Interpretable Representation Learning for Healthcare via Capturing Disease Progression through Time

APA：Bai, T., Zhang, S., Egleston, B. L., & Vucetic, S. (2018, July). Interpretable Representation Learning for Healthcare via Capturing Disease Progression through Time. In *Proceedings of the 24th ACM SIGKDD International Conference on Knowledge Discovery & Data Mining* (pp. 43-51). ACM.
Advisor：Jia-Ling, Koh
Speaker：Pei-Hsuan Lin
Source：KDD,2018
Date：2019/01/29

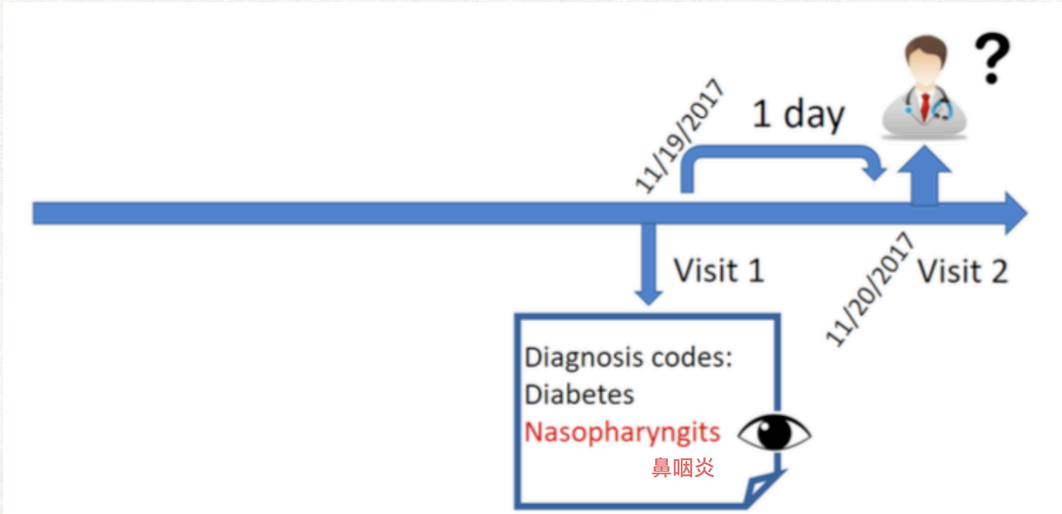
Outline

- Introduction
- Method
- Experiment
- Conclusion

Introduction

- To predict what is the primary diagnosis category for the hospital visit

(a) For a visit record long time ago, doctors may put more attention to chronic diagnosis since they have long-term effect.



(b) For a recent visit record, doctors may put more attention to the acute diagnosis since they have strong short-term effect.

Challenges

The RNN model is lack of interpretability

-> Add attention layer into the model

+

Irregular sampling of patient visits

-> Consider visit interval in the hidden state

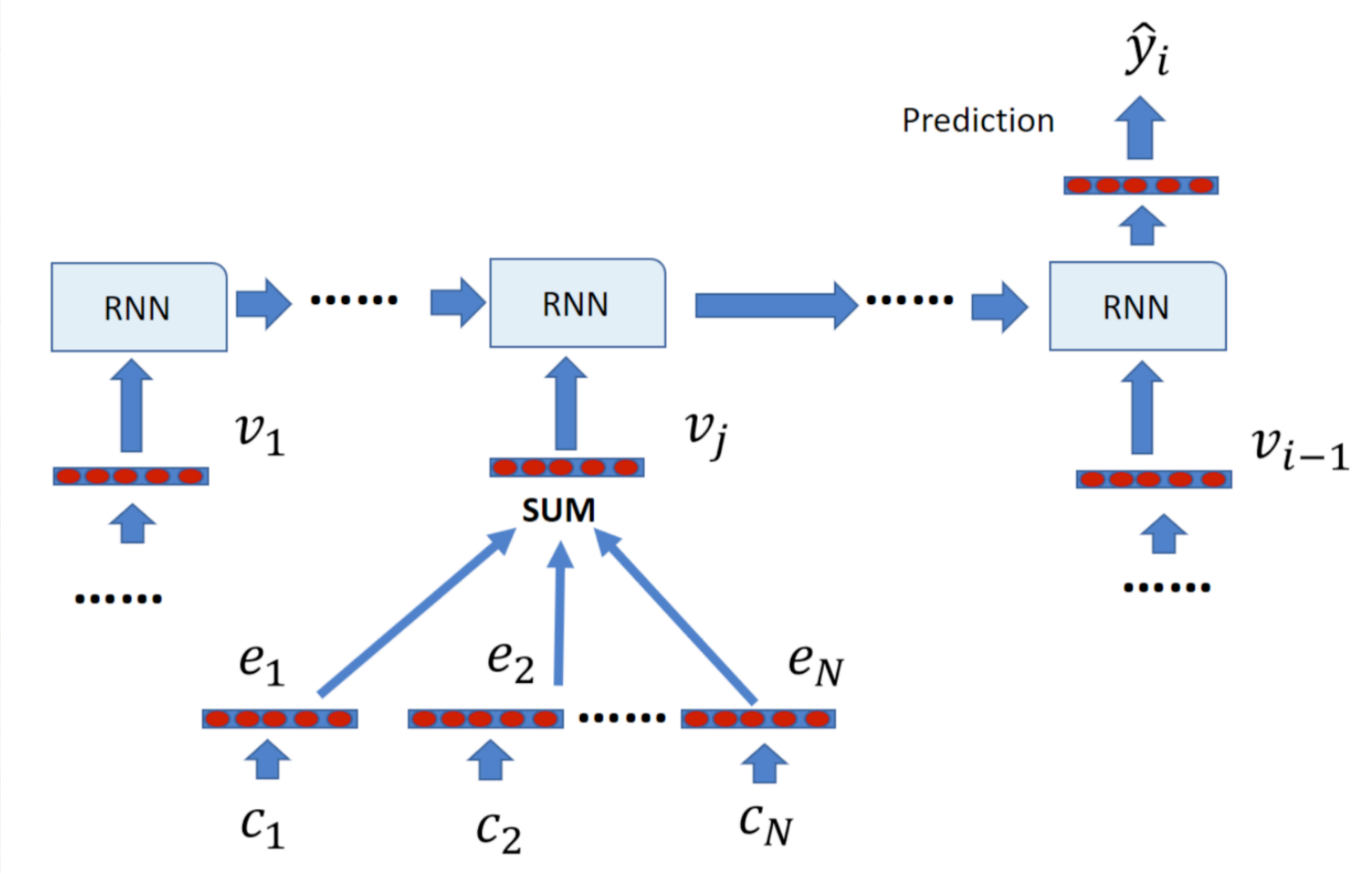
↓

Interpretable, time-aware, disease-sensitive RNN model :
Timeline

Problem setup

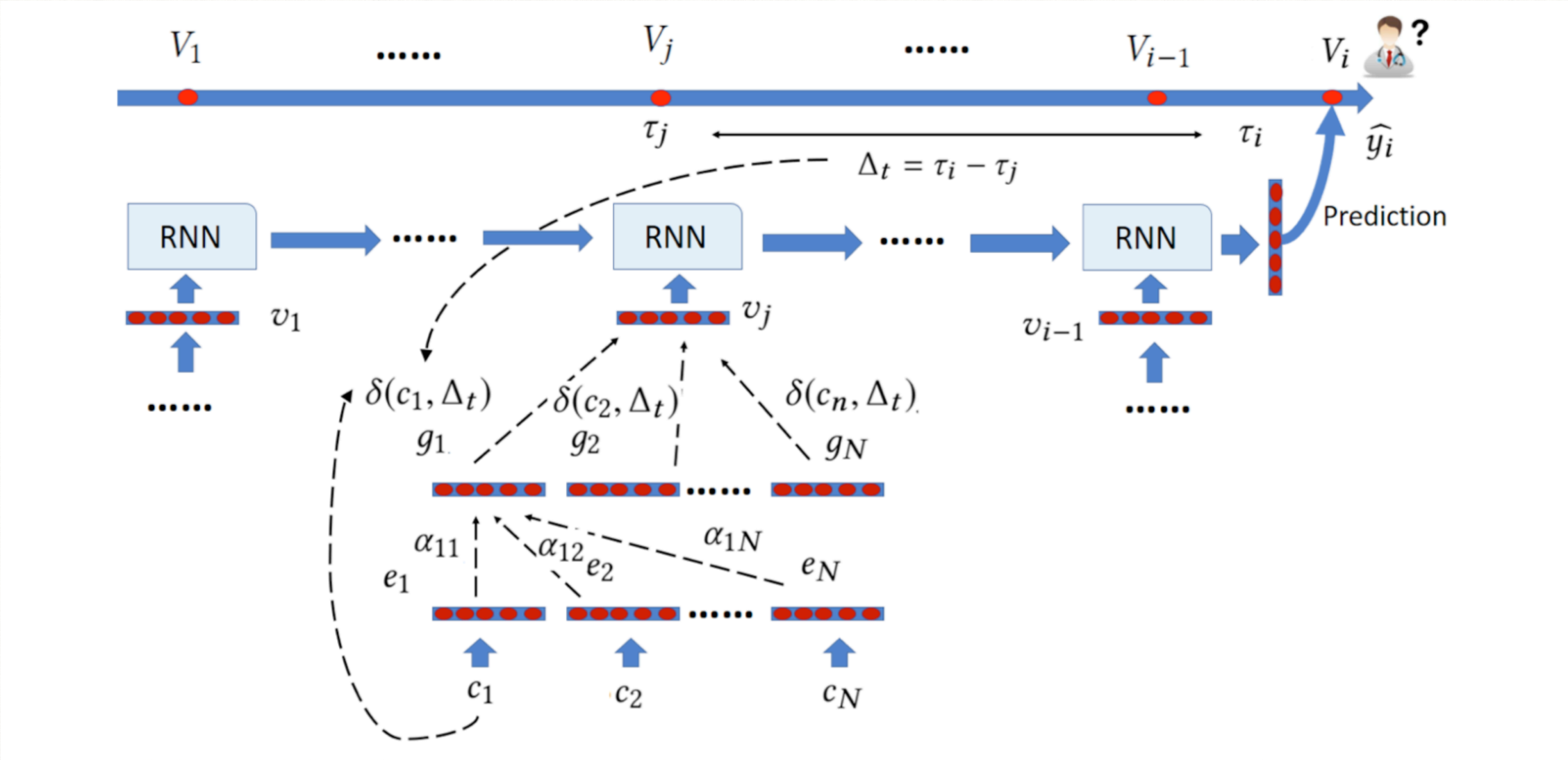
- The i-th patient consists of a sequence of T^i visits $V_1^i, V_2^i, V_3^i, \ldots, V_{T^i}^i$ ordered by the visiting time.
- The j-th visit V_j^i is a 2-tuple $V_j^i = (\xi_j^i, \tau_j^i)$
- ξ_j^i consists of a set of unordered medical codes $\xi_j = \{c_1, c_2, \ldots, c_{|\xi_j^i|}\}$
- τ_j^i is the admission day of the visit

The Similar Simple Framework

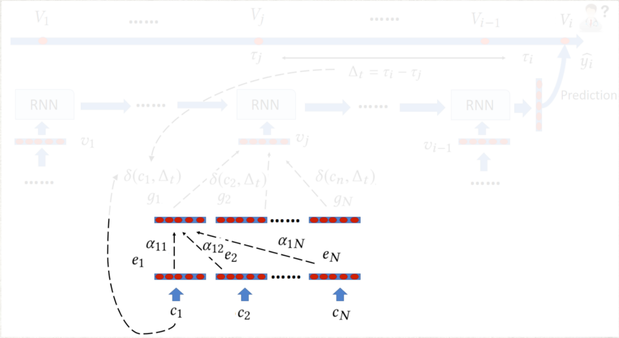


$$v_j = \sum_{n=1}^{N} e_n$$: **Each code contributes equally to the final visit representation.**

The Timeline Model

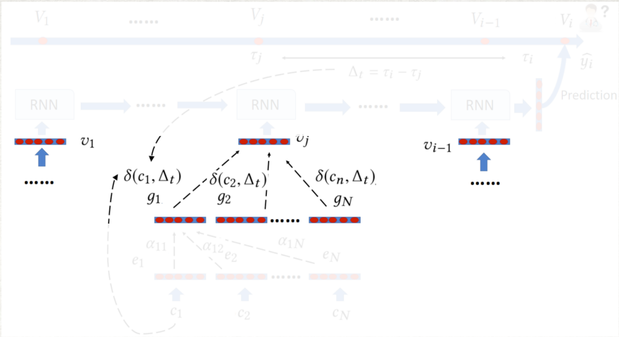


The Timeline Model - 1attention weight



- <u>query vector and key vector for c_n</u>
  - query vector : $q_n = W_Q e_n, W_Q \in R^{a \times m}$
  - key vector : $k_n = W_K e_n, W_k \in R^{a \times m}$
- <u>attention value</u> :
  - $$\alpha_{n1}, \alpha_{n2}, \ldots, \alpha_{nN} = softmax([\frac{q_n k_1}{\sqrt{a}}, \frac{q_n k_2}{\sqrt{a}}, \ldots, \frac{q_n k_N}{\sqrt{a}}]),$$
  - $\sqrt{a}$ is the scaling factor

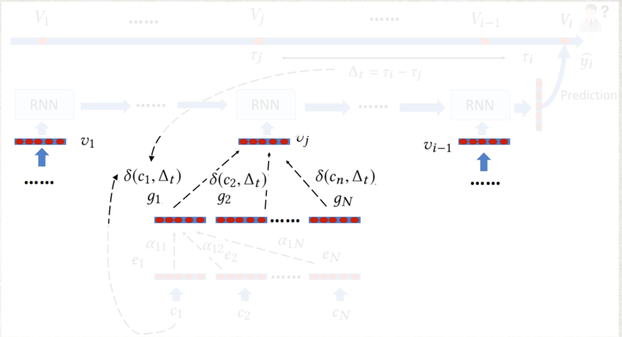
The Timeline Model - 2final visit representation



- <u>context vector gn</u> :
- $$g_n = \sum_{x=1}^{N} \alpha_{nx} e_x$$

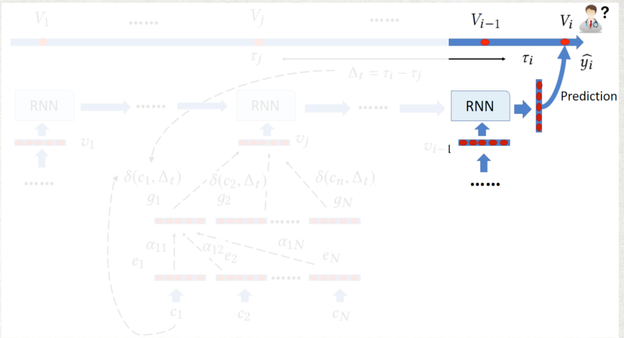
- <u>δ function</u> : representation how disease cn diagnosed at Δt ago affects the condition at the time of prediction
  - $\delta(c_n, \Delta_t) = S(\theta_{c_n} - \mu_{c_n} \Delta_t)$
  - μ_{c_n} , θ_{c_n} are disease-specific learnable scalar (initial and through-time influence)
  - Δt = τi − τj , time interval between Vj and the prediction Vi
  - sigmoid function

The Timeline Model - 2final visit representation



- <u>final visit representation</u>：
  - $$v_j = \sum_{n=1}^{N} \delta(c_n, \Delta_t) g_n$$

The Timeline Model - 3prediction



- <u>target label</u>：
  - $y_i \in R^L$, one-hot
- <u>prediction process</u>：
  - $h_1, h_2, \ldots, h_{i-1} = biLSTM(v_1, v_2, \ldots, v_{i-1}, \theta_{LSTM})$
  - $\widehat{y_i} = softmax(Wh_{i-1} + b)$
- <u>loss function</u>：
  - negative log likelihood：$L(y_i, \widehat{y_i}) = -y_i \log \widehat{y_i}$
    - average of instance losses for multiple instances in implementation

The Timeline Model - interpretation

- analysis weights associated with each embedding e of medical code c:
- $$v_j = \sum_{n=1}^{N} \delta(c_n, \Delta_t) g_n$$
$$= \sum_{n=1}^{N} \delta(c_n, \Delta_t)(\sum_{x=1}^{N} \alpha_{nx} e_x)$$
$$= \sum_{x=1}^{N} (\sum_{n=1}^{N} \delta(c_n, \Delta_t) \alpha_{nx} e_x)$$
- $\phi(c_x) = \sum_{n=1}^{N} \delta(c_n, \Delta_t) \alpha_{nx}$, if φ(cx) is large then it contributes to the final prediction more

$$v_j = \sum_{x=1}^{N} \phi(c_x) e_x$$

Data Sets

- SEER-Medicare Linked Database
  - records each visit if a patient as a set of diagnosis, procedure billing codes.
  - contains inpatients, outpatients and carrier claims from 161,366 patients from 2000-2010
- In this experiment, we use
  - inpatient dataset : ICD-9 diagnosis, procedure codes
  - mixed dataset : ICD-9, CPT codes
- to predict the primary diagnosis of future inpatient visits, ICD-9 diagnosis codes are grouped into 18 major groups

Data Sets

Dataset	Inpatient dataset	Mixed dataset
# of patients	45,104	93,123
# of visits	155,898	5,979,529
average # of visits per patient	3.46	64.21
max # of visits per visit	35	483
# of instances	45,104	200,892
# of unique medical codes	6,020	18,826
# of unique ICD-9 diagnosis codes	3,928	8,342
# of unique ICD-9 procedure codes	2,092	2,614
# of unique CPT codes	NA	7,870
Average # of medical codes per visit	8.01	6.21
Max # of medical codes per visit	29	105

Baselines

- Majority predictor : always predicts the majority class
- RNN-uni : uses the sum of code embeddings as visit embeddings and feeds into a unidirectional LSTM
- RNN-bi : uses the sum of code embeddings as visit embeddings and feeds into a bidirectional LSTM
- Dipole : uses location-based attention and feeds into a bidirectional RNN
- GRNN-HA : uses hierarchal attention ; calculates attention weights for medical codes and patient visits.

Results

	Inpatient dataset		Mixed dataset	
Method	Accuracy	F1	Accuracy	F1
Majority Predictor	0.212	NA	0.245	NA
RNN-uni	0.299	0.194	0.511	0.436
RNN-bi	0.298	0.199	0.516	0.442
Dipole	0.303	0.230	0.523	0.463
GRNN-HA	0.301	0.222	0.519	0.450
Timeline-uni	0.314	0.234	0.526	0.469
Timeline	**0.315**	**0.235**	**0.530**	**0.473**

- The benefits of bi-LSTM on inpatient dataset is small:
  - The claim number is smaller in inpatient dataset than in mixed dataset

Results

- Awareness of distance between visits

Table 3: Visits of synthetic patient 1. For each visit, all medical codes and weights associated with them are shown. CPT codes are prefixed by c_; ICD-9 diagnosis codes are prefixed by d_..

visit 1 (298 days ago)		
c_99213	0.0	Office, outpatient visit 門診訪問
d_2859	0.0	Anemia unspecified 貧血
c_92012	0.0	Eye exam 眼科檢查
visit 2 (185 days ago)		
c_99213	0.0002	Office, outpatient visit
d_4241	0.0002	Aortic valve disorders 主動脈瓣閉鎖不全
visit 3 (26 days ago)		
c_80061	0.03	Lipid panel 血脂檢查
d_6117	1.739	Signs and symptoms in breast disorders 乳癌症狀
visit 4 (10 days ago)		
d_V048	0.458	viral diseases 流行性感冒
c_G0008	0.601	Administration of influenza virus vaccine 流感疫苗注射
d_4019	0.0	Unspecified essential hypertension 原發性高血壓
visit 5 (8 days ago)		
d_1742	1.87079	Upper-inner quadrant of female breast cancer 上內部女性乳癌
c_99243	0.0	Office consultation 醫病諮詢
Prediction:	**Neoplasms (0.99)** 腫瘤	

Results

- The model learned which code has huge influence

Table 4: Visits of synthetic patient 2. For each visit, all medical codes and weights associated with them are shown. CPT codes are prefixed by c_; ICD-9 diagnosis codes are prefixed by d_.

visit 1 (153 days ago)		
d_4149	1.0	Chronic ischemic heart disease unspecified 慢性缺血性心臟病
d_7240	1.0	Spinal stenosis other than cervical 頸椎外的脊柱狹窄
d_4019	0.0	Unspecified essential hypertension
c_99213	0.0	Office, outpatient visit 原發性高血壓
visit 2 (143 days ago)		
d_2780	0.0	Obesity 肥胖
d_3751	0.0	Disorders of lacrimal gland 淚腺疾病
c_92012	0.0	Eye exam 眼科檢查
visit 3 (82 days ago)		
d_3771	1.94464	Pathologic fracture 病理性骨折
c_72080	1.739	Radiologic examination, spine 脊椎放射檢查
d_4019	0.0	Unspecified essential hypertension
visit 4 (18 days ago)		
d_4019	0.0	Unspecified essential hypertension
c_80048	0.017	Basic metabolic panel 基礎代謝檢查
c_85025	0.0	Blood count 血液常規檢查
d_V726	0.301	Special investigations and examinations 特殊檢查
Prediction:	**diseases of the musculoskeletal system and connective tissue (0.67)** 肌肉骨骼系統、結締組織疾病	

Results

- The model is sensitive to the exact time of past clinical events

Table 5: We generate two visits, one visit contains d_1749 and one visit contains d_2720, we change the time interval of the first visit in order to see how prediction changed.

visit 1 (t days ago)	
d_1749	female breast cancer unspecified
visit 2 (10 days ago)	
d_2720	Pure hypercholesterolemia 高膽固醇血症

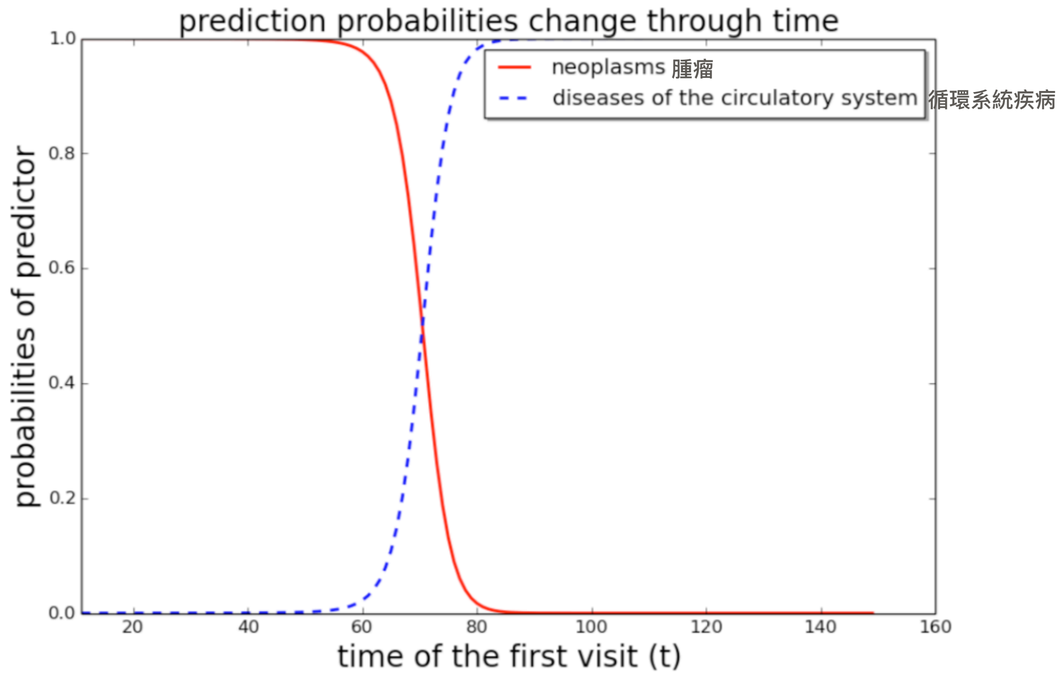


Figure 4: We change time interval t in Table 5 and show how prediction probabilities change with t.

Results

- Each disease has different progression function

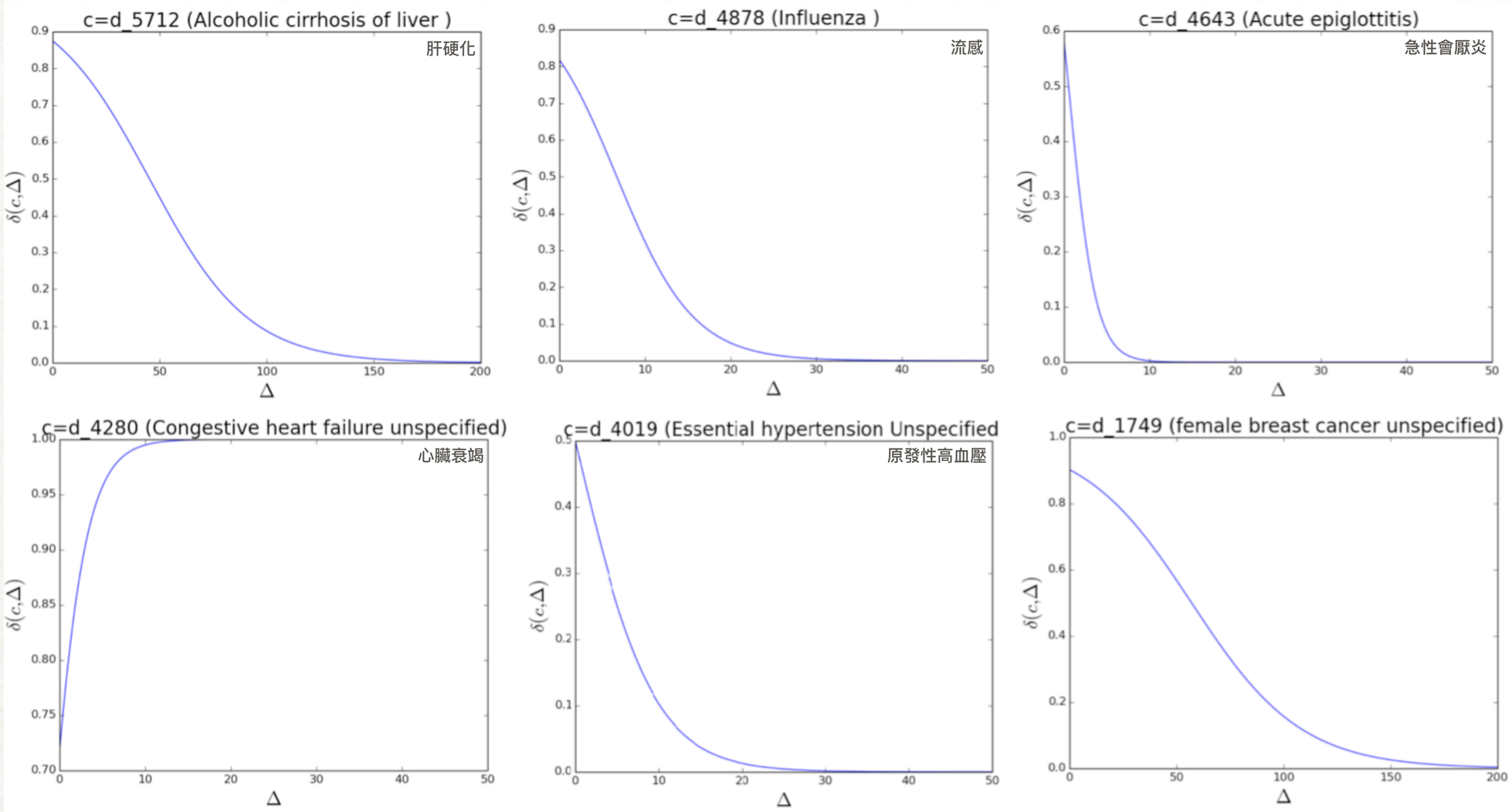


Figure 5: The $\delta(c, \Delta)$ function for six different codes.

Conclusions

- It is important to take sampling irregularity and different disease progression patterns into consideration.
- Uses an attention mechanism to aggregate context information of medical codes
- Uses time-aware disease-specific progression function to model how much information of each disease flows into the RNN.
- The interpretability of the model : Timeline