Language Models Are An Effective Patient Representation Learning Technique For Electronic Health Record Data

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Abstract

Widespread adoption of electronic health records (EHRs) has fueled development of clinical outcome models using machine learning. However, patient EHR data are complex, and how to optimally represent them is an open question. This complexity, along with often small training set sizes available to train these clinical outcome models, are two core challenges for training high quality models. In this paper, we demonstrate that learning generic representations from the data of all the patients in the EHR enables better performing prediction models for clinical outcomes, allowing for these challenges to be overcome. We adapt common representation learning techniques used in other domains and find that representations inspired by language models enable a 3.5% mean improvement in AUROC on five clinical outcomes compared to standard baselines, with the average improvement rising to 19% when only a small number of patients are available for training a prediction model for a given clinical outcome.

1 Introduction

The widespread adoption of electronic health records (EHRs) has created opportunities for using machine learning to reduce healthcare costs and improve quality of care. EHR data have been used to learn prediction models for clinical outcomes such as mortality [1], sepsis [2], 30-day readmission [3] and others [4, 5]. However, the complexity of patient data poses many obstacles to its effective use. Patient records in EHRs are variable length, high dimensional and sparse, with complex temporal and hierarchical structure. They are comprised of irregularly spaced visits spread across years, with each visit consisting of a subset of thousands of possible diagnosis, procedure, and medication codes as well as lab values and unstructured data such as text or images. In contrast, most off-the-shelf machine learning algorithms expect a fixed length vector of features as input. Manually defining a transformation of patient records into such a representation beyond simple binned counts is time consuming and outcome-dependent, leaving much of the temporal and hierarchical structure of EHRs underutilized when building machine learning models.

The challenge of representing EHR data can be addressed by using neural networks to automatically learn how to featurize patient data while learning a model for a given clinical outcome (e.g., mortality or 30 day readmissions) [4]. This “end-to-end” formulation is appealing because it has led to ground-breaking performance in computer vision and natural language processing (NLP) without manual feature engineering. However, it is unclear how this approach works in practice for EHR data. While prior work has reported that deep neural networks outperform models that use simple count-based features [6, 7], that work has not consistently evaluated against comprehensive baselines. In contrast, other researchers [4, 8] have found that such end-to-end neural models provide minimal or no benefit over count-based representations combined with simpler models such as logistic regression or gradient boosted trees. Our work investigates these apparently conflicting findings.

Deep learning models typically require large data sets to train, so the finding of minimal performance gains may be a result of using datasets that are simply too small for deep neural networks to shine. Recent machine learning research addresses the problem of limited training data with representation learning, which seeks to learn representations from large datasets that capture important, generally useful patterns. Once learned, these representations are then used as input to learn models for specific, potentially unrelated tasks. Representation learning is routinely used in settings in computer vision and NLP when limited data
is available. It is especially compelling for clinical outcome models using EHR data because it is often the case that the number of patients available in a training set for a given outcome is a small fraction of the total number of patients in an EHR. The core hypothesis (as demonstrated in Figure 1) is that it is possible to use these other patients to improve predictive performance for many clinical outcomes of interest. A variety of representation learning methods have been proposed for EHR data [9, 10, 11, 12]; however, the comparative performance of these methods, using a common set of shared clinical outcomes, against each other and against simple, count based representations is unknown.

In this work we empirically evaluate the effectiveness of three common representation learning approaches as a means of deriving features for learning prediction models for five clinical outcomes. We use only coded EHR data (diagnosis, procedure, medication, and lab order codes) due to IRB restrictions on the use of images and clinical notes. We compare against carefully tuned baseline models using simple count representations and end-to-end trained neural nets for the same outcomes. We also perform subsampling experiments to investigate the performance gains resulting from using the different representations as a function of the amount of data available to train the clinical outcome model. We find that clinical language model based representations (CLMBR) inspired by NLP outperform all other representations for all outcomes and training set sizes. Surprisingly, models using CLMBR even outperformed end-to-end trained neural nets. The advantage of CLMBR over others grows as training set size decreases. However, at the largest dataset sizes, simple count based representations can perform almost as well when used with a flexible model class such as gradient boosted trees. In contrast, other representation learning methods provided only marginal benefits over simple count based representations, and only in situations with small sample sizes. These results show that it is possible to learn general purpose EHR representations that enable training better performing models for a range of clinical outcomes. The benefits are especially great when labeled training data for the clinical outcomes are limited. However, CLMBR is expensive to learn (we spent 54 GPU-days tuning the CLMBR setup), and when labeled training data for the clinical outcomes are plentiful, simple
count based representations paired with flexible off-the-shelf models, such as gradient boosted trees, can perform almost as well.

1.1 Related Work

1.1.1 Predictions Using The Electronic Health Record

Recent work on learning clinical prediction models using EHR data focuses on complex neural network models trained in an end-to-end manner on the outcome of interest. This approach has been applied to many clinical outcomes, such as all-causes mortality [1], heart failure [7, 13, 6], COPD [14], readmissions [15, 16], and future hospital admissions [17]. These works generally propose novel neural net architectures and report performance gains over baseline models. However, Rajkomar et al [4] reports that logistic regression using a simple bag of words based representation that ignored time and encoded patient time lines as counts of the medical codes occurring in the timeline performed very close to or within the margin of error of an ensemble of three complex neural net models for three clinical outcomes (inpatient mortality, readmissions, and length of stay). Considerable effort went into developing the neural net models, but it seems that with appropriate care a relatively simple baseline can perform almost as well. Similarly, Chen et al [8] found that neural nets were consistently outperformed by gradient boosted trees and random forests on a range of clinical outcomes with smaller datasets. Together, these seemingly conflicting results require further investigation of the performance benefits of using neural networks over other methods.

1.1.2 Representation Learning

Representation learning is often used in computer vision and NLP to mitigate the impact of having limited training data. Prior work on representation learning for EHR data primarily follows work in NLP because of similarities in the structure of data. Both natural language and EHR data fundamentally concern sequences of tokens. In NLP, each element in a dataset is a document which in turn contains a sequence of words. Analogously, a patient’s EHR can be seen as a sequence of interactions with the hospital, where each interaction generates diagnosis, procedure, medication, and laboratory codes. In both cases, we most often wish to learn representations of high level units such as documents (patients) so that we can make a decision on the document (patient) as a whole. In this section, we briefly discuss representation learning techniques for text, starting from words and working our way up to documents, and then describe how those techniques have been adapted for coded EHR data.

Representation Learning For Text

Text can be viewed as a sequence of words, and representations can be learned for both the words and the sequences themselves. Representation learning for text can generally be broken down into two categories: word level representations and document level representations.

Word level representations are fixed length vectors for each word learned through information theory and linear algebra [18] or neural networks [19]. In both cases, the aim is to learn a representation that is useful for anticipating surrounding context words (e.g., in this sentence, the context of “representation” includes “learn” and “useful”). The end result is a fixed length vector representation of each individual word which can then be used for tasks such as question answering and sentiment analysis [20, 21].

In contrast, document level representations are fixed length vectors that capture salient properties of the document as a whole. A classic linear algebra technique for this is Latent Semantic Indexing (LSI) [22], which combines both SVD and TF-IDF to learn a low dimensional vector representation of a document with the goal of maximizing the ability to reconstruct document term frequencies.

Currently, the most effective representation learning techniques for text expand on document level representations by learning language models. A language model is a probabilistic model of sequences of words, as opposed to LSI, which models only the count matrix, or word2vec, which models only the probability of individual words given context. These language models are often formulated with complex neural networks with millions of parameters that capture the language generation process by predicting a word at a time, either sequentially with recurrent neural networks [23] or via masking with Transformer models [24].

Representation Learning For Electronic Health Records
Table 1: Clinical Outcome Definitions

| Outcome Name         | Outcome Definition                                                                 | Prediction Time                  |
|----------------------|-------------------------------------------------------------------------------------|----------------------------------|
| Inpatient Mortality  | Whether a patient will die during an inpatient stay                                | Time of admission                |
| Long Admission       | Whether a patient will stay seven or more days in the hospital                     | Time of admission                |
| ICU Transfer         | Whether a patient will be transferred to the ICU the following day                 | Every day of an inpatient stay before transfer |
| 30-day Readmission   | Whether a patient will be readmitted to the hospital within 30 days                | Time of discharge                |
| Abnormal HbA1c       | Whether an HbA1c test will be positive (> 6.5%) for a non-diabetic patient         | Before the test results are returned |

Table 2: Characteristics of Clinical Outcomes

| Outcome Name         | Num Labels | Num Positives | Num Unique Patients |
|----------------------|------------|---------------|---------------------|
| Inpatient Mortality  | 212,599    | 4,294         | 130,708             |
| Long Admission       | 212,636    | 48,508        | 130,719             |
| ICU Transfer         | 761,658    | 8,094         | 101,999             |
| 30-day Readmission   | 187,866    | 29,693        | 112,264             |
| Abnormal HbA1c       | 83,550     | 1,651         | 51,654              |

Work on representation learning for EHR data has focused on adapting methods successfully used in NLP. One family of approaches treats medical codes as words, and learns representations for medical codes [11, 12] by adapting word2vec to deal with the lack of intrinsic ordering of medical codes within an encounter. Choi et al [12] takes the next step and uses the code vectors to predict heart failure. In follow up work, Choi et al extend this approach to simultaneously learn medical code and patient level representations [10]. However, later evaluations on clinical outcomes found this approach was little better than several other baselines in predicting heart failure [25]. Finally, Miotto et al [9] learns patient level representations using autoencoders, reporting significantly better performance than their baselines on the task of predicting future new diagnosis codes. However, in Choi et al [10], stacked autoencoders were found to be no better than other baselines at predicting next encounter diagnosis codes. Therefore, the utility of learning general purpose representations of EHR data for better predicting clinical outcomes remains unclear.

There has also been some initial work on applying language modeling to electronic health records. Prior work by Choi et al [26] proposes models that predict a simplified subset of the medical codes appearing in the next step of a sequence of patient encounters. They report that simple Gated Recurrent Unit (GRU) models perform quite well on this task. However, the resulting representation is not evaluated for effectiveness on learning better predictive models for clinical outcomes such as in-patient mortality or readmissions.

2 Results

We evaluate a wide range of simple count based and learned representations in terms of their ability to enable learning models for five clinical outcomes across a range of training set sizes. Table 1 provides a description of the clinical outcomes; Table 2 provides some descriptive statistics about the characteristics of the datasets for each clinical outcome. We conduct four experiments, aimed at the following questions. First, what is the relative performance of prediction models trained using alternative representations of EHR data with large sample sizes? Second, how does the relative performance gains resulting from using alternative representations of EHR data vary with sample size available for training the clinical outcome model? Third, what impact does the model class (such as logistic regression or gradient boosted trees) have on the contribution of each representation to performance of the clinical outcome model? Finally, our language model builds on prior work so we ask what is the relative contribution of our effort compared to the prior work?
Table 3: AUROC Of The Clinical Outcome Models As A Function Of The Representation

| Outcome Name          | Counts | Word2Vec | LSI     | CLMBR   | End-to-end GRU |
|-----------------------|--------|----------|---------|---------|----------------|
| Inpatient Mortality   | 0.834  | -0.010 ± 0.006 | -0.046 ± 0.007 | **0.018 ± 0.006** | -0.030 ± 0.008 |
| Long Admission        | 0.783  | -0.020 ± 0.002 | -0.055 ± 0.002 | **0.009 ± 0.002** | -0.013 ± 0.002 |
| ICU Transfer          | 0.792  | -0.041 ± 0.006 | -0.086 ± 0.007 | **0.045 ± 0.005** | 0.039 ± 0.006  |
| 30-day Readmission    | 0.809  | -0.018 ± 0.002 | -0.051 ± 0.003 | **0.005 ± 0.002** | -0.001 ± 0.002 |
| Abnormal HbA1c        | 0.700  | 0.015 ± 0.015 | -0.011 ± 0.016 | **0.056 ± 0.013** | -0.019 ± 0.017 |

We report the performance of four categories of representations (Counts, Word2Vec, LSI, and CLMBR) used as inputs to two classes of clinical outcome models: logistic regression and gradient boosted trees. As an additional baseline, we also report results of a clinical outcome model trained as an end-to-end GRU, which directly uses the raw EHR data and internally learns a fixed length representation during the process of training a prediction model for the given clinical outcome.

2.1 Effect Of Representation With Large Amounts Of Data

We evaluated the performance of the alternative representations when large amounts of training data are available. Each outcome in the pool of five clinical outcome was chosen on the basis of having a large number of labels to both aid this analysis and to reduce the variance of our performance estimates. Table 3 shows the AUROC on the test set for each representation category when trained with all of the data, with the best performing representation presented in bold font. All performance metrics are calculated pair-wise, relative to the counts representation, in order to reduce variance and better quantify differences between representations. We report standard deviations estimated by bootstrap sampling of the test set. Appendix E lists the best hyperparameter settings for each outcome and representation combination. We find that CLMBR performed best in helping build models for all five outcomes, although the improvement over alternatives is minimal for some of the outcomes. Surprisingly, CLMBR is uniformly superior to the end-to-end GRU models. Word2vec and LSI representations on the other hand are usually worse than other representations.

2.2 Effect Of Training Set Size

We also perform experiments in which we artificially reduce the dataset set sizes used for clinical outcome model training through subsampling the training and development sets. These experiments explore the hypothesis that learned representations are especially effective when there is only a limited amount of training data available for developing a clinical outcome model. Figure 2 shows the performance measured by AUROC of each representation category as a function of dataset size for each clinical outcome. We calculate the average AUROC across ten subsamples of the training set and show the 95% t-distribution confidence interval for the average AUROC. We find that all representations suffer with small data set sizes, but, as expected, the CLMBR fares best. The other learned representation classes, word2vec and LSI, do seem to provide some benefit relative to counts at smaller sample sizes (with word2vec working better than LSI), but fail to reach the performance of CLMBR. Overall, the magnitude of the benefit from CLMBR is highly outcome dependent, and in all cases, count based representations appear to converge on similar performance. We also note that there is sometimes considerable variance in the estimated performance with very small datasets, probably due to difficulties in hyperparameter tuning and model selection (performance estimates are estimated on the full hold out test set and have relatively little variance due to test set sampling because of the size of the test set).
Figure 2: Clinical outcome AUROC (y-axis) for each representation type as a function of training/development set size (x-axis). Note that CLMBR (red) matched or outperformed all prior approaches. The dashed lines show performance of clinical outcome models trained using CLMBR on the full dataset, and represents best case performance given available data. We find that the CLMBR provides benefit for all outcomes and training set sizes, but the magnitude of the benefit is much larger for smaller sample sizes, and diminishes relative to simple count based representations at larger sample sizes.

2.3 Effect Of The Choice Of Clinical Outcome Model Class

We evaluate both L2 regularized logistic regression and gradient boosted tree for training clinical outcome models. Comparing the relative performance of these two model classes can provide insight into which types of models perform best with which types of representations. Figure 3 shows the relative performance of these model types across clinical outcomes and sample sizes for counts and CLMBR. As before, we compute the mean AUROC from 10 subsamples of the training set and report the 95% t confidence interval for that mean. When using count based representations, we find that there is a consistent, often quite large, performance benefit from using gradient boosted tree models versus logistic regression, with gaps ranging from 4% for 30 day readmission to 20.7% for inpatient mortality. With CLMBR, the best clinical outcome model is often
simply logistic regression; more complex gradient boosted tree models offer no improvement even with large sample sizes and often hurt performance at smaller N.

![Figure 3: AUROC for logistic regression and gradient boosted tree prediction models for the five clinical outcomes trained using counts and CLMBR. For count based representations, we observe significant benefits from using gradient boosted trees versus L2 regularized logistic regression. In contrast, we find that CLMBR does not benefit from using a more complex prediction model for any clinical outcome, and logistic regression is sufficient to take advantage of the extra information captured in the representation. The dashed lines show performance of prediction models trained on the full clinical outcomes datasets using CLMBR, and represents best case performance given available data.](image)

### 2.4 Relative Effect Of The Full Language Model Compared To A Simplified Version

We perform ablation experiments aimed at understanding the importance of the full language modeling objective. We implement a simplified language modeling objective used in prior work [26] and measure the performance of the resulting representation for training clinical outcome models. Table 4 shows the performance of this representation relative to the full language model representation using all data for each clinical outcome. Standard deviations are estimated from bootstrapping the test set. There is a consistent improvement across outcome for the more complicated language modeling objective, but the magnitude of that improvement is relatively small compared to the overall gain due to using a language model.
Table 4: AUROC Of Clinical Outcome Models On CLMBR Comparing The Full Language Model To The Simplified Language Model

| Outcome Name       | Full Language Model | Simplified Language Model |
|--------------------|---------------------|---------------------------|
| Inpatient Mortality| 0.852               | −0.008 ± 0.003            |
| Long Admission     | 0.792               | −0.004 ± 0.001            |
| ICU Transfer       | 0.837               | −0.024 ± 0.002            |
| 30-day Readmission | 0.814               | −0.007 ± 0.002            |
| Abnormal HbA1c     | 0.756               | −0.014 ± 0.008            |

3 Discussion

Prior work employing deep neural nets to train clinical outcome models using EHR data mostly focused on end-to-end clinical outcome models and used large datasets; there has been much less work on learning general purpose representations using the entire EHR dataset that can then be used to learn better clinical outcome models. We have shown that CLMBR, which captures the sequential nature of EHR data, are significantly better than a wide array of alternative representations for training clinical outcome models, and across a range of training set sizes. The benefits are largest with small sample sizes (with an average improvement of 19% in AUROC), but continue to hold to quite large sample sizes, including when training clinical outcome models with over 200,000 samples.

Somewhat surprisingly, CLMBR also proved superior to end-to-end trained neural nets in the large sample regime. In contrast, other learned representations proved to be of little value relative to simpler count based representations when sufficient data is available. Finally, we found that with enough labeled training data, clinical outcome models using simple count based representations can perform very well, only performing 3.5% worse than models trained using the more complicated CLMBR. However, with count based representations, it is important to use a model class with sufficient expressive power. Note that gradient boosted trees performed much better than L2 regularized logistic regression with the simple counts based representations. This observation may explain some of the large discrepancies in reported performance gaps between neural network models and simpler baselines in prior work [4, 8, 27, 7].

Together, these results suggest an interesting tradeoff between computation and clinical outcome model performance. Language modeling has significant computational costs and requires substantial (unlabeled) data. We spent a total of 54 GPU-days (NVIDIA V100 GPUs) tuning the language model, and early experiments suggested that this computational cost was necessary to the success of learning generic representations because less well tuned language model based representations did not perform as well as count based representations. When the absolute best performance is a priority, or when there is little labeled training data for the clinical outcome, CLMBR offers significant benefits. However, the performance gains need to be weighed against the additional cost and complexity of learning a more sophisticated representation. In addition, complex models may be less robust to distributional shifts, and healthcare is highly non-stationary. Complex models often incur technical debt and are harder to keep running in a real deployment [28]. Given these realities, it is important to question whether or not marginal gains in performance are worthwhile in practice.

Our conclusions have important limitations. First, our findings are limited to the five clinical outcomes used in this work and findings may not generalize to all other possible EHR-based model types. Second, this work does not explore how well CLMBR learned from data from one institution will work well at other sites. In addition, we can expect the volume of EHR data available for predictive modeling to increase steadily, which might erode the gains from using fancier representation regimes. In particular, we note that end-to-end neural net models may regain the advantage when more training data is available.

Nevertheless, this work suggests the following guidelines for how to represent patient EHR data for clinical outcomes similar to those in this work. When one has a large computational budget and sufficient data for carefully tuning CLMBR, those representations combined with logistic regression can be a very effective choice, providing larger gains in predictive performance when the dataset to train the predictor is smaller.
However, if there is a large dataset available for training the clinical outcome model and it is desirable to avoid the "technical burden" of complex language modeling, simple count based representations combined with a gradient boosted tree model often do almost as well.

4 Conclusion

In this work we explore the utility of various representation learning schemes for EHR data in learning five distinct clinical outcome models at a variety of simulated dataset sizes. We find that clinical language model based representations (CLMBR) perform quite well, beating out both simpler count representation schemes as well as end-to-end neural network models for all clinical outcomes and dataset sizes. However, at large dataset sizes, the difference between CLMBR and simple count based representations diminishes, with the gap falling to only a couple of AUROC points. These results suggest that when labels are abundant and computational resources are scarce, gradient boosted tree models on count representations offer a useful balance between prediction performance and compute cost. Otherwise, if either labels are scarce or computational resources are available, logistic regression models combined with CLMBR can provide significant gains in prediction performance.

5 Methods

We evaluate the performance of four categories of representations (Counts, Word2Vec, LSI, and CLMBR) used as inputs to two classes of clinical outcome models: logistic regression and gradient boosted trees. In order to tune the various hyperparameters available for each representation category, we independently determine the best hyperparameters on the development set and report performance of representations using those settings on the hold out test set. The hyperparameters for the final clinical outcome model are likewise tuned on development set data. As an additional baseline, we also report results of clinical outcome model trained as an end-to-end GRU, which directly uses the raw EHR data and internally learns a fixed length representation during the process of training on a particular clinical outcome. Figure shows an overview of the experimental set up.

| EHR Data          | Representation | Experiments | Clinical Task Model Type |
|-------------------|----------------|-------------|--------------------------|
| Demographics      | Counts         | Logistic Regression | Mortality               |
| Diagnoses         | LSI            | Gradient Boosted Trees | Long Admission          |
| Procedures        | Word2Vec       |                          | ICU Transfer            |
| Med orders        | Language Model |                          | Readmission             |
| Lab test orders   |                |                          | HbA1c                    |

Figure 4: Overview of our experiments for evaluating representation learning methods using EHR data (col 1). We evaluate four representation methods (col 2) using two model classes (col 3) to train models for five clinical outcomes (col 4).

5.1 Data

All experiments are conducted on de-identified EHR data from Stanford Hospital and Lucile Packard Children’s Hospital. The data comprises 3.4 million patient records spanning roughly from 1990 through 2018.
Data usage was reviewed by Stanford University’s institutional review board with waiver of informed patient consent. We treat each patient’s electronic health record as a sequence of days $d_1, \ldots, d_N$, ordered by time but ignoring the interval between successive days. Each day is associated with a set of medical codes representing diagnoses, procedures, medication orders, and laboratory test orders (ICD10, CPT or HCPCS, RXCUI, and LOINC codes respectively) recorded on that day. In this study, we do not use quantitative information such as laboratory test results or vital sign measurements. We also do not use the text notes, images, or explicit linkages between codes (e.g., diagnosis codes entered to justify procedures, as used in Choi et al [25]). In total, there were 21,664 codes after filtering for codes that occur in the electronic health records of at least 25 patients. Patient demographic data (gender, race and ethnicity) was encoded by assigning corresponding codes to the date of birth of the patient.

5.2 Representations

5.2.1 Count Based Representations

The simplest representation we consider is similar to a bag of words except that we count the number of occurrences of each code in the electronic health record instead of using binary indicators for presence/absence. This representation is widely used as a baseline, and in Rajkomar et al [4] it achieved excellent performance with a regularized logistic regression model for three clinical outcomes.

We also evaluate two enhancements to the basic counts representation: time binning and ontology rollup. Time binning counts occurrences of a code in different time buckets separately, and has been used in prior work [1, 4]. We use time buckets of 0-30 days, 30-180 days, 180-365 days, and 365+ days from the reference time. These representations are very high dimensional and sparse because there are very many codes, most of which occur in a very few patients. Ontology rollup is a commonly used technique that mitigates this problem by using ontologies (knowledge bases that specify hierarchical relationships between concepts, e.g., ”Type 1 diabetes mellitus with ketoacidosis” is a type of ”Type 1 diabetes mellitus”) to ”densify” these representations [7]. For example, if we observe the ICD10 code E10.1 ("Type 1 diabetes mellitus"), we also count that as an occurrence of the ancestor codes E10 ("Type 1 diabetes mellitus") and E08-E13 ("Diabetes mellitus"). We use the Unified Medical Language System (UMLS) [29] and map codes to their ancestors within their respective hierarchies when applicable (ICD10 for diagnoses, CPT or MTHH for procedures, and ATC for medications). Note that this procedure can increase the dimensionality of the representation to 36,617 codes because many ancestor codes were not present in the original representation.

We thus evaluate four variations of count based representations, one for each combination of ontology roll up and time binning. These representations are our baselines for simple, non-learned representations.

5.2.2 Word2Vec Representation

One way to approach representing a patient’s EHR data is to first learn representations of each possible code, and then combine the representations for codes actually occurring in a patient’s timeline in some manner. In NLP applications, it has been shown that very simple methods of combining word representations learned by, e.g., taking the element-wise mean of a set of word embeddings, can yield surprisingly effective representations of sentences or documents [20]. Adapting this approach to patient EHR data requires some way of dealing with the unordered nature of codes occurring on a given day. Prior work [12, 11] recommends simply randomly ordering the codes observed on a given day and treating them as a sequence for input to word2vec. We implement this algorithm to construct embeddings for every code in our data, with an embedding size of 300. We use gensim’s [30] word2vec implementation for our experiments. We also evaluate code embeddings on data augmented by ontology rollup as described above. Finally, in order to construct patient level representations from the code representations, we test combining code representations by taking the element-wise mean, and also by concatenating the element-wise min, max and mean vectors as described in [20]. These two possibilities combined with the ontology flag result in four variations of word2vec representations.
5.2.3 Latent Semantic Indexing Representations

Latent semantic indexing (LSI) is a long-standing technique used in information retrieval to construct representations of documents. LSI starts with the counts of words in each document, weights them using TF-IDF \cite{TF-IDF}, and then uses a singular value decomposition \cite{SVD} on the resulting matrix for dimensionality reduction. We apply LSI to construct patient level representations by treating each patient’s electronic health record up to a randomly sampled time point as a document with each code counting as a word. Following our count based representations \ref{count-based}, we run LSI with and without ontology rollup and test representation sizes of 400 and 800. We thus evaluate four different LSI representations. We use gensim’s \cite{gensim} implementation of LSI.

5.2.4 Clinical Language Model Based Representations

The core idea behind language model based representations is that language models can capture global information about the sequence of tokens (such as words or disease codes) that is useful for predicting clinical outcomes. This generic global information can then be extracted in the form of dense representations that can be used directly when training a clinical outcome model. In an EHR, the elements of the sequence that we are trying to capture consist of days where the patient interacts with the hospital. Mathematically, the language modeling objective can be seen as trying to estimate the probability of seeing a particular patient record, i.e., \( p(d_1, \ldots, d_N) \). The primary key technique for learning language models is that probability distributions over sequences can be factorized into a sequence of predictions where only a single element of the sequence is predicted at a time. In an EHR, this boils down to predicting the next day in a patient record given all of the previous days, i.e., \( p(d_i|d_1, \ldots, d_{i-1}) \). The main complication with EHRs is that unlike in other settings, each \( d_i \) is composed of a set of codes as opposed to a single token. Thus, the problem is a multi-label prediction problem instead of a multi-class prediction problem. There is a large body of literature on multi-label problems and a number of techniques for modeling them. For the purposes of our experiments, we choose the simplest possible technique of transforming this problem into a binary classification problem through the binary relevance method \cite{binary-relevance}. We model \( p(d_i|d_1, \ldots, d_{i-1}) = \prod_{c \in C} I(c \in d_i)p(c|d_1, \ldots, d_{i-1}) + I(c \notin d_i)(1 - p(c|d_1, \ldots, d_{i-1})) \). One issue with this approach is that this factorization will only be able to correctly model \( p(d_i|d_1, \ldots, d_{i-1}) \) when the probability of the codes are independent given the prior history. That assumption is unlikely to be the case in our data, where we know that there are strong correlations among certain codes due to adverse drug reactions and limited time during visits. Nonetheless, we found that this approach seems to work well in practice.

Similar to prior work, we use a GRU-based neural network as our language model \cite{GRU}. Figure 5 shows an overview of the model architecture. The main modification we make is that we introduce a linear layer after the GRU layer in order to extract representations of a lower dimension from the internal GRU state. The first layer of our network is an embedding bag layer which takes as input the sets of codes for each day and outputs the mean embedding for that day using an embedding matrix \( W \) with a tuned embedding size. As in Rajkomar et al \cite{Rajkomar}, day embeddings are then concatenated with a five element vector for each day that contains the age at a particular day, the log transform of the age at that particular day, the time delta from the previous day, the log transform of that time delta and a binary indicator of whether or not that day is the first day of the sequence. All of these variables are normalized to 0 mean and 1 standard deviation. The purpose of adding these variables is to provide some time information to the neural network due to the fact that there are different amounts of real time passing between each day. The day embeddings plus demographic data are then fed into a single layer GRU with a set number of hidden units. A patient embedding at each time step is computed by passing the output of the GRU through a GELU \cite{GELU} activation function and a linear layer with output size equal to the embedding size.

This patient embedding is then used to compute the probability of each code in the code set in order to satisfy the language modeling objective. Intuitively, we would like to compute these probabilities as a sigmoid transformation of the dot product between the patient embedding and the code embedding. However, computing this naively is problematic due to both memory and computational needs caused by the large number of codes. Prior work \cite{HIDEN} has shown that it is possible to use a hierarchical decomposition for computing large scale softmax operations when there is pre-existing hierarchical structure. We apply a hierarchical decomposition to our code probability space using the ontologies in UMLS. We then apply that algorithm on a code matrix and a patient embedding in order to obtain the probability of each code.
Following prior work on text language models, we use the same embedding matrix for both this computation and when computing our mean embeddings on the input side. After the language model is trained, we extract patient representations by taking the output of the linear layer prior to the hierarchical sigmoid layer. More sophisticated approaches involving layer-wise fine-tuning were investigated, but did not appear to perform better than this simpler approach. Thus, we use the trained language model as a fixed feature extractor.

Clinical Language Model-based Representation (CLMBR)

We implement this model in PyTorch and optimize it using OpenAI’s version of the Adam algorithm [36] using L2 regularization. We apply dropout between the input embedding and the GRU and between the GRU and the linear layer. Two models are tested: a small model with an embedding size of 400, and a larger model with an embedding size of 800. For each model, the learning rate, dropout rate, L2 regularization strength, and hidden layer size are tuned using grid search. We train each model for 50 epochs with linear learning rate decay to zero with a two epoch linear learning rate warmup. A batch size of 2,000 days (using as many patients as possible in a greedy manner) is used. Xavier initialization is used for the code embeddings and the default Pytorch initialization is used for the other parameters. The full grid of tested hyperparameters is specified in Appendix A.

We also implement and test the simpler language modeling objective used in DoctorAI [26] to study the effect of the choice of the language modeling objective. Following DoctorAI, we ignore the multi-label nature of the problem and instead use a softmax loss function. In addition, we mirror DoctorAI by simplifying our target space by only predicting high level diagnosis (3 token ICD10) and medication codes (leaf ATC) as opposed to the full code space considered in our main language model. We use a simplified flat softmax as the reduced code space renders techniques like hierarchical softmax unnecessary. For the sake of time, we only evaluated the simplified language model with a fixed embedding size of 800. We performed the same hyperparameter grid search as for our baseline language model for that particular embedding size.

Figure 5: An overall diagram of our clinical language model and how CLMBRs are constructed. CLMBRs for individual patients are created by extracting the fixed length vectors generated by the linear layer after the GRU.
5.3 Clinical Outcome Models

We use each representation as input to two classes of models to learn a predictor for each clinical outcome. The first is a simple linear model: logistic regression with L2 regularization. The L2 parameter is swept in a grid for every power of 10 between 10\(^{-6}\) to 10\(^6\). We use the sklearn's LogisticRegression implementation with the lbfgs algorithm. The second model class is gradient boosted trees, which can model interactions and non-linearities in the data. We performed hyperparameter tuning by grid search, varying the learning rate between 0.02, 0.1, and 0.5; and the number of leaf nodes in each base tree between 10, 25, and 100. Early stopping with 500 max trees is used for selecting the number of trees. We used the LightGBM implementation of gradient boosting.

5.4 End-to-End Neural Network Models

When one assesses the utility of general purpose learned representations, it is important to quantify the degree to which they differ from the frequently used alternatives, especially with large sample sizes. To this end, we train end-to-end recurrent neural net models for each clinical outcome. These models do not use any of the learned representations described above, and instead operate directly on the raw data representation itself, i.e., a sequence of observed codes. We use the same architecture as the language models except that the patient representation is fed directly into a simple logistic regression layer to predict the clinical outcomes. As for the language models, a hyperparameter search was performed independently for each outcome in order to provide a fair comparison. This hyperparameter search is of roughly the same size as the language model hyperparameter search grid, with one change being more exploration of smaller model sizes to counter rampant overfitting caused by the reduced sample count. See Appendix B for the hyperparameter grid of the end-to-end GRU models. See Appendix D for the best performing hyperparameters for each clinical outcome model.

5.5 Experimental Setup

5.5.1 Data Splits

Data was split into training, development, and test sets by time: data through December 31, 2015 was used for training, data from January 1, 2016 through July 1, 2016 was used as the development set, and data from August 1, 2016 through August 1, 2017 was used as a held out test set. Note that even though patients may appear in multiple splits, each prediction time for such patients will appear in only one split. We adopted this design because of potential non-stationarity in electronic health records - this scheme provides more unbiased estimates of real world performance than time-agnostic patient splits.

5.5.2 Tuning And Evaluation

Experiments were carried out in three stages: representation tuning, model tuning, and final evaluation on the held out test set. The representation tuning stage only applies to the language model because it has many parameters that need to be intrinsically tuned. In this stage we run a hyperparameter grid (see Appendix A) on the training set and select the best hyperparameters based on the intrinsic language modeling loss. After the representation tuning stage, we perform model tuning. During model tuning, we train representations on the training set and use the resulting representation model to generate training and development set representations which are then used for training clinical outcome models. Hyperparameters for the clinical outcome models are selected on the basis of Area Under the Receiver Operating Characteristics curve (AUROC).

Finally, we perform an evaluation phase where we train the representations on both the training and development sets and apply the learned representation model to all three splits of the data. A final clinical outcome model is trained using the training and development set data and is applied to the test set in order to obtain final performance (measured in AUROC). Uncertainty estimates are computed by performing 1,001 test set bootstrap samples.
5.6 Subsampling Experiments

We also evaluate the representations with clinical outcome models trained on smaller datasets to test the hypothesis that representation learning provides greater benefits as sample sizes decrease. We perform experiments in which training and development sets are subsampled without replacement, with stratified sampling of the training and development sets to enforce a fixed positive label prevalence of 10%. The total sample sizes were 100, 200, 400, 800, 1,600, and 3,200, with 70% and 30% of each sample drawn from the training and development splits respectively. The subsampled training and development splits were then used for clinical outcome model tuning and fitting in place of the full training and development splits as described above. This process was repeated 10 times in order to provide estimates of variance due to sampling of the training and development sets for the performance metrics. End-to-end GRU predictive models are excluded from this experiment due to observed poor performance with small sample sizes and the high relative cost of training end-to-end GRU models.

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Data Availability

The EHR data used in this study cannot be made publicly available due to patient privacy constraints.

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Contributions
E.S. designed and conducted the primary experiments and created the initial drafts of the manuscript. K.J. helped work on further drafts and helped contribute code for some experiments. C.C. and S.P. contributed code for some of the experiments. J.F. and N.S. provided helpful discussion and helped design some of the figures. All authors contributed to revising the paper.

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Competing Interests

The authors have no conflicts of interest to declare.

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A  Language Model Hyperparameter Grid

Table 5: Language Model Hyperparameters

| Hyperparameter Name | Hyperparameter Values |
|---------------------|-----------------------|
| Embedding Size      | [400, 800]            |
| GRU Hidden Size     | [400, 800, 1600]      |
| LR                  | [10^{-2}, 10^{-3}, 10^{-4}, 10^{-5}] |
| L2                  | [0.1, 0.01, 0.001]    |
| Dropout             | [0, 0.1, 0.2]         |

B  End To End GRU Model Hyperparameter Grid

Table 6: End To End GRU Model Model Hyperparameters

| Hyperparameter Name | Hyperparameter Values |
|---------------------|-----------------------|
| Embedding Size      | [100, 200, 400]       |
| GRU Hidden Size     | [100, 200, 400]       |
| LR                  | [10^{-2}, 10^{-3}, 10^{-4}, 10^{-5}] |
| L2                  | [0.1, 0.01, 0.001]    |
| Dropout             | [0, 0.1, 0.2]         |

C  Best Language Model Hyperparameters

Table 7: Best Language Model Hyperparameters

| Hyperparameter Name | Size 400 Model Value | Size 800 Model Value |
|---------------------|----------------------|----------------------|
| Embedding Size      | 400                  | 800                  |
| GRU Hidden Size     | 800                  | 1600                 |
| LR                  | 10^{-3}              | 10^{-3}              |
| L2                  | 0.01                 | 0.1                  |
| Dropout             | 0.1                  | 0.1                  |
| Epochs              | 20                   | 40                   |

D  Best End To End GRU Model Hyperparameters

Table 8: Inpatient Mortality GRU Best Hyperparameters

| Hyperparameter Name | Value |
|---------------------|-------|
| Embedding Size      | 100   |
| GRU Hidden Size     | 400   |
| LR                  | 10^{-2}|
| L2                  | 0.1   |
| Dropout             | 0.1   |
| Epochs              | 21    |
Table 9: Long Admission GRU Best Hyperparameters

| Hyperparameter Name | Value  |
|---------------------|--------|
| Embedding Size      | 400    |
| GRU Hidden Size     | 100    |
| LR                  | $10^{-2}$ |
| L2                  | 0.1    |
| Dropout             | 0.1    |
| Epochs              | 28     |

Table 10: ICU Transfer GRU Best Hyperparameters

| Hyperparameter Name | Value  |
|---------------------|--------|
| Embedding Size      | 400    |
| GRU Hidden Size     | 400    |
| LR                  | $10^{-3}$ |
| L2                  | 0.001  |
| Dropout             | 0      |
| Epochs              | 0      |

Table 11: 30-day Readmission GRU Best Hyperparameters

| Hyperparameter Name | Value  |
|---------------------|--------|
| Embedding Size      | 400    |
| GRU Hidden Size     | 100    |
| LR                  | $10^{-2}$ |
| L2                  | 0.1    |
| Dropout             | 0      |
| Epochs              | 24     |

Table 12: Abnormal HbA1c GRU Best Hyperparameters

| Hyperparameter Name | Value  |
|---------------------|--------|
| Embedding Size      | 400    |
| GRU Hidden Size     | 200    |
| LR                  | $10^{-3}$ |
| L2                  | 0.01   |
| Dropout             | 0.1    |
| Epochs              | 1      |
### E Best Outcome Model/Representation Hyperparameters On All Data

#### Table 13: Inpatient Mortality Best Hyperparameters

| Representation Name | Representation Hyperparameters | Best Model Class | Best Hyperparameters |
|---------------------|--------------------------------|------------------|----------------------|
| Counts              | with_ontology_rollup           | LightGBM         | num_leaves: 100      |
|                     |                                |                  | num_boost_round: 317 |
|                     |                                |                  | learning_rate: 0.02  |
| Word2Vec            | concat_max_mean_min            | Logistic         | C: 0.01              |
| LSI                 | size: 800                      | LightGBM         | num_leaves: 10       |
|                     |                                |                  | num_boost_round: 250 |
|                     |                                |                  | learning_rate: 0.02  |
| CLMBR               | size: 800                      | Logistic         | C: 0.001             |

#### Table 14: Long Admission Best Hyperparameters

| Representation Name | Representation Hyperparameters | Best Model Class | Best Hyperparameters |
|---------------------|--------------------------------|------------------|----------------------|
| Counts              | with_time_bins                 | LightGBM         | num_leaves: 100      |
|                     |                                |                  | num_boost_round: 292 |
|                     |                                |                  | learning_rate: 0.02  |
| Word2Vec            | concat_max_mean_min            | LightGBM         | num_leaves: 100      |
|                     |                                |                  | num_boost_round: 360 |
|                     |                                |                  | learning_rate: 0.02  |
| LSI                 | size: 800                      | LightGBM         | num_leaves: 100      |
|                     |                                |                  | num_boost_round: 494 |
|                     |                                |                  | learning_rate: 0.02  |
| CLMBR               | size: 800                      | LightGBM         | num_leaves: 100      |
|                     |                                |                  | num_boost_round: 397 |
|                     |                                |                  | learning_rate: 0.02  |

#### Table 15: ICU Transfer Best Hyperparameters

| Representation Name | Representation Hyperparameters | Best Model Class | Best Hyperparameters |
|---------------------|--------------------------------|------------------|----------------------|
| Counts              | with_time_bins                 | LightGBM         | num_leaves: 100      |
|                     |                                |                  | num_boost_round: 43  |
|                     |                                |                  | learning_rate: 0.02  |
| Word2Vec            | with_ontology_rollup,concat_max_mean_min | Logistic | C: 1.0 |
| LSI                 | size: 800                      | Logistic         | C: 1000000.0         |
| CLMBR               | size: 800                      | Logistic         | C: 1e-05             |
### Table 16: 30-day Readmission Best Hyperparameters

| Representation Name | Representation Hyperparameters | Best Model Class | Best Hyperparameters       |
|---------------------|--------------------------------|-----------------|----------------------------|
| Counts              | with_time_bins                 | LightGBM        | num_leaves: 100            |
|                     |                                |                 | num_boost_round: 159       |
|                     |                                |                 | learning_rate: 0.02        |
| Word2Vec            | concat_max_mean_min            | LightGBM        | num_leaves: 100            |
|                     |                                |                 | num_boost_round: 215       |
|                     |                                |                 | learning_rate: 0.02        |
| LSI                 | size: 400                      | LightGBM        | num_leaves: 100            |
|                     |                                |                 | num_boost_round: 188       |
|                     |                                |                 | learning_rate: 0.02        |
| CLBMR               | size: 800                      | LightGBM        | num_leaves: 100            |
|                     |                                |                 | num_boost_round: 282       |
|                     |                                |                 | learning_rate: 0.02        |

### Table 17: Abnormal HbA1c Best Hyperparameters

| Representation Name | Representation Hyperparameters | Best Model Class | Best Hyperparameters       |
|---------------------|--------------------------------|-----------------|----------------------------|
| Counts              | with_ontology_rollup           | LightGBM        | num_leaves: 100            |
|                     |                                |                 | num_boost_round: 73        |
|                     |                                |                 | learning_rate: 0.1         |
| Word2Vec            | concat_max_mean_min            | LightGBM        | num_leaves: 25             |
|                     |                                |                 | num_boost_round: 21        |
|                     |                                |                 | learning_rate: 0.1         |
| LSI                 | size: 800                      | LightGBM        | num_leaves: 10             |
|                     |                                |                 | num_boost_round: 63        |
|                     |                                |                 | learning_rate: 0.1         |
| CLBMR               | size: 800                      | Logistic        | C: 0.01                    |