [5] to embed medical notes. The self-attention mechanism [11] is adopted to encode information from the medical notes for disease risk prediction.
- LERP: Our LERP model² is a label-dependent and eventguided approach to make interpretable risk predictions. Medical notes, names of disease risk labels, and clinical events are embedded by Clinical-BERT. The crossattention mechanism is introduced to assign attention weights to words from medical notes based on the semantic similarities among words, events, and names of disease risk labels.
- LERP⁻: This is a modified version of LERP that clinical events are not included in the risk prediction model. Attentions of words from medical notes are determined by their semantic similarities with names of disease risk labels.

C. Quantitative analysis

The performance of all comparative models is evaluated using the following metrics: precision, recall, and ROC AUC score. We compute both micro- and macro-averages for these metrics. Table I shows the results of all comparative methods, from which we have the following observations:

- Compared with LEAM which does not use Clinical-BERT for textual information embedding, our LERP model returns higher values for most evaluation metrics. Especially, LEAM has much lower recall values. This is because Clinical-BERT can be useful in learning semantic representations of medical textual information. This observation demonstrates the power of incorporating the pretrained language model for the risk prediction.
- Compared with TS which is not label-dependent, LERP returns higher values in most evaluation metrics as well. This observation indicates that the cross-attention mechanism, making the predictive model label-dependent, would work better than the self-attention mechanism.
- Compared with LERP⁻ which does not use the information from clinical events, the values of evaluation metrics obtained from our full model are slightly lower but the difference in ROC AUC values is trivial. This

TABLE I Performance of comparative methods

	Evaluation Metrics			
Models	Micro Precision	Macro Precision	Micro Recall	
LEAM	0.7526	0.6308	0.4958	
TS	0.7256	0.6533	0.5968	
LERP	0.7231	0.6645	0.6075	
LERP-	0.7075	0.6598	0.6305	
Models	Macro Recall	Micro ROC AUC	Macro ROC AUC	
LEAM	0.4347	0.8898	0.8587	
TS	0.5404	0.8969	0.8642	
LERP	0.5424	0.9001	0.8729	
LERP-	0.581	0.9013	0.8737	

²https://github.com/finnickniu/LERP

is because LERP⁻ learns the attentions of words from medical notes fully dependent on the prediction tasks. In our full LERP model, attentions are also guided by clinical events. Although our full model has sacrificed a little bit of performance, it would give better interpretable results which will be shown in the following subsection.

D. Qualitative analysis

In this subsection, we carried out case studies to show the interpretability of our model by investigating which words from medical notes have gained high attention from our model and checking whether these words are clinically relevant to the risks. Three EHRs for patients with different disease risks have been randomly selected from the MIMIC-III dataset. Fig. 2 shows fragments of medical notes, clinical events, and risks that have been recorded in each EHR. Words from EHR fragments are highlighted in red, whose darkness are determined by their attention scores derived from the cross-attention mechanism. Clinical events and disease risks that are associated with the given medical note fragments are given as well. To show whether the event-guided approach would improve interpretability, we compare results from LERP with LERP⁻.

The patient recorded in 'EHR 1' has the risks of 'Coronary atherosclerosis ...' and 'Cardiac dysrhythmias'. By comparing the results from LERP⁻ and LERP, we can find that LERP, for example, gives higher attentions to the following two words from medical notes: 'Amiodarone' and 'hypotensive'. 'Amiodarone' is a medicine frequently used to treat both 'Coronary atherosclerosis ...' and 'Cardiac dysrhythmias' (

	0% 1%	20%	40% 60%	80% 100%
EHR ID	Event	Risk	Medical note highlighted by LERP	Medical note highlighted by LERP-
EHR 1	Propofol, Amiodarone	Coronary atherosclerosis and other heart, Cardiac dysrhythmias	was interest to the arruin stable condition on neal and arrotatine was actuated on his postportative night and had his prestruted of d and was fransformed to the ford on and on and he was in after and was very hypotensistic and was iterated on the arrotation of the arrow of the arrow in a statistication of the arrow of the ar	was transferred to the transferred in stable condition on the and according to the stable stutbated on this postportative night and had his there there is a stable of the on post the stable of the floor on post on post here is the start of the stable of the on post here is the start of the start of the on post of the start of the start of the on according and converted to she was transferred back to the term on post
EHR 2	Dopamine	Acute myocardial infarction, Coronary atherosclerosis and other heart disease, Congestive heart failure	was transferred to the ccu on dopamine for hypotensin he was weaned from dopamins drg and transferred to general medicine floor for further observation, he was continued on his sas attern plavk no episodes of dist plan post procedure and was tischarged with follow up with a <u>sardiological</u> and prescriptions for the plavix state	was transferred to the ccu on dopamine for hypotension he was weared from dopamine drip and transferred to general flucture floor for further <u>observations</u> floor for further <u>observations</u> he was continued on his as a statin plavity, no <u>episodes</u> of <u>fluest pain post</u> <u>procedure</u> and was <u>flucture</u> with follow up with a cardiologistic and prescriptions for <u>ass</u> plavity statin,
EHR 3	Chest X ray	Coronary atherosclerosis and other heart disease	was transformed to the teamsety floor for further recovery charactulies and teams wires were discontinued without complication the patient/was evaluated by the physical therapy service for assistance with thready and mobility by the time of discharge on pod	was transferred to the telemetry floor for further tecamo created to the and pacing time were discontinued without complication the patient was evaluated by the physical through service for transferred with technoli and mobility by the time of discharge on pade

Fig. 2. Case studies to compare the interpretable results from LERP and LERP⁻. The colour map on the top of this figure maps the colours to normalized attention scores (ranging from 0% to 100%). In the result table, the second/third column contains the clinical events/disease risks associated with the selected fragments of medical notes.

[10]), while 'hypotensive' is a typical symptom of these risks [9]. For the rest cases, we can also find similar result that LERP can capture more related clinical phases than LERP⁻.

V. CONCLUSIONS

This study presents an interpretable label-dependent and event-guided prediction model to predict the presence of various disease risks by using the names of disease risks, clinical events, and medical notes from EHRs. We employ Clinical-BERT as an embedding layer to assist our LERP model in extracting information from raw textual data. With the adoption of the cross-attention mechanism, representations of medical notes are generated by learning attention influenced by both clinical events and names of disease risk labels. We evaluate our model LERP using the MIMIC-III dataset to show its predictive power and interpretability. Case studies have been conducted to show that the medical terms that are clinically relevant to the disease risks gain high attention weights. In the future, we will invite domain experts to manually annotate our results, for example, to specify which words from medical notes are relevant to risk labels. As such, we can quantitatively evaluate the degree of interpretability.

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