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Knowledge Base Completion for Constructing Problem-Oriented Medical Records

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Abstract

Both electronic health records and personal health records are typically organized by data type, with medical problems, medications, procedures, and laboratory results chronologically sorted in separate areas of the chart. As a result, it can be difficult to find all of the relevant information for answering a clinical question about a given medical problem. A promising alternative is to instead organize by problems, with related medications, procedures, and other pertinent information all grouped together. A recent effort by Buchanan (2017) manually defined, through expert consensus, 11 medical problems and the relevant labs and medications for each. We show how to use machine learning on electronic health records to instead automatically construct these problem-based groupings of relevant medications, procedures, and laboratory tests. We formulate the learning task as one of knowledge base completion, and annotate a dataset that expands the set of problems from 11 to 32. We develop a model architecture that exploits both pre-trained concept embeddings and usage data relating the concepts contained in a longitudinal dataset from a large health system. We evaluate our algorithms ability to suggest relevant medications, procedures, and lab tests, and find that the approach provides feasible suggestions even for problems that are hidden during training. The dataset, along with code to reproduce our results, is available at https://github.com/asappresearch/kbc-pomr.

1. Introduction

Clinical medicine is a complex task, with each patient representing a unique compilation of health problems involving overlapping biological systems, complicated care plans, and uncertain states of dynamic progression (Kannampallil et al., 2011). In the electronic health records (EHR) that store patients' data, information about each medical problem may be spread across views that correspond to different data types such as past diagnoses, medications, and procedures (Buchanan, 2017). Meanwhile, physicians spend at least as much time interacting with the EHR as they spend interacting with patients (Tai-Seale et al., 2017; Sinsky et al., 2016), which may contribute to physician burnout and worse patient
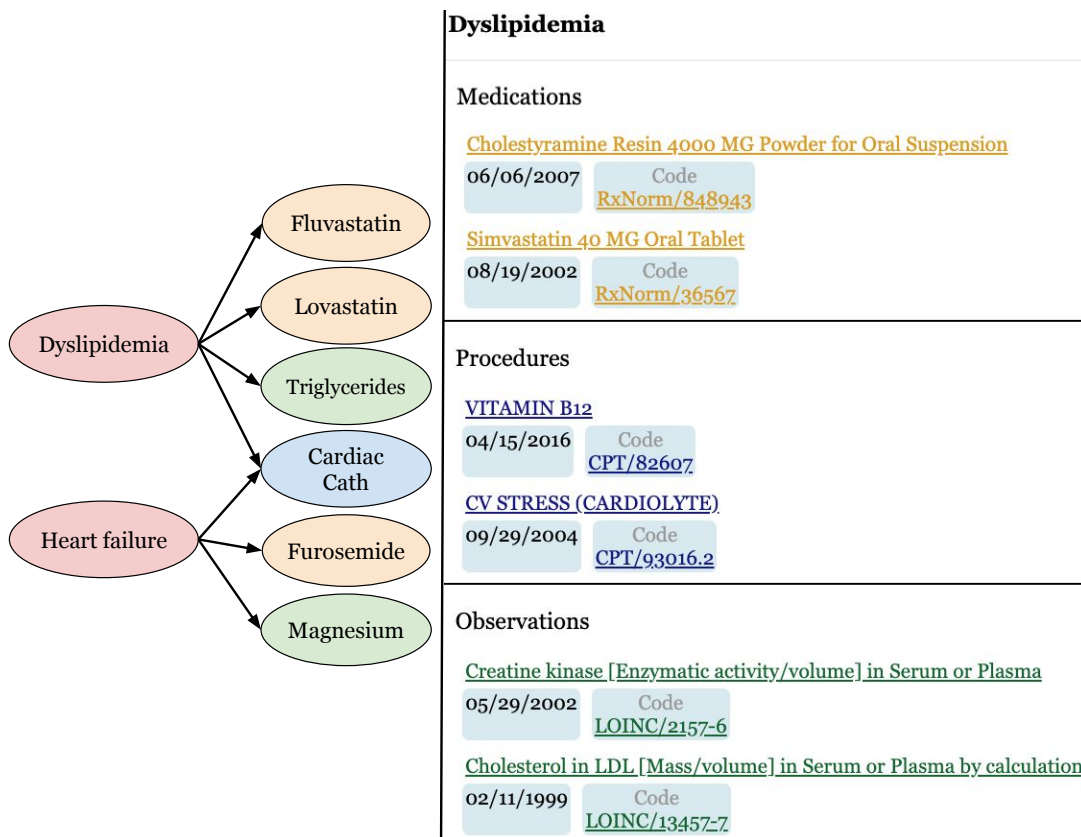
Figure 1: (left) A portion of our annotated knowledge base, as a graph. (right) A mockup of how a POMR might look in practice. The problem, dyslipidemia, is listed as a header, with sections listing relevant data elements of each type. In both figures, gold coloring denotes a medication, blue a procedure, and green a lab result.

outcomes. The problem-oriented medical record (POMR) is a paradigm for presenting medical information that, in contrast to chronological presentations, organizes data around the patient's problem list. This idea predates the widespread use of EHRs and was first introduced by Weed (1968), who argued that such an organization would improve physicians' ability to reason about each of their patients' problems.

To give a motivating example, many patients who suffer from atrial fibrillation, a heart rhythm abnormality, take blood thinners to reduce the likelihood of developing a blood clot. In order for a physician to determine whether the dose of the blood thinner is adequate, they would have to first have to review the problem list of the EHR to see that atrial fibrillation is one of the patient's current medical problems, then scan the medication section to determine what dose the patient is on, and finally navigate to the laboratory section to determine the patient's blood clotting parameters, all of which involves multiple clicks and time. In the POMR model, all relevant information pertaining to atrial fibrillation would be displayed in the same location within the EHR. We illustrate this concept in Figure 1.

We create a seed knowledge base to be used for POMR creation by drafting new problem definitions based on real data and having physician annotators select items pertinent to

the management of those problems in an emergency department setting. We then describe and evaluate neural network-based models that are trained to suggest new relations in the knowledge base, and demonstrate the effectiveness of our approach. Constructing a POMR can be construed as a two-step process, in which the first step is identifying the problems or phenotypes in a patient's record, and the second is associating the relevant medications, lab results, and other data to those problems. Our work focuses on the second step, and may be used in conjunction with phenotyping algorithms to form an end-to-end POMR creation pipeline.

Technical Significance In this paper, we frame the problem of constructing a problem-oriented view of a medical record as knowledge base completion, where the entities represent problems, medications, procedures, and laboratory results from patients' structured data. The relations connect problems to the other three entity types, and the relation types simply represent the data source of the target entity type (i.e., `medication`, `procedure`, or `lab`). Then the knowledge base can be represented as lists of medications, procedures, and labs for each problem entity. These lists can then be used downstream as a set of rules to organize patient data around the defined problems; for example, an algorithm could identify diagnosis codes that belong to the problem definition, then attach all co-occurring data elements in the lists. Prior work created lists through manual specification from experts (Buchanan, 2017), and in this work we enable automatic creation of these lists by tackling the knowledge base completion task with machine learning.

We develop neural network models that adapt pre-trained medical concept embeddings and learn from both an annotated knowledge base as well as a longitudinal dataset of inpatient and outpatient encounters for 10,000 patients from a regional health system. We evaluate not just on randomly masked entries of the knowledge base, but also by holding out and predicting on entire problems, to test our model's ability to generalize to new diseases.

Clinical Relevance Having a current and comprehensive problem-oriented view into a patient's data may improve clinician efficiency in retrieving relevant information, answering clinical questions, and completing administrative tasks. This can give time back to physicians, who may spend up to two hours per day working in the EHR outside of working hours (Sinsky et al., 2016). Moreover, a less usable EHR is correlated with increased risk of burnout (Melnick et al., 2019), and burnout in turn has been associated with poorer quality of care and increased risk of medical error (Panagioti et al., 2018).

In this work, we conjecture that automatically linking problems to their associated labs, medications, and procedures will be speedier than the otherwise manual process of determining which items belong to a given medical problem, which involves multiple experts coming to agreement, while maintaining an adequate level of accuracy.

Generalizable Insights about Machine Learning in the Context of Healthcare

Through our annotation effort, we show that physicians with similar specialties, given a similar situation, often agree on which medications, labs, and procedures in a patient's record are relevant to the treatment of the patient's problems, which is an encouraging sign that automatic construction of a POMR is feasible. We also show that with some fine-tuning, medical concept embeddings initially trained in an unsupervised way can be adapted to

predict useful concept relations, which can be leveraged to transform a chronological EHR into a problem-oriented medical record. The result that fine-tuning of embeddings trained on co-occurrence data improves performance for this task also demonstrates that co-occurrence patterns alone are not enough to predict which medications (as an example) are relevant to the treatment of which health problem. Our results also show that using publicly available concept embeddings trained over administrative insurance claims data gives competitive performance to embeddings trained with health system EHR data.

2. Dataset and Task

2.1. Data description

Though our goal and methods are agnostic to the site at which such models may be deployed, we ground our methods in a dataset of longitudinal health records, covering inpatient, outpatient, and emergency department settings from a large regional health system. The data is anonymized and dates are randomly shifted. The data is encounter-based, and each encounter may contain sets of diagnosis codes and procedure, medication, and lab orders. Additionally, some of the procedure, medication, and lab order entries list a corresponding diagnosis code, forming a relation between these diagnoses with the other types of data. When such a relation exists between a diagnosis and medication, lab, or procedure, we call it an *explicit relation*.

Diagnosis codes are recorded primarily using an internal coding system, with some usage of ICD-9 and ICD-10 (International Classification of Diseases). We use provided mappings to convert internal codes to ICD-10, or to SNOMED (Systematized Nomenclature of Medicine) or ICD-9 if no mapping to ICD-10 exists for a code. Procedure orders are recorded using a mixture of CPT (Current Procedural Terminology) and internal codes; however, no mapping is available from internal codes to CPT or other systems. Medication orders are recorded using internal codes with a mapping to RxNorm, which we use. Lab results are recorded using LOINC (Logical Observation Identifiers Names and Codes).

Statistics   Our dataset has a total of 10,000 patients, with 1.4 million unique encounters, 1.4 million medication orders, 2.0 million procedure orders, and 6.5 million laboratory results. Of the encounters, 1.6% are in inpatient or emergency department settings, and 51% of patients have at least one encounter of those types.

2.2. Annotation process

To learn to suggest sets of medications, procedures, and lab tests for a medical problem, we collect a set of annotated triplets (problem, relation, target). One could also simply use the lists created by Buchanan (2017), but those lists are limited to a set of 11 problems, the codes chosen are not to our knowledge based on real usage data, and we do not know what guidelines were provided to the experts when choosing medication and lab codes. In order to expand the set of problems we may train on while ensuring consistency in the guidelines used to select codes and the codes presented for annotation, we make our own set of annotations.

Problem definition   For the annotation task, we present for each problem a list of candidate medication, lab, and procedure codes derived from the dataset. First, we expand

the set of problems by defining new ones. Defining problems is not strictly necessary, as one could use groupings from the Clinical Classifications Software (CCS) or Diagnosis Related Groups (DRG), but we aimed to ensure our problems had sufficient examples in our dataset. Here we follow Buchanan (2017) in creating a problem definition as a set of diagnosis codes. To define new problems, we presented an annotator, an emergency medicine attending physician, with a list of diagnosis codes ranked by how many unique patients in the dataset had the code at any point in their history, limited to codes that appear in at least 50 patient records. The annotator then browsed the list in this order and defined new problems as they appeared, by assigning a diagnosis code to a new problem definition as appropriate. After this, the annotator expanded the problem definitions by assigning codes from the rest of the list. After this process we have a set of 32 problems, listed in Appendix A.

Candidate generation   Then, using these problem definitions, we develop lists of candidate codes based on the dataset. To reduce annotator effort, we aim to provide short lists of likely candidates, so we rank candidate codes using an importance score and provide the top 50 of each data type. We compute the following importance score (Rotmensch et al., 2017) between a problem and a medication, procedure, or lab:

$$IMPT = \log\left(p(x_i = 1 | y_j = 1)\right) - \log\left(p(x_i = 1 | y_j = 0)\right) \tag{1}$$

where x_i is a binary variable denoting the existence of medication, procedure, or lab i occurring in an encounter record with a reported diagnosis code, and y_j is a binary variable denoting the presence of a diagnosis code in the definition of problem j in an encounter record. This importance score captures the increase in likelihood of a medication, procedure, or lab appearing in an encounter record when a given problem is also recorded in that record.

To expand beyond this initial set of suggestions, we also perform a second round of annotation using a model trained on the first set. We replace the importance score with the score given by the model in Equation 2 (see subsection 3.1), and present the top 20 suggestions for each (problem, relation) pair.

Guidelines   In initial investigations, we found that a coherent framing led to improved inter-annotator agreement. So we have annotators score each (problem, candidate) pair with a 0 or 1, with the following guidelines: "1 means this item would be of interest to an emergency medicine physician for the vast majority of cases, when seeing a patient with the condition for the first time. 0 means the item is rarely of interest for this condition" This framing matches our intended use case of providing a POMR to more efficiently on-board a care provider to a new patient, and matches our annotators' specialty of emergency medicine. To calculate inter-annotator agreement, we had two annotators independently provide labels for a subset of the codes suggested first round of annotations. There were 100 codes, and the resulting Cohen's Kappa score was 0.847, demonstrating the feasibility of achieving high agreement for this task.

Our final dataset consists of 1,740 positive and 5,024 negative annotations across 32 health problems.

3. Methods

3.1. DistMult Model

The task of POMR construction consists of two main steps: identifying the problems, and identifying the data that are relevant to each problem; this work focuses on the latter task. We frame the problem of relevant data suggestion as knowledge base completion, also known as link prediction, wherein one suggests new relations between existing entities in a knowledge base. This task has seen increasing interest since the successful use of low-dimensional embeddings for the entities and relations in the knowledge base. DistMult (Yang et al., 2015) was a successful early approach that learns embeddings by applying a relation-specific scoring function g_r to each triplet using a three-way dot product:

$$g_{EMB}^{(r)} = (\boldsymbol{e_s}, \boldsymbol{e_t}) = \sum_{i}^{d} e_{s_i} e_{r_i} e_{t_i} \tag{2}$$

where $\boldsymbol{e_s}$ is a source embedding, $\boldsymbol{e_t}$ is a target embedding, and d is the dimensionality of embeddings. Based on more recent work (Kadlec et al., 2017) in knowledge base completion which showed that DistMult, when well-tuned, is competitive with more sophisticated approaches, we base our model on DistMult.

3.2. Initialization and pre-processing

Pre-trained embeddings We use pre-trained embeddings for diagnosis, medication, procedure, and laboratory codes to sensibly initialize the model. Prior work (Choi et al., 2016) learns embeddings for medical concepts from a dataset of insurance claims for 4 million people, exploiting longitudinal aspects of the data. We use the RxNorm, CPT, and LOINC embeddings from this set to initialize the parameters for medication, procedure, and lab codes, respectively, when the embedding code is also present in our dataset. For codes not present in these embeddings, we initialize randomly. To initialize problem embeddings, we combine embeddings for the codes in a problem's definition. We translate any definitions code in SNOMED or ICD-10 to ICD-9, keeping only codes with one-to-one mappings, for use with the embeddings from Choi et al. (2016). Embeddings are initialized as the weighted average of each definition code, with weights defined as the frequency of the code in our dataset, normalized across definition codes so the weights sum to 1. Relation embeddings are always initialized to be the all-ones vector, such that the scoring function (Equation 2) reduces to a dot product between the source and target embeddings, at the start of training.

Site-specific embeddings We also consider the scenario in which a site trains and uses its own embeddings, which then allows for greater coverage of the codes used and the possibility of usefully including internal codes without mapping. We simulate this scenario by training embeddings on our dataset of 10,000 patients. Specifically, we use Gensim (Řehůřek and Sojka, 2010) to train a skip-gram model which treats each encounter as a unit, using the entire set of codes in an encounter as context for a given code. Problem embeddings are initialized using the unweighted average of definition code embeddings. Both sets of embeddings are of dimension 300.

Vocab	Statistic	Value
Site-specific	# Medication codes	2,294
Site-specific	# Procedure codes	2,655
Site-specific	# Lab codes	1,335
Choi et al. (2016)	# Medication (RxNorm) codes	802
Choi et al. (2016)	# Procedure (CPT) codes	11,746
Choi et al. (2016)	# Lab (LOINC) codes	3,093
Intersection	Fraction of site-specific medication codes	25.8%
Intersection	Fraction of site-specific procedure codes	54.8%
Intersection	Fraction of site-specific lab codes	55.4%

Table 1: Statistics regarding code sets

Vocabulary The set of RxNorm, LOINC, CPT, and internal codes we use to train models derives from our dataset—it is the set of medication, lab, and procedure codes that occurs at least 5 times. We make this choice to simulate how our globally annotated data would likely be most useful in deployment. The externally trained embeddings are generated from a distinct vocabulary which does not overlap perfectly with our dataset's vocabulary. To ensure a fair comparison, at inference time we evaluate over all codes in the *intersection* of both code sets. Some statistics characterizing the vocabularies and their intersection are in Table 1. After translating problem definitions to ICD-9, 98.3% of definition codes have embeddings from Choi et al. (2016).

Feature engineering Hypothesizing that any POMR implementation is likely to be highly institution-specific, we aim to learn not just from concept-level information, but also from site-level information. We accomplish this by building features from the statistics of our dataset. We count co-occurrences of each (problem, target) pair in the dataset, and normalize by the count of the target. Each occurrence is counted at most once per patient. We compute these features for varying definitions of co-occurrence. A problem and target are said to co-occur when:

- An *explicit relation* exists between the two in the data.
- The two appear in the same encounter.
- The problem appears within two weeks before or after the target, at the same facility.
- The problem appears within two weeks before or after the target, at any facility.

We also use data on the specialties of providers listed on encounters. For each problem and target, we count the number of times a provider with a given specialty is listed on an encounter with the problem or target. We use a limited vocabulary of 24 specialties which encompasses 90% of all encounters that have a provider specialty recorded. Thus for each problem and target we construct a vector of features.

Finally, we use the number of patients for which each problem and target code is recorded as a feature.

Combining embedding sources with nearest neighbors   Open-source embeddings such as those from Choi et al. (2016) are a useful starting point for models, but those models will have limited efficacy on any site-specific codes from an internal vocabulary, and even standardized codes that don't appear in the embeddings' vocabularies. For codes missing from the open-source vocabulary, naively we must randomly initialize embeddings. A more useful initialization for missing codes is to acquire embeddings for them by training on the internal dataset, and exploit their nearest neighbors. Specifically, for each code missing from the external vocabulary, we initialize its embedding by first finding the k nearest neighbors of the code in the internal embedding space, limited to those codes that do exist in the external vocabulary. Then we take the element-wise average of the corresponding *external* embeddings of those neighbor codes, and use that to initialize an embedding for the missing code. We conduct a separate set of experiments using this initialization technique to show its usefulness.

3.3. Training and Inference

Data splits   We divide the annotated triplets at random into training, validation, and test sets at a 70%, 15%, 15% share of the data, respectively. To show that our models are capable of generalizing to new problems, we also create separate train, validation, and test sets, where the test set and validation set consist of all triplets for 5 randomly chosen problems each, and the training set consists of all triplets for the remaining 22 problems.

Training   After initializing, we train the DistMult model using the ranking loss from the original paper (Yang et al., 2015), which guides the model to rank true triplets higher than randomly sampled negative triplets, with a margin. However, rather than sample at random from the vocabulary, as is common in knowledge base completion, our dataset has the benefit of having explicit negative examples that result from the annotation process, which we use for training. This has the potential benefit of providing negatives that are still ranked highly according to an importance score, which may improve learning. We shuffle the training set so that during training, each batch consists of a random selection of positive and negative examples. The model is implemented in PyTorch (Paszke et al., 2019) and trained with the Adam optimizer (Kingma and Ba, 2015). Learning rate and batch size are tuned by pilot experiments using the validation set.

Using engineered features   When we use the features we construct from our dataset, we must alter the scoring function. In addition to computing the embedding-based score in Equation 2, the model also computes a similar bilinear term to combine the specialty feature vectors for problem and target, using a separate set of relational parameters.

$$g_{SPEC}^{(r)} = (\boldsymbol{v}_s, \boldsymbol{v}_t) = \sum_i^d v_{s_i} v_{r_i} v_{t_i} \tag{3}$$

The relational parameters v_{r_i} are similarly initialized to all ones. The other features $\boldsymbol{f}(s,t)$ are concatenated with the scores from embeddings and specialty feature vectors, and a final linear layer is used to provide a final score $g^{(r)}$:

Model	Overall		Medications		Procedures		Labs	
	MR	MRR	MRR	H@1	MRR	H@1	MRR	H@1
Choi et al. (2016) Frozen	1.83	0.749	0.753	0.571	0.824	0.688	0.601	0.371
Choi et al. (2016) ProblemOnly	1.67	0.803	0.785	0.631	0.884	0.797	0.697	0.543
Choi et al. (2016) RelationOnly	1.86	0.773	0.749	0.560	0.867	0.766	0.658	0.543
Choi et al. (2016)	1.56	0.826	0.814	0.690	0.892	0.812	0.736	0.571
Choi et al. (2016) + Features	1.52	0.832	0.866	0.786	0.840	0.719	0.737	0.543
Site-specific Frozen	2.93	0.570	0.597	0.381	0.611	0.438	0.429	0.200
Site-specific ProblemOnly	1.97	0.782	0.821	0.726	0.764	0.641	0.719	0.600
Site-specific RelationOnly	2.34	0.677	0.719	0.583	0.675	0.484	0.579	0.371
Site-specific	1.90	0.760	0.791	0.667	0.766	0.641	0.673	0.457
Site-specific + Features	1.74	0.797	0.807	0.702	0.816	0.734	0.740	0.543

Table 2: Results on held-out triplets. For MR, lower is better, and higher is better for all other metrics. Frozen means the embeddings are used as initialized with no further training. RelationOnly means that only the relation embeddings are updated during training, and ProblemOnly means that only problem embeddings are updated (see Equation 2).

$$g^{(r)}(s,t) = \boldsymbol{\theta}^\top \left[g_{EMB}^{(r)}(s,t) \oplus g_{SPEC}^{(r)}(s,t) \oplus \boldsymbol{f}(s,t) \right] \tag{4}$$

where $\oplus$ denotes concatenation.

Inference and Metrics At inference time, for each (source, relation, target) triplet in the validation or test set, we score it along with all negative triplets in the validation/test set with the same problem and relation type. For metrics, we evaluate the mean rank (MR) of the true triplet among the set, along with the mean reciprocal rank (MRR), Hits @ 1 (H@1; frequency of true triplet appearing in top 1), and Hits @ 5 (H@5). During training, we use early stopping using MR on the validation set to prevent overfitting.

3.4. Ontology Baselines

Medical ontologies such as the National Drug File Reference Terminology (NDF-RT) contain curated knowledge that can also be leveraged to help construct a POMR. We compare our learning-based methods to rule-based methods that leverage NDF-RT and CPT ontologies to infer medications and procedures, respectively, which are relevant to a problem. Though these ontologies are incomplete and inevitably miss internal codes, having a quantitative comparison can be illuminating. Implementation details on these baselines are described in Appendix B.

4. Results

4.1. Held-out triplets

We first aim to validate our approach by gauging our performance when predicting on randomly held-out triplets. We note that for the held-out problems evaluations, the set of

negatives includes all annotated negatives for a given problem and relation type, but in the held-out triplets evaluation, this set is a smaller, random sample of all negatives for the problem-relation type pair. This leads to results that are not directly comparable to held-out problems results.

Results for the held-out triplets evaluation are in Table 2. We first compare the two approaches to initializing the model - the externally trained embeddings from Choi et al. (2016), and the site-specific embeddings which we trained. To evaluate the impact of learning, we also report results using each set of embeddings as initialized without any training (Frozen). In this evaluation, site-specific embeddings lag the externally trained embeddings when frozen.

We perform two ablations to determine the source of performance gains from training. By freezing the relation and target embeddings and updating only the problem embedding parameters (ProblemOnly) during training, we evaluate how much performance comes from improved problem representations over their heuristic initializations. Here, the gain for site-specific embeddings is larger than the gain for external embeddings, perhaps suggesting that having more data to pre-train embeddings can lead to diagnosis code embeddings that are robust enough to combine linearly into a useful problem representation. For site-specific embeddings, we see that the list of the 5 most similar problems changes notably before and after training. For atrial fibrillation, before training, the nearest problems are [heart failure, arthritis, sleep apnea, asthma, dyslipidemia]. After training, they are [syncope, coronary artery disease, heart failure, hypertension, dyslipidemia]. This indicates closer alignment to clinical similarity. For arthritis, before training, the neighbor problems are [dyslipidemia, GERD, back pain, gout, hypertension]. After training, they are [back pain, rheumatoid arthritis, gout, kidney stone, and headache].

By training only the relation embedding parameters (RelationOnly), we can see how much performance derives from separately modeling the relevance of medications, labs, and procedures. We notice that the relation parameters do contribute to performance in terms of MRR, and by combining these gains with those from updating problem embeddings and target embeddings we can improve upon both ablations. Finally, we evaluate adding in our engineered features. This gives a strong boost to performance overall and to nearly all per-type metrics, also narrowing the gap in performance between models that use site-specific and external embeddings.

4.2. Held-out problems

To truly match our intended use case, we evaluate on problems that the model has not encountered during training. These results are in Table 3.

Again, we first compare Choi et al. (2016)'s embeddings with our site-specific ones without further training. Again in this case, the externally trained embeddings provide better performance, emphasizing their usefulness in the absence of labeled data. We also see that directly applying embeddings in this way is more effective than relying on ontologies. The relatively weak performance of the NDF-RT heuristic on medications in particular seems to be due in large part to the brittleness of the code matching heuristic. Although 65% of test set medication codes have at least one associated diagnosis code, only 19% of test set medication codes ultimately end up matching to one of the defined problems.

Model	Overall MR	Overall MRR	Medications MRR	Medications H@5	Procedures MRR	Procedures H@5	Labs MRR	Labs H@5
Ontology baseline			0.066	0.023	0.150	0.270		
Choi et al. (2016) Frozen	7.4	0.302	0.268	0.534	0.432	0.629	0.262	0.706
Choi et al. (2016) RelationOnly	9.6	0.386	0.274	0.562	0.487	0.686	0.477	0.725
Choi et al. (2016) Relation+Target	7.2	0.387	0.359	0.493	0.430	0.771	0.396	0.745
Choi et al. (2016)	7.1	0.392	0.375	0.493	0.451	0.800	0.377	0.765
Choi et al. (2016) + Features	5.5	0.590	0.578	0.630	0.583	0.800	0.612	0.765
Site-specific Frozen	18.9	0.175	0.182	0.219	0.256	0.257	0.109	0.098
Site-specific RelationOnly	19.3	0.244	0.192	0.219	0.265	0.314	0.305	0.373
Site-specific Relation+Target	14.7	0.270	0.222	0.247	0.155	0.343	0.419	0.510
Site-specific	14.3	0.248	0.209	0.219	0.176	0.400	0.352	0.392
Site-specific + Features	7.8	0.460	0.414	0.329	0.373	0.143	0.584	0.510

Table 3: Results on held-out problems. Relation+Target means that relation and target embeddings are updating during training, and problem embeddings are kept frozen. "Ontology baseline" combines the results from using NDF-RT and CPT heuristics on the medications and procedures, respectively (see subsection 3.4).

We perform a similar set of ablation experiments on this evaluation, however we replace the ProblemOnly ablation with Relation+Target, in which we train just those sets of parameters and keep problems frozen. We make this change because we do not expect to see gains from ProblemOnly training when the validation set contains only problems not seen at train time. Despite this trait of the evaluation, when using Choi et al. (2016) embeddings we see an improvement in performance in nearly all metrics from Relation+Target training to all embeddings being trained. This gain could be because allowing the problem embeddings to be updated broadens the search space for relation and target parameters that the optimizer will explore.

Finally, we evaluate the addition of our engineered features, and the results show the usefulness of exploiting auxiliary information for new problems. Again, we see that with all embeddings trained, and using engineered features, the performance gap between models using site-specific and external embeddings becomes much smaller. An initial ablation analysis into the engineered features showed that of those features, most of the gains over models that do not use them came from the explicit relation-based feature.

Performance by problem Some medical problems are more strongly related with some types of entites. For example, urinary tract infection (UTI) is strongly associated with urinalysis and particular antibiotic medications, but there is not a routinely performed procedure for this common condition. In Table 4 we break down performance on the test set by problem, to help analyze results in this light. Poor performance in sleep apnea medications may not be important, as there are few medications that directly treat that problem. In designing the POMR, it is not expected that every problem would always have associated labs, medications, and procedures, and performing this analysis could be used to decide which suggested elements to turn on.

	Medication	Procedure	Lab
Sleep apnea	0.00	1.00	1.00
Hypokalemia	0.13	1.00	0.40
Thrombocytopenia	0.33	0.75	0.50
Hypertension	0.75	0.83	1.00
UTI	0.84	0.67	0.91

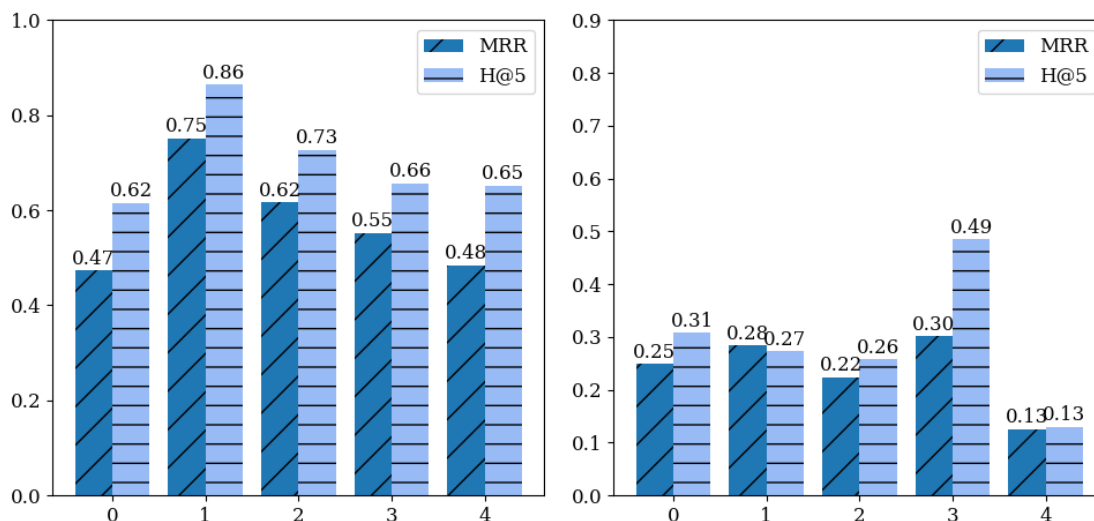Table 4: Hits@5 values for held-out problems, by data type. Results shown are for the best model in subsection 4.2.

Figure 2: Performance of Choi et al. (2016) + Features on held-out problems, grouped by the log of target occurrence counts in the dataset. Log counts are binned and increasing from left to right. On the left, we train as previously described in subsection 3.3, using annotations for negative examples. On the right, we train using negatives randomly sampled from the vocabulary. The bin sizes are (13, 22, 66, 35, 23).

Performance by frequency   In Figure 2 we plot the performance of the best model, Choi et al. (2016) + Features for different bins of target code frequency. We take the log of the count of each target code in the test set and group into bins before computing the metrics. We show two plots—one trained using annotated negatives (left), and one using negatives randomly sampled from the vocabulary (right). Perhaps counterintuitively, when training with annotated negatives we observe that the most frequent codes do not afford the best performance. Further analysis shows that performance is worse than average over target codes that appear in negative examples in the training set. A possible explanation is that during training, the model updates the embeddings for negative target codes to score them lower, but the resulting embeddings end up further in space from *all* problem embeddings. More frequent codes are more likely to show up as negative training examples, so performance suffers. To investigate this, we train the same model using the randomly

Medication	Procedure	Lab
Phenazopyridine	**Us-renal**	**Piperacillin+tazobactam [susceptibility]**
Ciprofloxacin	Bladder lavage/instillation, simple	**Bacteria identified in isolate by culture**
Nitrofurantoin	**Us - abdomen, complete**	**Bacteria identified in unspecified specimen by culture**
Trimethoprim	**Post void residual bladder us**	**Streptomycin [susceptibility]**
Sulfamethoxazole	**Cystoscopy**	Choriogonadotropin (pregnancy test) [presence] in urine
Levofloxacin	**Bladder cath insertion,temp indwell, simple**	**Ampicillin [susceptibility]**
Nystatin	**Cystoscopy/remove object, simple**	**Aztreonam [susceptibility]**
Tamsulosin	**Abdomen ct w/o iv and with po contrast**	**Cefoxitin [susceptibility]**
Cephalexin	**Abd/pelvis ct w/ + w/o iv contrast (no po)**	**Cefepime [susceptibility]**
Enoxaparin	**Cystoscopy/insertion of stent**	**Trimethoprim+sulfamethoxazole [susceptibility]**

Table 5: Example top-10 suggestions from the best-performing model from subsection 4.2 (Choi et al. (2016) + features) for the held-out test set problem UTI. Candidates are drawn from the set of all triplets in the test set. Suggestions in blue are positive examples. The medication nitrofurantoin is an antibiotic commonly used to treat a UTI, so knowing whether a patient was previously prescribed it may be important for current treatment due to antibiotic resistance considerations. The procedure "Us-renal" stands for a renal ultrasound, a commonly ordered procedure for patients who frequently have UTI's. Many of the lab tests are susceptibility tests, which are important to know for personalizing antibiotic recommendations.

sampled negatives. Though the degraded performance for common target codes still appears, the overall performance is notably degraded as well. We leave further investigations into this phenomenon for future work.

Qualitative examples We provide a list of top suggestions for the best model on this evaluation in Table 5. We see that many of the highest ranked suggestions are ground truth annotations. In medications, Nystatin is a medication to treat fungal infections, which may be correlated via the common cause of obesity. We also see "Pelvis US" (pelvic ultrasound), which may investigate pains that turn out to be a symptom of UTI. Knowing this procedure history would be especially useful for chronic UTI patients. "Bladder lavage" and "Cystoscopy/remove object, simple" suggestions describe bladder procedures that may be seen in similar contexts as UTI. There are still irrelevant suggestions, however, in this

Model	Overall			IV		OOV	
	MR	MRR	H@5	MRR	H@5	MRR	H@5
Site-specific Frozen	20.1	0.163	0.182	0.175	0.189	0.134	0.167
Choi et al. (2016) Frozen	21.1	0.224	0.431	0.302	0.610	0.035	0.000
Choi et al. (2016) Frozen 5-NN	14.5	0.209	0.276	0.250	0.346	0.110	0.106
Site-specific	17.8	0.199	0.249	0.196	0.252	0.208	0.242
Choi et al. (2016)	14.3	0.324	0.427	0.410	0.541	0.116	0.152
Choi et al. (2016) 5-NN	11.7	0.318	0.471	0.321	0.465	0.312	0.485

Table 6: Results on held-out problems, with no vocab restriction, to evaluate the k-NN embedding initialization approach. "IV" refers to codes that are **I**n the Choi et al. (2016) **V**ocabulary, while "OOV" refers to codes that are **O**ut **O**f **V**ocabulary.

case "Nebulizer treatments". Further examples for all test set problems are provided in Appendix C.

4.3. Combined embeddings evaluation

To evaluate our k-NN approach to initializing embeddings for out-of-vocabulary codes, we perform a separate evaluation. This is necessary because limiting the set of codes to those that are in both embedding sets, as we did in previous experiments, obviates the need for this approach. In this experiment, we evaluate on held-out problems, and do not limit the vocabulary, so the metrics should not be directly compared to those from previous experiments. Models are initialized using the k-NN approach for out-of-vocabulary codes and trained the same way as before. k is selected by experiments on the validation set, and is set to 5. Rankings are generated as before by comparing a given code to the full set of negatives for the same problem and relation type. Results are shown in Table 6.

Overall, we find that the k-NN approach provides better results in MR and Hits@5 than using either embedding source individually, while the overall effect is weak. After training, performance on out-of-vocabulary codes is better when initializing with Choi et al. (2016) embeddings and the k-NN approach than using the site-specific embeddings themselves. However, this comes at the cost of performance on in-vocabulary codes, which leads to only a weak improvement overall after training. The successful use of embeddings trained on disparate data sources for this application merits further study.

5. Related Work

Prior literature discusses the potential benefits of Weed's problem-oriented medical record (Xu and Papier, 2018; Buchanan, 2017). One review identified determinants that influence use and implementation of problem lists, the foundation of the POMR, concluding that a sociotechnical approach that considers both organizational and technical needs is important for successful implementation (Simons et al., 2016). Notably, Wright et al. (2015) find in a study of ten sites that problem-oriented charting is a factor leading to more complete problem lists.

We found that works that approach the technical aspects of the problem tend to focus on creating the problem list, without orienting the rest of a patient's data around those problems. For example, Devarakonda et al. (2017) create problem lists by extracting features from clinical notes and structured data and training decision-tree ensembles in a multilabel way. This work could be considered as part of the larger phenotyping literature, which seeks to usefully classify patients having certain characteristics, one of which may be active problems. Many techniques for phenotyping exist Banda et al. (2018); Ho et al. (2014); Halpern et al. (2016), which can be combined with our approach to form a POMR without having problem list entries. We found one other work that directly tackles organization of data around medical problems; Juarez et al. (2011) takes an expert systems approach and orients data around acute problems using temporal constraints. Much previous work (Choi et al., 2016; Beam et al., 2020; Finlayson et al., 2014) investigates how to learn representations of medical concepts in which related medications, procedures, and diagnoses are close in space. Although Choi et al. (2016) demonstrate that their trained representations are able to usefully group concepts together in a broad sense, they did not evaluate on the specific goal of POMR creation.

Another work (Rotmensch et al., 2017) sought to create a knowledge graph for healthcare automatically, using concepts extracted from clinical records and narratives. In this work, given the targeted nature of the knowledge we seek to capture, we instead initialize a knowledge graph manually, and then use models learned from clinical data to expand it. We also successfully exploit context from real data using engineered features.

In knowledge base completion, approaches typically focus on general-purpose knowledge bases. Many neural network-based models have been developed and evaluated (Yang et al., 2015; Kadlec et al., 2017), typically operating over triplets (source, target, relation), though recent successes also exploit information in the entities' neighborhoods (Nathani et al., 2019) and the global graph structure (Pinter and Eisenstein, 2018). These works have not, to our knowledge, exploited information about how the entities in the knowledge base appear in real-world data, beyond that included in embeddings, as our work does by using engineered features.

6. Discussion

We've shown that a knowledge base completion approach building on existing models and engineered features can produce a model that is able to usefully organize patient data around well-defined problems. It outperforms baselines that exploit existing medical knowledge bases such as NDF-RT, and those that directly apply pre-trained embeddings. Importantly, the approach performs well even for previously unseen health problems, such that scaling beyond the 32 initial problems we define for this proof of concept only entails defining a list of diagnosis codes for a problem.

A next step towards using this research in deployment would be to expand the set of problems, which could be done automatically, using CCS for example, and then directly run the model to rank the medications, procedures and labs in a patient record, using a threshold score to limit the number of suggestions. Then, each suggested element would be shown alongside the condition. Leftover data elements could then be presented either separately in traditional chronological views, or incorporated into the problems for which they have the

highest score. Though we do not evaluate on patient records, we note that the Hits@5 results for each data type in Table 3 are >0.5 for the best model. So the majority of the ground truth relevant codes, when compared to ≈70 negative codes each, are ranked in the top 5, which suggests these models may be fruitful for patients with a similar number of unique codes of each type. Alternatively, one could also simply repeat our iterated annotation procedure, by providing suggestions for each problem for experts to accept or reject, to save time and effort over less useful suggestions.

An auxiliary benefit of our annotated dataset is that it may be useful as a way to evaluate learned concept embeddings, similar to how Choi et al. (2016) evaluate using relations in NDF-RT. Although our dataset was not made for this purpose, the relations it captures would be desirable features of an embedding space. We also observe that the embeddings from Choi et al. (2016), trained on a much larger dataset than the site-specific embeddings, perform better without further training.

Prior work has shown that problem lists and problem-oriented medical records are desirable and useful in practice; we hope our work shows that POMR construction is feasible. By releasing our annotations and using open-source embeddings, we allow other researchers to reproduce our results from Table 2 and Table 3 (except those using site-specific embeddings or the engineered features), and hope this allows for further investigation into POMR construction.

Limitations Our approach is a first attempt at this problem and thus has some limitations. First, the usefulness of this model on organizing patient data around a problem relies on that problem having a definition which is strictly coded as a list of diagnosis codes, when in reality the phenotype of diseases are much more complex. However, one need not initialize a problem representation as a linear combination of diagnosis code representations as we do. In general, the adoption of POMR should consider both technical and organizational needs, as pointed out by Simons et al. (2016). Specifically, one would have to consider, for example, the reliability and accuracy of current problem lists, the ability to re-train physicians to use a new system for accessing patient data, and integration concerns such as using institution-internal vocabularies. Only the last of these is partially tackled in this work.

Additionally, this dataset was collected with the emergency medicine physician's perspective in mind, and what is deemed relevant will certainly vary across medical specialties. The relevance of certain data points may also vary from patient to patient, and even from visit to visit, so this work is most useful when limited to typical patients at initial appointments.

Finally, the success of this approach ultimately rests on a targeted evaluation that measures whether structuring patient data in this way allows clinicians to answer questions about a patient's medical problems more quickly and accurately than the chronological view. We hope to perform such an evaluation in future work.

Acknowledgments

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Appendix A. Defined Problems

See Table 7 for the list of all defined problems.

Appendix B. Ontology baseline implementation

Using NDF-RT   First, we convert every RxNorm medication code in the test set to a code in NDF-RT. Then, for each NDF-RT medication code we create a set of related NDF-RT diagnosis codes using the "May Treat" and "May Prevent" relations contained in NDF-RT. These NDF-RT diagnosis codes are then converted to SNOMED when possible, so that each medication code has a list of SNOMED diagnosis codes associated with it. Finally, we augment the list of SNOMED codes to include equivalent ICD-10 and ICD-9 codes. To determine if a medication is relevant to a problem, we look for a match between the problem's definition codes and the medication's associated diagnosis codes. 75% of test set medication codes are coded in RxNorm, of which 91% have equivalent NDF-RT codes, of which 95% have at least one "May Treat" or "May Prevent" relation. All triplets in the validation set are given a score of 1 if they are deemed relevant by this baseline, and 0 otherwise. Since there are ties with this scoring function, we choose a rank by picking the median position of the example in the set of examples with the same score. For example, suppose there are 10 total triplets in an evaluation step, 1 positive and 9 negative. Suppose 4 negative triplets are deemed relevant and 5 are not. If the positive triplet is relevant, it gets rank 3. If it is not relevant, it gets rank 7.5.

Using CPT   We could not find a relation analogous to the "May Treat" and "May Prevent" relations in NDF-RT that would connect procedure concepts to diagnosis codes; however, we use a proxy based on the hierarchy of both CPT and ICD codes. We had a physician provide annotations connecting which parts of the CPT and ICD hierarchy correspond to the same medical disciplines. For example, CPT hierarchy code `1006056` "Surgical Procedures on the Cardiovascular System" falls into the same discipline as ICD-10 code `I0-I99`, "Diseases of the circulatory system". Then, we use this to apply the heuristic that a procedure is relevant to a problem if the CPT's parent code is under the same discipline as any of the problem's definition ICD codes.

Appendix C. Test set problem examples

Tables 8, 9, 10, and 11 contain examples suggestions for all test set problems.

Anemia
Arthritis
Asthma
Atrial fibrillation
Back pain
Cholelithiasis
Chronic kidney disease
Chronic obstructive pulmonary disease
Coronary artery disease
Cough
Dermatitis
Diabetes
Diverticulosis/Diverticulitis
Dyslipidemia
Gastroesophageal reflux disease
Gout
Headache
Heart failure
Hematuria
Hypertension
Hypokalemia
Kidney stone
Mood disorders, including depression
Osteoporosis
Rheumatoid Arthritis
Seizure disorder
Sleep apnea
Syncope
Thrombocytopenia
Thyroid hormone disorders
Uterine fibroid
Urinary tract infection

Table 7: All problems. Those in bold are those initially defined by Buchanan (2017)
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Medication	Procedure	Lab
Atenolol	**Ekg complete (tracing and interp)**	**Creatinine [mass/volume] in serum or plasma**
Diltiazem	**Ekg (hospital based)**	Potassium [moles/volume] in serum or plasma
Metoprolol	Holter complete (comm prac)	Inr in platelet poor plasma by coagulation assay
Lisinopril	**Echo, stress (exercise)**	Platelets [#/volume] in blood by automated count
Doxazosin	Methylprednisolone acetate inj 40 mg	Digoxin [mass/volume] in serum or plasma
Nitroglycerin	Pulse oximetry sngl determin (op)	Leukocytes [#/volume] in blood by automated count
Olmesartan	Mri-brain without contrast	Glucose [mass/volume] in serum or plasma
Chlorthalidone	Abdomen ct w/o iv and with po contrast	Natriuretic peptide b [mass/volume] in serum or plasma
Amlodipine	Pacemaker with interpretation	Prothrombin time (pt)
Hydrochlorothiazide	**Echo, complete (2d), trans-thoracic**	Sodium [moles/volume] in serum or plasma

Table 8: Example top-10 suggestions from the best-performing model (Choi et al. (2016) + features) for the held-out test set problem Hypertension. Candidates are drawn from the set of all triplets in the test set. Suggestions in blue are positive examples. Note that for hypertension, there is only 1 positive annotated lab.

Medication	Procedure	Lab
Metoprolol	**Ekg (hospital based)**	Lipase [enzymatic activity/volume] in serum or plasma
Enoxaparin	**(ekg) tracing only**	Natriuretic peptide b [mass/volume] in serum or plasma
Labetalol	Dual-lead pacemaker + reprogram	Prothrombin time (pt)
Nitroglycerin	Echo, complete (2d), transthoracic	**Creatinine [mass/volume] in serum or plasma**
Heparin	Holter hook-up (comm prac)	Inr in platelet poor plasma by coagulation assay
Lorazepam	Chest ct, no contrast	Bilirubin.total [mass/volume] in serum or plasma
Amlodipine	**Ekg complete (tracing and interp)**	Leukocytes [#/volume] in blood by automated count
Carvedilol	Dual-lead defibrillator + reprogram	**Potassium [moles/volume] in serum or plasma**
Clopidogrel	Nuc med, myocardial stress - pharmacologic	Creatine kinase.mb [mass/volume] in serum or plasma
Oxygen	Defibrillator remote interrogation eval/interp,to 90d	Renin [enzymatic activity/volume] in plasma

Table 9: Example top-10 suggestions from the best-performing model (Choi et al. (2016) + features) for the held-out test set problem Hypokalemia. Candidates are drawn from the set of all triplets in the test set. Suggestions in blue are positive examples.

Medication	Procedure	Lab
Metoprolol	Us - abdomen, complete	Reticulocytes/100 erythrocytes in blood by automated count
Prednisone	**Filgrastim inj 480 mcg**	**Hemoglobin [mass/volume] in blood**
Sulfamethoxazole	Abdomen ct w/o iv and with po contrast	Creatinine [mass/volume] in serum or plasma
Acetaminophen	Us - abdomen, limited	**Inr in platelet poor plasma by coagulation assay**
Cephalexin	**Bone marrow biopsy**	Ferritin [mass/volume] in serum or plasma
Pegfilgrastim	**Bone marrow aspiration**	Bacteria identified in isolate by culture
Ferrous sulfate	**Filgrastim inj 300 mcg**	Circulating tumor cells.breast [#/volume] in blood
Enalapril	**Ct - head/brain w/o contrast**	Sodium [moles/volume] in serum or plasma
Ibuprofen	Alteplase recomb 1mg	Natriuretic peptide b [mass/volume] in serum or plasma
Tamsulosin	**Cbc w/o plt**	Leukocytes [#/volume] in blood by automated count

Table 10: Example top-10 suggestions from the best-performing model (Choi et al. (2016) + features) for the held-out test set problem Thrombocytopenia. Candidates are drawn from the set of all triplets in the test set. Suggestions in blue are positive examples.

Medication	Procedure	Lab
Montelukast	**Sleep study, w/ cpap (treatment settings)**	Natriuretic peptide.b prohormone n-terminal [mass/volume] in serum or plasma
Ipratropium	**Positive airway pressure (cpap)**	**Natriuretic peptide b [mass/volume] in serum or plasma**
Enoxaparin	**Sleep study, w/o cpap**	Nicotine [mass/volume] in urine
Exenatide	Pulse ox w/ rest/exercise, multiple (op)	Inr in platelet poor plasma by coagulation assay
Lamotrigine	Basic spirometry	Creatinine [mass/volume] in serum or plasma
Oxycodone	(ekg) tracing only	Leukocytes [#/volume] in blood by automated count
Albuterol	Ekg complete (tracing and interp)	Cotinine [mass/volume] in urine
Fluticasone	Pneumogram, peds multichannel	Hemoglobin [mass/volume] in blood
Azithromycin	Ekg (hospital based)	Opiates [presence] in urine by screen method
Clonazepam	Intervene hlth/behave, indiv	Ferritin [mass/volume] in serum or plasma

Table 11: Example top-10 suggestions from the best-performing model (Choi et al. (2016) + features) for the held-out test set problem Sleep apnea. Candidates are drawn from the set of all triplets in the test set. Suggestions in blue are positive examples.