PrTransH: Embedding Probabilistic Medical Knowledge from Real World EMR Data

Lin Feng Li¹,²,§, Peng Wang³, §, Yao Wang², Jinpeng Jiang², Buzhou Tang⁴, Jun Yan², Shenghui Wang¹, Yuting Liu⁵

¹Institute of Information Science, Beijing Jiaotong University, Beijing, China
²Yidu Cloud Technology Inc., Beijing, China
³The First Hospital Affiliated to AMU, Chongqing, China
⁴Department of Computer Science, Harbin Institute of Technology Shenzhen Graduate School, Shenzhen, China
⁵School of Science, Beijing Jiaotong University, Beijing, China
§Linfeng Li and Peng Wang contributed equally

ABSTRACT This paper proposes an algorithm named as PrTransH to learn embedding vectors from real world EMR data based medical knowledge. The unique challenge in embedding medical knowledge graph from real world EMR data is that the uncertainty of knowledge triplets blurs the border between "correct triplet" and "wrong triplet", changing the fundamental assumption of many existing algorithms. To address the challenge, some enhancements are made to existing TransH algorithm, including: 1) involve probability of medical knowledge triplet into training objective; 2) replace the margin-based ranking loss with unified loss calculation considering both valid and corrupted triplets; 3) augment training data set with medical background knowledge. Verifications on real world EMR data based medical knowledge graph prove that PrTransH outperforms TransH in link prediction task. To the best of our survey, this paper is the first one to learn and verify knowledge embedding on probabilistic knowledge graphs.

INDEX TERMS embedding multi-relational data, medical knowledge graph, probabilistic knowledge triplet, representation learning,

I. INTRODUCTION

In medical fields, knowledge graph is the core underlying component for clinical decision supporting system (CDSS) [1]. Some recent works report CDSS applications in different scenarios, such as medicine recommendation [2], drug-to-drug similarity measurement [3], etc. Medical knowledge graph could be built either by human experts or by unsupervised data mining algorithms from Electronic Medical Records (EMRs). The first approach is too labor-consuming to be feasible in building large-scale knowledge graph. Therefore, unsupervised data mining from EMR data is a promising approach [4].

Modeling multi-relational data in knowledge graphs by learning embedding vectors of entities and relations provides improvements for knowledge completion [5]-[8] and other common NLP tasks [9]. In medicine, the embedding of medical knowledge graphs is reported to be capable of improving diagnosis inference task [10].

The most unique challenge in learning embedding vectors from real world EMR data based medical knowledge graph is to learn probability of each triplets. For example, considering triplet (pneumonia, disease_to_symptom, fever), symptom "fever" is common but not always present among patients with disease "pneumonia (ICD10: J18.901)"; hence the co-occurrences of "fever" and "pneumonia" can be counted on training data set, which can be further extended to conditional probability:

\[ P(\text{symptom} = \text{fever} | \text{disease} = \text{pneumonia}) \]

In previous works, the label of each triplet is either correct or wrong when training embedding vectors. However, the probabilistic nature in medical knowledge blurs the border, leading to changes in fundamental design of embedding learning algorithm.

• The existing loss function, which is margin-based ranking criterion, is not able to express relationships among probabilities of triplets.

As labels of triplets are binary in previous works, the training target are designed to be "the score value of positive triplet" should be higher or lower than "the score value of (random selected) negative triplet" by some margin. However,
it does not work for probabilistic knowledge graph because there is no way to guarantee the score value of triplet with high probability is higher than the score value of triplet with low probability.

- Requirements on mapping score values to probability.

As discussed in loss function, the score value (also named as energy level) of each triplet \((h, r, t)\) should be compared with probability of the triplet, requiring mapping from score values to probability and vice versa. However, in distance-based TransX embedding algorithms \([5]\), \([6]\), \([8]\) and DIST_MULT \([7]\), there is no such mapping. \([11]\) introduced logistic reverse link function as mapping, but it has not been verified on probabilistic knowledge graph.

To address these challenges, this paper proposes two enhancements to embedding learning algorithms. First of all, the mapping function between the existing distance-based score value and probability value is defined. Second, based on the mapping function, the target distance of positive triplets (those from training data set) is changed from relative condition to absolute mapping value derived from probability, ensuring the relative relationship among positive triplets are incorporated into embedding. The proposed PrTransH algorithm is verified on real world EMR data based knowledge graphs, proving better result in link prediction task.

The main contributions of this paper are: 1) Design of PrTransH algorithm to learn probability information in medical knowledge graph triplets; 2) Verification on real world EMR data based knowledge graph to prove the improvement of embedding. To the best of our survey, this paper is the first one to learn and verify knowledge embedding on probability knowledge graphs. Such improvements also indicate potentials of applying proposed embedding algorithm to the pre-trained vector representation of high-level concepts in complex medical CDSS application.

The rest of paper is organized as following. In the next section, the system of building probabilistic knowledge graph is presented. In section 3, the methodology of designing PrTransH is described. Then it comes with experiments and discussion on results. Finally, the conclusion and future works are stated in the last section.

II. OVERVIEW OF PROBABILISTIC KNOWLEDGE TRIPLET EXTRACTION

Real world EMR data could be viewed as a collection of visit records, each consists of all medical records generated from one particular visit paid by one patient, such as patient information / chief complain / history of present illness / medical orders / etc. In each visit record, there are probably multiple medical entities. The term medical entity refers to the concrete instances of diagnosis, symptoms, laboratory tests, examinations, drugs and surgeries. For example, considering the visit in Figure 1, diagnosis Pneumonia, unspecified organism, symptom cough, medicine cefathiamidine, and other medical entities co-exist in that visit record.

Relationships expressed in \((h, r, t)\) triplet are derived from the medical entities co-existing in each single visit. Take the visit record above as an example, several triplets can be generated: such as \((J18.9, \text{disease}\_\text{to}\_\text{symptom}, \text{cough})\), \((J18.9, \text{disease}\_\text{to}\_\text{medicine}, \text{cefathiamidine})\), etc.

Considering the triplets from all visits, the probability of each triplet \((h, r, t)\) can be calculated as below:

\[
p_{(h,r,t)} = \frac{N_{(h,r,t)}}{N_h}
\]
Where $N_{(h,r,t)}$ represents the number of $(h, r, t)$ triplets in total training data set, $N_h$ represents the number of $h$ entities in training data set. If $(h, r, t)$ is a valid triplet, the condition $P_{(h,r,t)} \in (0,1]$ holds; otherwise, $P_{(h,r,t)} = 0$.

### III. RELATED WORKS

#### A. MODELING MULTI-RELATIONAL DATA

[5] proposed translations in embedding space (TransE) to $(h, r, t)$ triplets in knowledge graph. The principle of TransE algorithm could be represented by the geometric relationships among embedding vectors of entity and relation: if $(h, r, t)$ holds, the embedding vector of tail entity should be close enough to the head entity plus some vectors depending on relation. The score function is defined as the distance between $h + r$ and $t$. The loss function is defined by margin-based ranking criterion, targeting the score of positive triplets is lower than one of the negative triplets by a margin. TransE features a model with less complexity while achieving relatively good predictive performance.

**TransH** [6] is an improved version of TransE. As stated in TransH, the major flaw of TransE is the incapability to handle reflexive / one-to-many / many-to-one / many-to-many relations since the representation of entities are the same when involved in many relations. To solve the problem, relation-dependent hyperplanes are introduced to the score function. Experiment result proves that projecting the embedding vector to different hyperplanes improves the performance in predicting reflexive / one-to-many / many-to-one / many-to-many relations.

**TransR** [8] proposes to project embedding vector into relation-specific space, instead of projecting to hyperplanes in the same space presented in TransH. The distance-based score function is evaluated in the relation-specific space. Introduction of relation-specific space makes TransR more expressive to model difference among relation and entities.

**DIST_MULT** [7] and **ComplEx** [11] do not use distance-based score function, but bilinear scoring function within real vector space or complex vector space. The loss functions are the same as TransX mentioned before. Bilinear scoring function is more expressive as the experiment results show that the DIST_MULT outperforms all TransX in predicting tail entity in 1-to-N relations. ComplEx further surpassed DIST MULT because the asymmetry in the product of complex embeddings betters the asymmetric relationships expression.

In medical knowledge graph, predicting tail entities in 1-to-N relation is the most important because one-to-many relation is the most common relation among different types of medical entities. For example, one disease is related with multiple symptoms / medicines / etc.

Based on these requirements, TransH / TransR / DIST_MULT / ComplEx are candidates.

On one hand, according to the evaluation result in TransR [8], it has not achieved better performance than TransH in predicting tail entities in 1-to-N relations.

On the other hand, although DIST_MULT and ComplEx are reported to be better in modeling, but their score functions are not distance-based. In [11], it is clarified that each relation embedding $w_r$ is an anisotropic scaling of the basis defined by the entity embeddings $E$, followed by a projection onto the real subspace. Such mathematical property makes it more difficult than the distance-based score function to explain and understand the embedding of relations. In medical field, explainable distance-based score function could help doctors understand how the embedding works and improve trust in any application built by embedding algorithm.

Based on the two considerations above, TransH is selected to be the most suitable candidate algorithm.

The target of TransH training is to minimize a margin-based ranking loss over training set:

$$L = \sum_{(h,r,t) \in A} \sum_{(h,r,t') \in A^c} \left[ f_r(h, t) + \gamma - f_r(h', t') \right]_+, \quad (2)$$

Where

$$f_r(h, t) = \left\| h + d_r - t \right\|_2$$

$$h = h - w_r^T h w_r, t = t - w_r^2 t w_r$$

#### B. BUILD KNOWLEDGE GRAPH FROM EMR

[4] presents methodology to automatically build knowledge graphs using maximum likelihood estimation (MLE) of probabilistic models. Only disease to symptom relation is studied in the paper. Compared against logistic regression and naive Bayes model, noisy OR is proposed to be better in rank symptom for randomly selected diseases.

The major limitation of this paper is that the proposed algorithm is not capable of predicting unseen tail entities. Taking the noisy OR algorithm as an example, if there is no link between symptom $i$ and disease $j$, the probability $f_{ij}$ (probability that disease fails to turn on its child symptom) cannot be calculated.

[10] presents construction of medical knowledge graphs from EMR and applications such as inference diagnosis based on symptom and tests. This paper introduces distributed representation, i.e. knowledge embedding, of medical concepts to the MRF inference architecture, including TransE and LFM score functions. However, this paper has no research on integrating conditional probability into the score function and loss for training embedding.

### IV. METHOD

#### A. MAPPING BETWEEN DISTANCE AND PROBABILITY

In previous works, if two or more relationships are "right", there is no way to tell which relation is more relevant than others. Such a weakness can also be explained from formal representation of loss functions based on existing algorithms. Take TransH as an example, it uses "margin-based ranking
To avoid expressed as minimizing the component below:

\[ f_r(h, t, i) = \gamma = f_r(h', t') \] (3)

Because \((h', r, t')\) are randomly selected, given the number of training iteration is large enough, the distance of each "right" triplet \((h, r, t)\) is expected to be lower than any "wrong" triplet. However, there is no way to guarantee the relationship among distances of "right" triplets.

Therefore, to address this challenge, involving probability of triplet into the embedding learning algorithm is necessary. Intuitively, if a triplet has higher probability than other triplet, the distance between triplets with probability 1.0, but training would be solely reducing the value of loss function, the target of optimization is to maximize the distance of corrupted triplets.

Therefore, the training procedure, the distance between corrupted triplets with probability 1.0, but training would be solely reducing the value of \(|\Theta|\). Moreover, since the optimizer is constrained by the type of relation. For example, given "diagnosis-to-symptom" relation, the head entity must be in type "diagnosis" and the type of tail entity must be "symptom". If the constraint is broken, say (diagnosis_1, diagnosis-to-symptom, medicine_1), this triplet does not make any sense. Therefore, when building corrupted triplet for medical knowledge graph, the space to sample corrupted triplet should not be the entire entity space, but only in the sub space in which the entity type meets the requirements.

B. NECESSITY OF CORRUPTED TRIPLETS IN LOSS FUNCTION

**Corrupted Triplets** refer to the triplets not existing in training data, usually generated by some sampling algorithms with entity and relation space.

If ignoring corrupted triplets in loss function, the target of training would be solely reducing the value of \(f_r(h, t, i) = \ln \frac{1}{p(h, r, t)}\). Assume that both \((h_1, r, t_1)\) and \((h_2, r, t_2)\) are valid triplets with probability 1.0, but \((h_i, r, t_j)\) does not hold in medical knowledge. The training target only requires \(f_r(h_i, t_1) \approx 0\), but sets no requirement on \(f_r(h_1, t_j)\). In this case, the distance between \(h_1\) and \(t_j\) is out of control in training procedure, and it probably be a random value. Such a random effect definitely harms the accuracy of link prediction.

Therefore, in addition to reducing \(f_r(h, t, i) = \ln \frac{1}{p(h, r, t)}\) for valid triplet \((h, r, t)\), the targets of training should also include maximizing the distance of corrupted triplets \((h, r, t)\), i.e. \(f_r(h', t')\). Moreover, since the optimizer is to minimize the value of loss function, maximizing the distance can be expressed as minimizing the component below:

\[ \ln \frac{1}{p(h, r, t)} - f_r(h', t') \] (6)

To avoid zero denominator, for corrupted triplet, it is defined:

\[ p_{(h, r, t)} \approx \varepsilon_n \]

Where \(\varepsilon_n > 0\) is a hyperparameter.

Furthermore, to avoid the situation that probability of valid triplet \((h, r, t)\) is less than \(\varepsilon_n\), minimum probability of valid triplet is introduced as \(\varepsilon_p\).

\[ p_{(h, r, t)} = \begin{cases} p(h, r, t) & \text{for } p(h, r, t) \geq \varepsilon_p \\ \varepsilon_p & \text{otherwise} \end{cases} \] (7)

Where

\[ 0 < \varepsilon_n < \varepsilon_p \]

Both \(\varepsilon_n\) and \(\varepsilon_p\) are hyperparameters.

C. SAMPLING MEANINGFUL NEGATIVE TRIPLETS

In medical knowledge graph, the type of head and tail entities is constrained by the type of relation. For example, given "diagnosis-to-symptom" relation, the head entity must be in type "diagnosis" and the type of tail entity must be "symptom". If the constraint is broken, say (diagnosis_1, diagnosis-to-symptom, medicine_1), this triplet does not make any sense. Therefore, when building corrupted triplet for medical knowledge graph, the space to sample corrupted triplet should not be the entire entity space, but only in the sub space in which the entity type meets the requirements.

D. FORMAL REPRESENTATION OF ENHANCED ALGORITHM

Based on the mapping function \(\Phi(x)\), the enhanced loss function is defined as below.

\[ L = \sum_{i \in D} \sum_{(h', r, t) \in D'} \left[ \ln \frac{1}{p(h, r, t)} - f_r(h, t, i) \right] + \gamma * \left[ \ln \frac{1}{p(h', r, t')} - f_r(h', t') \right] \] (8)

E. DATA AUGMENTATION: INCORPORATING EXISTING DOMAIN KNOWLEDGE

Since this paper focuses on knowledge graph in medical field, existing domain knowledge could be leveraged to provide richer information than only training data set.

For all diagnosis from training data set, the relationships among those diagnosis can be derived from the ICD-10 [12] code of each diagnosis.

Here is a concrete example scenario. The diagnosis pneumonia unspecified (ICD10: J18) has a series of similar diagnosis as hyponym. Suppose that in one hospital, doctors always use pneumonia (ICD10: J18.901) as diagnosis, only (J18.901, diagnosis-to-symptom, symptom_i) can be learned from training data. Based on medical domain knowledge, even if (J18.902, diagnosis-to-symptom, symptom_i) is not mentioned in training, the relation is expected to be learned.

Triplet (J18, upper disease to lower disease, J18.902) with probability 1.0 could be added into training data set to achieve the goal mentioned above. The value 1.0 means we are fully confident that the triplet is correct. With additional triplet, the similarity between embedding vectors of J18 and J18.902 is expected to be learned. The similarity could help to
PACS (Picture Archiving data from EMR (electronic medical record), HIS (hospital architecture in hospital private cloud, it aggregates medical the platform is built based on distributed technology Affiliated to AMU Application Platform) platform of The First Hospital A.

This study is performed based on DPAP (Data Platform and Application Platform) platform of The First Hospital Affiliated to AMU (Southwest Hospital, Chongqing, China), the platform is built based on distributed technology architecture in hospital private cloud, it aggregates medical data from EMR (electronic medical record), HIS (hospital information system), LIS (laboratory information system), PACS (Picture Archiving and Communication Systems) and other isolated sub systems. Eventually, the platform organizes all related medical data into "Visit" level and "Patient" level. Visit level data contains records from all sub systems for same visit, including chief complain, and present illness history from EMR, examination order, drug prescription from HIS, laboratory exam result from LIS and so on. Patient level data contains all "Visit" data of same patient.

Only EMR records from year 2015 to 2018 are collected into data set. The data set consists of 3,767,198 patients and 16,217,270 visits. Based on the data set, triplets of 5 relationships are extracted. Moreover, as mentioned in section "Data Augmentation: Incorporating existing domain knowledge", relation "upper_disease_to_lower_disease" is added to relation list as in Table 1.

The disease entity is identified by its unique ICD-10 [12] code. ICD-10 hierarchical relationships are considered with extracting triplets. For example, assume the main diagnosis in a visit is C16.902 (Gastric cancer NOS) and medicine m1 is prescribed by doctor, a list of triplets will be generated, including (C16.902, disease_to_medicine, m1), (C16.9, disease_to_medicine, m1), (C16, disease_to_medicine, m1).

Table 2 lists the number of triplets by different relations. Note that the original number of triplets from data set is larger than the number in Table 2 because the probability of triplets is distributed in long tail manner. To reduce noise from data and improve training efficiency, we only select a subset of triplets for each given head and relation pair using the rules below:

- no more than 20 triplets would be selected, AND
- sort triplets in descending order of probability, select elements from first element, AND
- a triplet is selected if it occurs in at least 10 visits

The total number of distinct entities in training set is listed as in Table 3.

### V. EVALUATION AND DISCUSSION

#### A. DATA COLLECTION AND TRIPLETS EXTRACTION

This study is performed based on DPAP (Data Platform and Application Platform) platform of The First Hospital Affiliated to AMU (Southwest Hospital, Chongqing, China), the platform is built based on distributed technology architecture in hospital private cloud, it aggregates medical data from EMR (electronic medical record), HIS (hospital information system), LIS (laboratory information system), PACS (Picture Archiving and Communication Systems) and

### Table 1

| Relation ID | Relation Name               | Source          | Head Entity Type | Tail Entity Type | Comments                                                                 |
|-------------|------------------------------|-----------------|------------------|------------------|---------------------------------------------------------------------------|
| 0           | disease_to_medicine          | EMR data set    | disease          | medicine         | the disease and medicine are from same visit in EMR data                  |
| 1           | disease_to_symptom           | EMR data set    | disease          | symptom          | the disease and symptom are from same visit in EMR data                  |
| 2           | disease_to_operation         | EMR data set    | disease          | operation        | the disease and operation are from same visit in EMR data                |
| 3           | disease_to_laboratory        | EMR data set    | disease          | laboratory       | the disease and laboratory test are from same visit in EMR data          |
| 4           | disease_to_examination       | EMR data set    | disease          | examination      | the disease and examination (such as X-ray/CT/MRI) are from same visit in EMR data |
| 5           | upper_disease_to_lower_disease | domain knowledge: ICD10 | disease | disease |                                                                 |

### Table 2

| Relation Name               | Triplet Count |
|----------------------------|---------------|
| disease_to_medicine         | 74,835        |
| disease_to_symptom          | 53,885        |
| disease_to_operation        | 13,292        |
| disease_to_laboratory       | 71,805        |
| disease_to_examination      | 38,061        |
| upper_disease_to_lower_disease | 6,455        |
| TOTAL                      | 258,333       |

### Table 3

| Entity Type | Entity Count | Comments                              |
|-------------|--------------|---------------------------------------|
| disease     | 7,465        | identified by its unique ICD-10 code  |
| medicine    | 1,588        | identified by its chemical ingredient. TCM (Traditional Chinese Medicine) is included |
| symptom     | 9,767        |                                       |
| operation   | 1,540        |                                       |
| laboratory  | 1,121        | identified by the names of lab test set name in medical order, some different names refer to same test items |
| examination | 219          |                                       |
| TOTAL       | 21,700       |                                       |

make distance of (J18.902, diagnosis-to-symptom, symptom_1) short enough to discover the relation.

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TABLE 4
OVERALL EVALUATION RESULTS ON FILTERED TEST SET

|               | Hits@10 | Mean Rank | NDCG@10 |
|---------------|---------|-----------|---------|
|               | TransH | PrTransH | TransH | PrTransH | TransH | PrTransH |
| disease to medicine | 0.280  | 0.500  | 53     | 40    | 0.255  | 0.561  |
| disease to symptom | 0.417  | 0.550  | 79     | 40    | 0.397  | 0.542  |
| disease to operation | 0.460  | 0.480  | 66     | 23    | 0.525  | 0.511  |
| disease to laboratory | 0.200  | 0.285  | 65     | 60    | 0.267  | 0.390  |
| disease to examination | 0.2960 | 0.360  | 23     | 16    | 0.343  | 0.600  |
| All relations    | 0.323  | 0.438  | 61     | 31    | 0.359  | 0.523  |

TABLE 5
TOp 5 PREDICTION LIST ON RANDOMLY SELECTED HEAD AND RELATIONS.

| Head Entity      | TransH | PrTransH |
|------------------|--------|----------|
| disease to medicine | E11.901 (Type 2 diabetes mellitus without complications) | Metoprolol (无盐洛尔), voglibose (伏格列波糖)**, atorvastatin (阿托伐他汀), meclozolamine (甲氯胺) songlining xuekang capsule (TCM: 松龄血脉康胶囊) |
|                  | C34 (Malignant neoplasm of bronchus and lung) (支气管恶性肿瘤) | Erythra at head (头皮炎), cough (咳痰)**, bloody sputum (痰中带血)**, coughing up blood (咳血)**, hemoptysis (咯血)** |
|                  | C16 (Malignant neoplasm of stomach) (胃恶性肿瘤) | partial gastrectomy (胃部分切除术)**, Laparoscopic gastrectomy (腹腔镜下胃部分切除术)**, excision lesion bile ducts (胆管病损切除术), radical gastrectomy (根治性胃切除术)**, Esophagectomy (食管病损切除术)** |
|                  | E11.9 (Type 2 diabetes mellitus without complications) (非胰岛素依赖型糖尿病不伴有并发症状) | Blood Routine Test (空腹血糖), Renal Function Test type 2 (餐后Ⅱ号), Blood Routine Test (餐后血糖), Renal Function Test (甲功五项), Renal Function Test (甲功Ⅰ号) |
|                  | S82.282 (Fracture of shaft of tibia) (胫骨骨折) | Chest X-ray (胸部X线检查), MRT at lower extremities (下肢磁共振检查)**, cervical spine X-Ray (颈椎X线检查), Chest CT (胸肺CT检查), lower limb blood vessels CT (下肢血管CT显像) |
|                  |                  | Diformin (二甲双胍)**, aspart (门冬胰岛素30)**, epalrestat (依帕司他)**, acarbose (阿卡波糖)**, ibesartan (厄贝沙坦) |
|                  |                  | HBA1C (糖化血红蛋白)**, serum lipid (血脂Ⅱ号), fasting glucose (空腹血糖), Thyroid Function Test (甲功五项), Thyroid Function Test (甲功Ⅰ号), 2-hour post-meal blood glucose (餐后2小时血糖)** |
|                  |                  | MRT at lower extremities (下肢磁共振检查)**, knee joint X-ray (膝关节X线检查)**, lower extremities X-ray (股及下肢骨骨折X光摄片)**, foot X-ray (足X线检查)**, ankle X-ray (踝关节X线检查)** |

The number of marks * indicate the relevance level. ** indicate the most relevant tail entity according to medical knowledge, *** and * indicate less relevant tail entity. If a term is not marked with *, it does not match with any label.

Dialog group is used as the minimum unit of separation between training set and test set. The term dialog group refers to all triplets which share the same head and relation. For example, all symptoms (symptom1) related to disease C16.902 (Gastric cancer NOS) is a dialog group, containing (C16.902, disease_to_symptom, symptom1), (C16.902, disease_to_symptom, symptom2), etc. Therefore, given head entity and relation, all tail entities are either in training data or in test data.

During evaluation, for each triplet group in test set, the head entity and relation are used as test input, the target is to predict a sequence of all tail entities in valid entity type. The task is defined as to rank strong relevant tail entities prior to less relevant entities.

Algorithm in testing would transform head entity, relation and each potential tail entity into embedding vectors, calculate score functions of each potential triplets, rank the potential triplets using score value in ascending order.

C. DATA SPLIT AND LABEL CORRECTION

Based on the two rules below, 205,877 triplets are split into training set, while 49,756 triplets into test set.

- For relation with the name "disease_to_xxx", 20% of the triplet groups are randomly selected as test set.
- For relation "upper_disease_to_lower_disease", all of such triplets are included in training set.

Noise is inevitable in real world data. In medical case, the common noise in extracted triplets are unspecific triplets. Considering E11.901 (Type 2 diabetes) as head entity and disease_to_laboratory as relation, triplets with routine lab test items (such as blood routine test) usually have higher probability than specific triplets (such as Hemoglobin A1c (HbA1c)). The reason is that, in addition to specific tests, physicians are more likely to prescribe routine lab test items to lower the risk of missing any abnormal indicators. However, according to medical domain knowledge, Hemoglobin A1c (HbA1c) is expected to be related to E11.901 (Type 2 diabetes), while blood routine test is not expected to link with E11.901 (Type 2 diabetes).
Obviously, noise makes labels (i.e., tail entities in triplets from test data set) unreliable. To accurately evaluate the performance, the tail entities in test data set are corrected manually. As manually correction is quite labor-intensive, only a triplet groups subset of test data is randomly selected and corrected. This subset is named as **Filtered Test Set**.

### D. BENCHMARK & TRAINING

The TransH algorithm is selected as benchmark of proposed PrTransH. Both TransH and PrTransH are trained on the same training set until the losses of which are converged at a steady level. The hyperparameter $\lambda$ in TransH is set to 1. The hyperparameters in PrTransH are set to be: $\lambda = 1$, $\epsilon_n = 10^{-7}$, $\epsilon_p = 10^{-5}$.

The same negative triplets sampling algorithm, described in **Sampling Meaningful Negative Triplets** section, is used for both TransH and PrTransH.

### E. EVALUATION PROTOCOL

Similar to [5], the mean value of those correctly predicted ranks and the hits@10 are reported. The term "correctly predicted" or "hit" refers to the predicted item existing in tail entities in test set, regardless of the relevance level.

Since different tail entities in test set may have different relevance levels to head entity, the model which ranks stronger relevant tail entity prior to less relevant tail entity is better. To evaluate such difference in ranking accurately, NDCG [13] is reported for the top 10 tail entities predicted by models.

### F. RESULTS AND DISCUSSIONS

The overall verification result on filtered test set is reported in Table 4.

PrTransH outperforms TransH in almost all relations and metrics except for the NDCG@10 of "disease_to_operation" relation. Regarding NDCG@10, PrTransH performs the best in relation "disease_to_medicine", and doubles the NDCG@10 of TransH.

To analyze detailed results, sample predictions from both algorithms are listed in Table 5.

Based thorough investigation on results above, we believe that the improvements root in several factors in design and training procedure of PrTransH:

1. Involving probability into training objective of distance-based score value of positive triplet, which helps the embedding vectors accurately model the probability of each positive training triplet. In contrast, in TransH, the differences among positive training triplets are not considered. Since high probability implies strong ties between head and tail entities, PrTransH is able to learn such strong relationships.

2. Embedding absolute probability helps PrTransH tend to train medicines / symptoms / operations / lab tests / examinations which are specific to head entity nearer than other tail entities. For a specific tail entity, assuming it only links to one head entity in training data, it would be trained to locate at exact distance (expected frequency-based distance) from head. Otherwise, if it links to a huge amount of head entities with short expected distance (high probability), its embedding vector will not be trained to locate near any of those head entities.

### VI. CONCLUSION AND FUTURE WORKS

In this paper, we propose PrTransH and prove its performance on medical knowledge graph derived from real world EMR data. The proposed PrTransH successfully incorporates uncertainty of knowledge triplets into translational learning algorithms, and embeds uncertainty information into the vectors in embedding space. Experiments results prove that PrTransH outperforms TransH in terms of almost all indicators.

It should be noted that the application scenarios of embedding vectors from entities and relation are far richer than link prediction. In state-of-art NLP research, it is verified that using both text context and knowledge graph to train model to represent words could achieve significant improvements on various knowledge-driven tasks [9]. Similar work in medical field [10] is also reported, where the embedding from TransE and LFM is used in MRF inference architecture to infer possible diagnosis based on test results and symptoms. Considering the significant advantages compared with TransH, adopting embedding vectors from PrTransH into CDSS inference system is worthy to be explored in future, which includes recommending the most possible diagnosis, lab test / examination orders, drug orders, auditing any error in medical records.

### REFERENCES

[1] G. Kong, D.-L. Xu, and J.-B. Yang, “Clinical decision support systems: A review on knowledge representation and inference under uncertainties,” International Journal of Computational Intelligence Systems, vol. 1, no. 2, pp. 159–167, 2008.

[2] M. Wang, M. Liu, J. Liu, S. Wang, G. Long, and B. Qian, “Safe medicine recommendation via medical knowledge graph embedding,” arXiv preprint arXiv:1710.05980, 2017.

[3] Y. Shen, K. Yuan, J. Dai, B. Tang, M. Yang, and K. Lei, “KGDDS: A system for drug-drug similarity measure in therapeutic substitution based on knowledge graph curation,” Journal of medical systems, vol. 43, no. 4, p. 92, 2019.

[4] M. Rotmensch, Y. Halpern, A. Tlimat, S. Horng, and D. Sontag, “Learning a health knowledge graph from electronic medical records,” Scientific reports, vol. 7, no. 1, p. 5994, 2017.

[5] A. Bordes, N. Usunier, A. Garcia-Duran, J. Weston, and O. Yakhnenko, “Translating embeddings for modeling multi-relational data,” in Advances in neural information processing systems, 2013, pp. 2787–2795.

[6] Z. Wang, J. Zhang, J. Feng, and Z. Chen, “Knowledge graph embedding by translating on hyperplanes,” in Twenty-eighth aaai conference on artificial intelligence, 2014.
[7] B. Yang, W.-t. Yih, X. He, J. Gao, and L. Deng, “Embedding entities and relations for learning and inference in knowledge bases,” *arXiv preprint arXiv:1412.6575*, 2014.

[8] Y. Lin, Z. Liu, M. Sun, Y. Liu, and X. Zhu, “Learning entity and relation embeddings for knowledge graph completion,” in *Twenty-ninth aaai conference on artificial intelligence*, 2015.

[9] Z. Zhang, X. Han, Z. Liu, X. Jiang, M. Sun, and Q. Liu, “ERNIE: Enhanced language representation with informative entities,” *arXiv preprint arXiv:1905.07129*, 2019.

[10] C. Zhao, J. Jiang, Y. Guan, X. Guo, and B. He, “EMR-based medical knowledge representation and inference via markov random fields and distributed representation learning,” *Artificial intelligence in medicine*, vol. 87, pp. 49–59, 2018.

[11] T. Trouillon, J. Welbl, S. Riedel, É. Gaussier, and G. Bouchard, “Complex embeddings for simple link prediction,” in *International conference on machine learning*, 2016, pp. 2071–2080.

[12] W. H. Organization, *International statistical classification of diseases and related health problems*, vol. 1. World Health Organization, 2004.

[13] K. Järvelin and J. Kekäläinen, “Cumulated gain-based evaluation of ir techniques,” *ACM Transactions on Information Systems (TOIS)*, vol. 20, no. 4, pp. 422–446, 2002.