Deep learning facilitates rapid classification of human and veterinary clinical narratives

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ABSTRACT

Objective: Currently, dedicated tagging staff spend considerable effort assigning clinical codes to patient summaries for public health purposes, and machine-learning automated tagging is bottlenecked by availability of electronic medical records. Veterinary medical records, a largely untapped data source that could benefit both human and non-human patients, could fill the gap.

Materials and Methods: In this retrospective study, we trained long short-term memory (LSTM) recurrent neural networks (RNNs) on 52,722 human and 89,591 veterinary records. We established relevant baselines by training Decision Trees (DT) and Random Forests (RF) on the same data. We finally investigated the effect of merging data across clinical settings and probed model portability.

Results: We show that the LSTM-RNNs accurately classify veterinary/human text narratives into top-level categories with an average weighted macro F_1 score of 0.735/0.675 respectively. The evaluation metric for the LSTM was 7 and 8% higher than that of the DT and RF models respectively. We generally did not find evidence of model portability albeit moderate performance increases in select categories.

Discussion: We see a strong positive correlation between number of training samples and classification performance, which is promising for future efforts. The use of LSTM-RNN models represents a scalable structure that could prove useful in cohort selection, which could in turn better address emerging public health concerns.

Conclusion: Digitization of human and veterinary health information will continue to be a reality. Our approach is a step forward for these two domains to learn from, and inform, one another.

1. OBJECTIVE

The Classification Problem

Rapid identification of standardized cohorts through automatic text classification techniques is an emerging field that uses a combination of tools such as human medical coding, rule-based systems queries [1], natural language processing (NLP), statistical analyses, data mining, and machine learning (ML) [2]. These techniques are not used in clinical practice, however. Generally, dedicated tagging staff assign clinical codes, either from the International Classification of Diseases (ICD) [3] or the Systematized Nomenclature of Medicine (SNOMED), after reading patient summaries. This time-consuming, error-prone task leads to only 60–80% of the assigned codes reflecting actual patient diagnoses [4], misjudgment of severity of conditions, and omission of codes altogether. Thus, significant effort is still required to close the gap between care and coding.

The problem also exists in in veterinary medicine. Although the American Animal Hospital Association (AAHA) has constructed SNOMED-CT-Vet, a veterinary extension of SNOMED-CT maintained by the Veterinary Terminology Services Laboratory at the Virginia-Maryland Regional College of Veterinary Medicine [5], neither clinicians nor medical coders in the United States regularly apply diagnosis codes to veterinary visits, possibly due to the lack of a substantial veterinary third-party payer system. There is no veterinary equivalent of the U.S. Health Information Technology for Economic and Clinical Health (HITECH) Act of 2009 (which enforces higher standards of electronic healthcare systems), leaving few incentives for veterinary clinicians or hospitals to annotate their records. Billing codes are thus rarely applicable across veterinary institutions unless hospitals share the same management structure and records system; even then, hospital-specific modifications exist. Less than five academic veterinary centers of a total of 30 veterinary schools in the United States have dedicated medical coding staff to annotate records using SNOMED-CT-Vet [6].

The fact that the vast majority of veterinary clinical data is stored as free-text fields with very low rates of formal data curation exacerbates the problem. Further increasing variance in the data, veterinary patients necessarily come from many different environments, including hospitals [7], practices [8], zoos [9], wildlife reserves [10], army facilities [11], research facilities [12], breeders, dealers, exhibitors [13], livestock farms, and ranches [14]. With the development of new wearable and sensory technology for animals [15], the amount of animal health data will continue to grow exponentially. Since the integration of veterinary data streams with those concerning humans could benefit public health, it is imperative that automatic text classification of veterinary data is achieved soon.

One-health approach

Said integration has the potential to improve both veterinary and human clinical settings. For example, as a result of well-annotated records and downstream work, human clinical decision support tools could be implemented in veterinary hospitals. Better harmonization could also directly address emerging public health concerns through biosurveillance of zoonotic diseases (which comprise 60–70% of all emerging diseases [16]) and early detection of environmental pollution factors. Human and veterinary cohorts identified through automatic text classification could also elucidate disease-specific patterns consistent across species or isolate features of diseases specific to human variants, both of which would favor downstream translational applications.

In a previous study [17], we have shown the feasibility of automatic annotation of veterinary clinical narratives across a broad range of diagnoses with minimal preprocessing, but further exploration is needed to probe what we can learn from human-veterinary comparisons. Automatically adding meaningful disease-related tags to human and veterinary clinical notes using the same machinery would be a huge step forward in that exploration and could facilitate cross-species findings downstream.

2. BACKGROUND AND SIGNIFICANCE

Automatic medical text classification aims to reduce the human burden of handling unstructured narratives. These computational natural language processing (NLP) methods can be divided into two groups: a) semantic processing and subsequent ML; and b) deep learning.

Semantic processing and subsequent ML. These methods range from simple dictionary-based keyword-matching techniques and/or direct database queries to tools capable of interpreting the semantics of human language through lemmatization (removal of inflectional word endings), part-of-speech tagging, parsing, sentence breaking, word segmentation, and entity recognition [18]. Building the underlying dictionaries and manually crafting the rules that capture these diverse lexical elements both require time and domain expertise.

There is a growing interest in medical concept classification for clinical text; as such, many domain-specific semantic NLP tools (with various objectives, frameworks, licensing conditions, source code availabilities, language supports, and learning curves) have been developed for the medical setting. Such tools include MedLEE [19], MPLUS [20], MetaMap [21], KMCI [22], SPIN [23], HITEX [24], MCVS [25], ONYX [26], MedEx [27], cTAKES [28], pyConTextNLP [29], Topaz [30], TextHunter [31], NOBLE [32], and CLAMP [33].

ML downstream of the methods above requires featurization (concept extraction into columns and subsequent feature selection) in order to characterize text narratives in a machine-processable way. This can be done via term frequency-inverse document frequency (tf-idf), other vectorization techniques like Word2Vec, or manually curated rules. Semantic processing and downstream ML models have been shown to achieve high classification accuracy in human [34,35] and veterinary [36] free-text narratives for diseases well represented in training datasets (e.g. diabetes, influenza, and diarrhea). Additional success has been achieved in overall classification of clinical narratives with Decision Trees (DTs), Random Forests (RFs), and Support Vector Machines (SVMs) [37].

Deep learning. Deep learning (DL) methods eliminate the need of feature engineering, harmonization, or rule creation. They learn hierarchical feature representations from raw data in an end-to-end fashion, requiring significantly less domain expertise than traditional machine-learning approaches [38].

DL is quickly emerging in the literature as a viable alternative method to traditional ML for the classification of clinical narratives, even in situations where limited labeled data is available [37]. The technique can help in the recognition of a limited number of categories from biomedical text [39,40]; identify psychiatric conditions of patients based on short clinical histories [41]; and accurately classify whether or not radiology reports indicate pulmonary embolism [42,43] whilst outperforming baseline methods (e.g. RFs or DTs). Previous studies have shown the possibility of using DL to label clinical narratives with medical subspecialties [44] (e.g. cardiology or neurology) or medical conditions [45] (e.g. advanced cancer or chronic pain), outperforming concept-extraction based methods. Furthermore, the use of DL to analyze clinical narratives has also facilitated the prediction of relevant patient attributes, such as in-hospital mortality, 30-day unplanned readmission, prolonged length of stay, and final discharge diagnosis [46].

Significance: Text classification of human and veterinary medical records

Traditional NLP methods boast interpretability and flexibility, but come at the steep cost of data quality control, formatting, normalization, domain knowledge, and time needed to generate meaningful heuristics (which oftentimes are not even generalizable to other datasets). Automatic text classification is thus a logical choice to bypass these steps, classifying medical narratives from the electronic health record (EHR) by leveraging supervised deep learning on big data. We expect that our efforts could facilitate rapid triaging of documents and cohort identification for biosurveillance.

3. METHODS

Study Design

This is a retrospective cross-sectional chart review study that uses medical records collected routinely as part of clinical care from two clinical settings: the veterinary teaching hospital at Colorado State University (CSU) and the Medical Information Mart for Intensive Care (MIMIC-III) from the Beth Israel Deaconess Medical Center in Boston, Massachusetts [47].

Figure 1 shows a diagram of our study design. Both datasets were divided in two smaller datasets - training datasets containing 70% of the original datasets (used to build TensorFlow [48] deep learning models) and validation datasets containing 30% of the original datasets. We calculated the F_1 score of each top-level disease category to measure accuracy. We additionally investigated the effect of using MetaMap [21], a NLP tool that extracts clinically-relevant terms, on the accuracy of our models. We also explored the possibility of out-of-domain generalization, testing the MIMIC-trained model on the CSU validation data and vice versa (and ran separate tests for MetaMapped versions, as well). Finally, we investigated the effect of merging the MIMIC and CSU training datasets to test the efficacy of data augmentation.

Our code to run all models can be found in a public repository (https://github.com/rivas-lab/clinicalNoteTagger).

Clinical Settings

Veterinary Medical Hospital at Colorado State University (CSU). This is a tertiary care referral teaching hospital with inpatient and outpatient facilities, serving all specialties of veterinary medicine. After consultation, veterinarians enter patient information into a custom-built veterinary EHR, including structured fields such as entry and discharge dates, patient signalment (species, breed, age, sex, etc.), and SNOMED-CT-Vet codes. There are also options to input free-text clinical narratives with various sections including history, assessment, diagnosis, prognosis, and medications. These records are subsequently coded; the final diagnostic codes represent single or multiple specific diagnoses or post-coordinated expressions (a combination of two or more concepts).

Medical Information Mart for Intensive Care (MIMIC-III). The Beth Israel Deaconess Medical Center is a tertiary care teaching hospital at Harvard Medical School in Boston, Massachusetts. The MIMIC-III database, a publicly available dataset which we utilize in this study, contains information on patients

admitted to the critical care unit at the hospital [47]. We were interested in the free-text hospital discharge summaries in this database. These records are coded for billing purposes, and have complete diagnoses per patient (the database is publicly available, and thus represents the best possible medical coding annotation scenario for a hospital). Free-text fields in this database contain no protected health information.

Top level disease categories

Mapping between ICD and SNOMED codes is a challenging task, but can promote semantic interoperability. We used ICD top-level groups of diseases as the labels for the records that we aimed to extract. Table 1 shows the mapping between codes in ICD (versions 9 and 10) and SNOMED-CT (including the Veterinary extension).

Table 1. Top-level coding mapping between ICD 9, 10, and SNOMED-CT

Top-level category	Description	ICD 9	ICD 10	SNOMED-CT
1	Infectious and parasitic diseases	001-139	A00-B99	105714009, 68843000, 78885002, 344431000009103, 338591000009108, 40733004, 17322007
2	Neoplasms	140-239	C00-D49	723976005, 399981008
3	Endocrine, nutritional and metabolic diseases, and immunity disorders	240-279	E00-E90	85828009, 414029004, 473010000, 75934005, 363246002, 2492009, 414916001, 363247006, 420134006, 362969004
4	Diseases of blood and blood-forming organs	280-289	D50-D89	271737000, 414022008, 414026006, 362970003, 11888009, 212373009, 262938004, 405538007
5	Mental disorders	290-319	F00-F99	74732009
6	Diseases of the nervous system	320-359	G00-G99	118940003, 313891000009106
7	Diseases of sense organs	360-389	H00-H59, H60-H95	50611000119105, 87118001, 362966006, 128127008, 85972008
8	Diseases of the circulatory system	390-459	I00-I99	49601007
9	Diseases of the respiratory system	460-519	J00-J99	50043002
10	Diseases of the digestive system	520-579	K00-K93	370514003, 422400008, 53619000

11	Diseases of the genitourinary system	580-629 N00-N99	42030000
12	Complications of pregnancy, childbirth, and the puerperium	630-679 O00-O99	362972006, 173300003, 362973001
13	Diseases of the skin and subcutaneous tissue	680-709 L00-L99	404177007, 414032001, 128598002
14	Diseases of the musculoskeletal system and connective tissue	710-739 M00-M99	105969002, 928000
15	Congenital anomalies	740-759 Q00-Q99	111941005, 32895009, 66091009
16	Certain conditions originating in the perinatal period	760-779 P00-P96	414025005
17	Injury and poisoning	800-899 S00-T98	85983004, 75478009, 77434001, 417163006

Mappings were manually curated by two board-certified veterinarians trained in clinical coding.

Patients

The CSU dataset contains medical records from 33,124 patients and 89,591 hospital visits between February 2007 and July 2017. Patients encompassed seven mammalian species, including dogs (*Canis Lupus*, 80.8%), cats (*Felis Silvestris*, 11.4%), horses (*Equus Caballus*, 6.5%), cattle (*Bos Taurus*, 0.7%), pigs (*Sus Scrofa,* 0.3%), goats (*Capra hircus*, 0.2%), sheep (*Ovis Aries*, 0.1%), and other unspecified mammals (0.1%). In contrast, the MIMIC-III database contains medical records from 38,597 distinct human adult patients (aged 16 years or above) and 7,870 neonates admitted between 2001 and 2008, encompassing 52,722 unique hospital admissions to the critical care unit between 2001 and 2012. Table 2 summarizes the category breakdowns of both databases. Only those patients with a diagnosis in their record were considered.

Table 2. Database statistics of patients, records, and species (records with diagnosis).

	CSU	MIMIC
Medical Records	N = 89,591	N = 52,722
Patients	33,124	41,126
Hospital Visits	89,591	49,785

Species

Humans (*Homo Sapiens*)	n.a.	52,722
Dogs (*Canis Lupus*)	72,420	n.a.
Cats (*Felis Silvestris*)	10,205	n.a.
Horses (*Equus Caballus*)	5,819	n.a.
Other mammals	1,147	n.a.

Category

1. Infectious	11,454	10,074
2. Neoplasia	36,108	6,223
3. Endo-Immune	17,295	24,762
4. Blood	10,171	13,481
5. Mental	511	10,989
6. Nervous	7,488	9,168
7. Sense organs	15,085	2,688
8. Circulatory	8,733	30,054
9. Respiratory	11,322	17,667
10. Digestive	22,776	14,646
11. Genitourinary	8,892	14,932
12. Pregnancy	136	133
13. Skin	21,147	4,241
14. Musculoskeletal	22,921	6,739
15. Congenital	3,347	2,334
16. Perinatal	54	3,661
17. Injury	9,873	16,121

The mappings in Table 1 were used to generate the categories and numbers presented here in Table 2.
The seventeen categories represent the text classification labels.

Deep learning

We chose a long short-term memory (LSTM) recurrent neural network (RNN) architecture (which is able to handle variable-length sequences while using previous inputs to inform current time steps) for this multi-label text classification task [49]. The LSTM shares parameters across time steps as it unrolls, which allows it to handle sequences of variable length. In this case, these sequences are a series of word "embeddings" (created by mapping specific words to corresponding numeric vectors) from clinical narratives. Words are represented densely (rather than sparsely, as in Bag-of-Words or tf-idf models) using the Global Vectors for Word Representation (GloVe) [50] word embeddings. These embeddings learn a vector space representation of words such that words with similar contexts appear in a similar vector space, and also capture global statistical features of the training corpus.

LSTMs have proven to be flexible enough to be used in many different tasks, such as machine translation, image captioning, medication prescription, and forecasting disease diagnosis using structured data [49]. The RNN can efficiently capture sequential information and theoretically model long-range dependencies, but empirical evidence has shown this is difficult to do in practice [51]. The sequential nature of text lends itself well to LSTMs, which have memory cells that can maintain information for over multiple time steps and consist of a set of gates that control when information enters and exits memory, making them an ideal candidate architecture.

We first trained the model over a variety of hyperparameters for the model trained on MIMIC data and calculated the model's validation accuracy over all combinations of them, finding the set of [learning rate = 0.001, dropout rate = 0.5, batch size = 256, training epochs = 100, hidden layer size = 200, LSTM layers = 1] to be the optimal setting. We proceeded to use this hyperparameter set for all of the models trained, assuming that this set would be amenable to the task at hand regardless of training dataset. We then proceeded to train a set of six models on the MIMIC, CSU, and MIMIC+CSU data; one each in which MetaMap was used to map terms back to UMLS terms, and one each in which MetaMap was not. We finally determined F_1 scores on the corresponding validation sets for each of these models.

Baseline classifier comparison

A combination of several NLP and ML models have similarly aimed to classify clinical narratives [37, 52]. We selected two of these classifiers: DTs and RFs. DTs are ML models constructed around a branching boolean logic [53]. Each node in the tree can take a decision that leads to other nodes in a tree structure; there are no cycles allowed. The RF classifier is an ensemble of multiple decision trees created by

randomly selecting samples of the training data. The final prediction is done via a consensus voting mechanism of the trees in the forest.

We featurized the narratives using tf-idf, a statistic that reflects word importance in the context of other documents in a corpus and a standard ML modeling strategy for representing text, to convert the narratives into a tabular format [37]. The hyperparameters of both baseline models, like the LSTM, were tuned on the validation set.

MetaMap Feature Extraction

We used MetaMap Lite [54], a NLP tool which leverages the Unified Medical Language System (UMLS) Metathesaurus to identify SNOMED [55] and ICD [56] codes from clinical narratives. MetaMap's algorithm includes five steps: 1) parsing of text into simple noun phrases; 2) variant generation of phrases to include all derivations of words (i.e. synonyms, acronyms, meaningful spelling variants, combinations, etc.); 3) candidate retrieval of all UMLS strings that contains at least one variant from the previous step; 4) evaluation and ranking of each candidate, mapping between matched term and the Metathesaurus concept using metrics of centrality, variation, coverage, and cohesiveness; 5) construction of complete mappings to include those mappings that are involved in disjointed parts of the phrase (e.g. 'ocular' and 'complication' can together be mapped to a single term, 'ocular complication'). MetaMap incorporates the use of ConText [57], an algorithm for the identification of negation in clinical narratives.

Statistical analysis

Evaluation metric. For all models we trained (LSTM, DT, and RF), we used the same evaluation metrics previously reported for MetaMap Lite [54]: a) precision, defined as the proportion of documents which were assigned the correct category; b) recall, defined as the proportion of documents from a given category that were correctly identified; and c) F_1 score, defined as the harmonic average of precision and recall. Formulas for these metrics are provided below:

$$Precision = \frac{True\,Positive}{True\,Positive + False\,Positive} \qquad \text{Eq. 1}$$

$$Recall = \frac{True\,Positive}{True\,Positive + False\,Negative} \qquad \text{Eq. 2}$$

$$F_1 = 2 \cdot \frac{precision \cdot recall}{precision + recall} \qquad \text{Eq. 3}$$

Our task is framed as a multi-label classification problem, where each approach predicts multiple top-level categories for each observation using a single model. In order to combine all class-specific F_1 scores, we averaged the F_1 score for each label, weighting the labels by their supports (the number of true instances for each label, to account for label imbalance).

Domain adaptation. The portability of trained algorithms on independent domains has previously been used as a metric of model robustness in systems that leverage NLP and machine learning [58]. We evaluated the ability of our trained LSTM models to be used in a cross-species context. We utilized the MIMIC-trained model to classify the medical records in the CSU database, and vice versa, assessing performance as before. We also assess the classifier trained on the combined training sets.

4. RESULTS

We investigated the application of deep learning to free-text unstructured clinical narratives on two cohorts: veterinary medical records from CSU, and human medical records in the MIMIC-III database [47]. First, we present an evaluation of MetaMap Lite applied to veterinary records, and then we show the evaluation of the deep learning models built using human and veterinary records, as well as the portability between them.

Evaluation of MetaMap on veterinary records

MetaMap Lite has not previously been applied to veterinary data. As such, we endeavored to verify that the software works as expected when applied in this context. Two board-certified veterinarians trained in clinical coding independently evaluated MetaMap-extracted terms from 19 randomly-selected records. Disagreements were resolved via in-depth discussion and consensus. Evaluation of the NLP was done using a confusion matrix for each record. The ground truth in this evaluation was considered to be the human experts; terms selected by MetaMap but not by reviewers were considered false positives, terms selected by reviewers but not by MetaMap were considered false negatives, and terms selected by both the reviewers and MetaMap were considered true positives. We assumed there were no true negatives. This process resulted in a weighted-average precision of 0.62, recall of 0.82, and F_1 score of 0.71 for the CSU data, as compared to a previously reported weighted-average precision of 0.67, recall of 0.53, and F_1 score of 0.58 for human clinical narratives [54]. The results of this evaluation can be seen in Table 3.

Table 3. NLP (MetaMap) Evaluation.

Record No.	True positive	False positive	False negative	Total	Recall	Precision	F_1-score
1	29	3	11	43	0.73	0.91	0.81

2	86	23	66	175	0.57	0.79	0.66
3	103	11	103	217	0.50	0.90	0.64
4	208	43	81	332	0.72	0.83	0.77
5	96	18	38	152	0.72	0.84	0.77
6	55	19	20	94	0.73	0.74	0.74
7	127	22	124	273	0.51	0.85	0.64
8	50	16	34	100	0.60	0.76	0.67
9	97	25	79	201	0.55	0.80	0.65
10	66	5	26	97	0.72	0.93	0.81
11	84	28	58	170	0.59	0.75	0.66
12	32	8	26	66	0.55	0.80	0.65
13	112	29	93	234	0.55	0.79	0.65
14	156	27	88	271	0.64	0.85	0.73
15	61	6	14	81	0.81	0.91	0.86
16	124	24	53	201	0.70	0.84	0.76
17	114	37	51	202	0.69	0.75	0.72
18	108	24	47	179	0.70	0.82	0.75
19	126	30	100	256	0.56	0.81	0.66
				Weighted averages	**0.62**	**0.82**	**0.71**

Comparison of reviewer and MetaMap term extractions for 19 records. True Positive (TP) = MetaMap correctly matched term to code; False Negative (FN) = MetaMap did not extract a term the experts did; False Positive (FP) = MetaMap matched a term not identified by the expert; Total = Total number of terms matched in that document.

After MetaMap selected terms and assigned concept-unique identifiers (CUI), we only retained the matched term. The order in which terms appear in the original text was also preserved. Finally, we constructed MetaMap-matched clinical narratives, where those terms assigned "False" by the ConText algorithm are added a "no_" prefix. All terms were converted to lowercase, special characters (not alphanumeric) were removed, and extraneous spaces were simplified to single underscores. When multiple matched CUIs existed, duplicates of the word were kept in the new clinical narrative. This

process was conducted independently for each document before passed as input into the deep learning model. Table 4 shows an example of one free-text clinical narrative processed with MetaMap.

Table 4. Example of free-text and MetaMap-extracted veterinary record

Free-text clinical narrative	MetaMap-matched clinical terms
[PET_NAME], a 2 year old female spayed Bernese Mountain Dog, presented for evaluation of allergic dermatitis and otitis.	year old female bernese_mountain_dog evaluation allergic_dermatitis otitis.
[PET_NAME] had a history of recurrent UTI's as a puppy, but these problems have resolved.	history recurrent_utis puppy problems.
[PET_NAME] has a 1 year history of recurrent otitis externa and pruritus directed primarily at her feet and ears.	year history recurrent_otitis otitis_externa pruritus feet ears.
The pruritus and otitis problems appear to be more severe during the winter.	pruritus otitis problems more severe winter.
She also has a two month history of recurrent conjunctivitis that first developed after another dog in the house returned from a kennel.	month history recurrent conjunctivitis first dog house.
Her otitis, pruritus, and conjunctivitis have all respond well to therapy (prednisone, mometamax (for the ears), and neo/poly/dex solution (for the eyes), but signs usually recur within a couple of weeks of discontinuing the medication.	otitis pruritus conjunctivitis well therapy prednisone mometamax ears neo poly dex solution eyes signs usually recur couple weeks medication.
Most recently [PET_NAME] was treated with a course of prednisone that significantly helped her allergy signs.	most course prednisone allergy signs.

However, she had <u>significant</u> <u>side effects</u> from the <u>steroid</u> (including <u>aggressive behavior</u>).	significant side_effects steroid aggressive_behavior
[PET_NAME] was placed on a strict <u>diet</u> <u>trial</u> (Anallergen) about 6 <u>weeks</u> ago.	diet trial weeks.
[OWNER_NAME] does feel that [PET_NAME] may have improved since being on this <u>diet</u> (but is <u>unsure</u>, primarily because other therapies have also been enacted during this <u>time</u>).	diet unsure time.
[PET_NAME] has <u>now</u> been off <u>prednisone therapy</u> for just over a <u>week</u>.	now prednisone therapy week.

A 2-year old female dog patient with recurrent otitis and allergic dermatitis. Both the narrative (left) and the MetaMapped version (right) show that the treatment included prednisone (among other important clinical details). For the purposes of this manuscript, the pet and owner's name were manually de-identified.

Evaluation of Deep Learning models

We trained deep-learning models (as well as DT/RF baselines) for the human, veterinary, and merged (human and veterinary) datasets and tested each on their own domain, as well as the other domains. We built our LSTM model using the Python programming language (version 2.7), TensorFlow [48] (version 1.9), and the 'scikit-learn' library (version 0.19.2) [59]. The training was performed on an Amazon® Deep Learning AMI, a cloud-based platform running the Ubuntu operating system with pre-installed CUDA dependencies. Weighted macro F_1 scores for all models are shown in Table 5, and a full list of F_1 scores by category can be found in Supplementary Material 1.

Table 5. Weighted Macro F_1 scores using various training and validation dataset combinations.

Configuration			Model evaluation (Weighted F_1 score)		
Training	Validation	MetaMap	DT	RF	LSTM
MIMIC	MIMIC	No	0.60	0.64	**<u>0.65</u>**
		Yes	0.60	0.63	**<u>0.70</u>**

			DT	RF	LSTM-RNN
CSU	CSU	No	0.55	0.61	**<u>0.72</u>**
		Yes	0.54	0.60	**<u>0.75</u>**
MIMIC	CSU	No	0.22	0.24	**<u>0.28</u>**
		Yes	0.23	0.20	**<u>0.31</u>**
CSU	MIMIC	No	**<u>0.31</u>**	0.20	0.23
		Yes	0.28	0.19	**<u>0.36</u>**
MIMIC+CSU	CSU	No	0.57	0.62	**<u>0.67</u>**
		Yes	0.57	0.62	**<u>0.76</u>**
MIMIC+CSU	MIMIC	No	0.60	**<u>0.63</u>**	0.58
		Yes	0.60	**<u>0.63</u>**	0.60
MIMIC+CSU	MIMIC+CSU	No	0.59	0.64	**<u>0.68</u>**
		Yes	0.59	0.63	**<u>0.71</u>**
Average			0.489	0.506	**<u>0.571</u>**

Evaluation metrics for Decision Tree (DT), Random Forest (RF), and Long Short Term Memory Recurrent Neural Network (LSTM-RNN) on validation datasets with and without MetaMap term extraction. Bolded and underlined numbers represent the best scores for the specific configuration of training data, validation data, and MetaMap toggle.

5. DISCUSSION

Applying deep learning to unstructured free-text clinical narratives in electronic health records offers a relatively simple, low-effort means to bypass the traditional bottlenecks in electronic phenotyping. Besides creating a gold-standard veterinary corpus, none of our efforts involved any manual curation, feature generation, or data harmonization, all of which are time-consuming tasks. Circumventing the need for data harmonization was very important for the datasets, which contained a plethora of domain- and setting-specific misspellings, abbreviations, and jargon (these issues would have greatly impacted the performance of the LSTM and the NLP's entity recognition). MetaMap was useful in this regard, given its ability to parse clinical data.

The databases that we selected, MIMIC and CSU, represent vastly different clinical settings. The clinical narratives that arise in a critical care unit do not necessarily compare to those from a tertiary referral veterinary care facility. Moreover, the records were not coded in the same way, the clinicians did not receive the same training, and the documents apply to different species altogether. Despite these

differences, however, our LSTM model was general enough to be able to accurately classify medical narratives at the top level of depth independently in both datasets.

As indicated by Figure 2, models performed usually better on their respective validation datasets in those categories with more training samples. For example, the CSU-trained model (25,276 samples) had significantly better performance in the "neoplasia" category than the MIMIC-trained model (4,356 samples), while the MIMIC-trained model (21,038 samples) had better performance in the "Diseases of the circulatory system" category than the CSU-trained model (6,133 samples).

Figure 2 also makes apparent that CSU-trained models usually did better on CSU validation data and vice versa, with the combined "MIMIC+CSU"-trained model striking an average trendline between the two. Domain adaptation happened rarely and moderately only in those categories with enough training cases and similar descriptive narratives across species (e.g. in the "Diseases of the skin and subcutaneous tissue" category, the "MIMIC+CSU" model boosted performance relative to just the MIMIC model while validating on MIMIC). Further research, and more training examples, would be needed to provide a general model that is effective across domains.

The usefulness of even top-level characterizations in the veterinary setting cannot be understated; usually, a veterinarian must read the full, unstructured text in order to get any information about the patient they are treating. Rapid triaging from top-level categories could lead to more granular characterizations given sufficient data. The repeated use of a series of LSTM models for subsequent, increasingly-specific classifications thus represents a scalable, hierarchical tagging structure that could prove extremely useful in stratifying patients by specific departments, severities, and protocols.

Our study has several limitations, including sample size, number of databases investigated, and the focus on top-level (rather than more granular) categories. In the future, the increased availability of data from both the human and veterinary domains will facilitate more research in this field.

6. CONCLUSION

In this era of rapid digital health and deployment of health records, it is important to provide tools that facilitate cohort identification. Our deep learning approach (LSTM model) was able to automatically classify medical narratives without the use of any domain knowledge or manual feature curation. With enough training data, it is possible to foresee a scenario in which these models can accurately tag every clinical concept, regardless of data input. The expansion of veterinary data availability and the

subsequently enormous potential of domain adaptation could prove to be exciting chapters in reducing bottlenecks in public health research at large.

It is of critical importance to continue studying novel sources of information that can rapidly be used to generate classification models. A reliable alternative to existing rule-based and natural language processing strategies, deep learning is a promising tool for accelerating public health research.

DECLARATIONS

Data availability

Veterinary data presented here belongs to the Colorado State University, which may grant access to this data on a case-by-case basis to researchers who obtain the necessary Data Use Agreement (DUA) and IRB approvals.

Human data presented here belongs to the Beth Israel Deaconess Medical Center in Boston, Massachusetts, which can be accessed after signing a data usage agreement in the MIT Lab for Computational Physiology at https://mimic.physionet.org/

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Contributions

ALP, OBDW, GRV, and AMZ designed the study. RLP provided access to the veterinary data. OJBDW, GRV, ALP, AMZ, and SA extracted, formatted, and performed analysis of the data. AMZ, RLP, CDB and MAR provided interpretation of the results. ALP drafted the manuscript, and all authors contributed critically, read, revised and approved the final version.

Competing interests

CDB is Principal and Chairman of CDB Consulting LTD. He has advised Imprimed, Embark Vet and Etalon DX as a member of their respective Scientific Advisory Boards, and is a Director of Etalon DX. The remaining authors declare no conflicts of interest.

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Ethics approval

This research was reviewed and approved by Stanford's Institutional Review Board (IRB), which provided a non-human subject determination under eProtocol 46979. Consent was not required.

Bibliography

Gundlapalli AV, Redd D, Gibson BS, *et al.* Maximizing clinical cohort size using free text queries. *Comput Biol Med* 2015;**60**:1–7. doi:10.1016/j.compbiomed.2015.01.008

Shivade C, Raghavan P, Fosler-Lussier E, *et al.* A review of approaches to identifying patient phenotype cohorts using electronic health records. *J Am Med Inform Assoc* 2014;**21**:221–30. doi:10.1136/amiajnl-2013-001935

Moriyama IM, Loy RM, Robb-Smith AHT, *et al.* History of the statistical classification of diseases and causes of death. 2011.

Benesch C, Witter DM, Wilder AL, *et al.* Inaccuracy of the International Classification of Diseases (ICD-9-CM) in identifying the diagnosis of ischemic cerebrovascular disease. *Neurology* 1997;**49**:660–4. doi:10.1212/WNL.49.3.660

Virginia-Maryland Regional College of Veterinary Medicine. Veterinary Terminology Services Laboratory. httpsvtsl.vetmed.vt.edu. 2019.

Association of American Veterinary Medical Colleges. Association of American Veterinary Medical Colleges. 2019.

Cummings KJ, Rodriguez-Rivera LD, Mitchell KJ, *et al.* Salmonella enterica serovar Oranienburg outbreak in a veterinary medical teaching hospital with evidence of nosocomial and on-farm transmission. *Vector Borne Zoonotic Dis* 2014;**14**:496–502. doi:10.1089/vbz.2013.1467

Krone LM, Brown CM, Lindenmayer JM. Survey of electronic veterinary medical record adoption and use by independent small animal veterinary medical practices in Massachusetts. *J Am Vet Med Assoc* 2014;**245**:324–32. doi:10.2460/javma.245.3.324

Witte CL, Lamberski N, Rideout BA, *et al.* Development of a case definition for clinical feline herpesvirus infection in cheetahs (Acinonyx jubatus) housed in zoos. *J Zoo Wildl Med* 2013;**44**:634–44. doi:10.1638/2012-0183R.1

Griffith JE, Higgins DP. Diagnosis, treatment and outcomes for koala chlamydiosis at a rehabilitation facility (1995-2005). *Aust Vet J* 2012;**90**:457–63. doi:10.1111/j.1751-0813.2012.00963.x

Poppe JL. The US Army Veterinary Service 2020: knowledge and integrity. *US Army Med Dep J* 2013;:5–11.

Field K, Bailey M, Foresman LL, *et al.* Medical records for animals used in research, teaching, and testing: public statement from the American College of Laboratory Animal Medicine. *ILAR J* 2007;**48**:37–41.

Shalev M. USDA to require research facilities, dealers, and exhibitors to keep veterinary medical records. Lab Anim (NY). 2003;**32**:16. doi:10.1038/laban0603-16a

Robinson TP, Wint GRW, Conchedda G, *et al.* Mapping the global distribution of livestock. *PLoS One* 2014;**9**:e96084. doi:10.1371/journal.pone.0096084

Smith K, Martinez A, Craddolph R, *et al.* An integrated cattle health monitoring system. *Conf Proc IEEE Eng Med Biol Soc* 2006;**1**:4659–62. doi:10.1109/IEMBS.2006.259693

Gates MC, Holmstrom LK, Biggers KE, *et al.* Integrating novel data streams to support biosurveillance in commercial livestock production systems in developed countries: challenges and opportunities. *Front Public Health* 2015;**3**:74. doi:10.3389/fpubh.2015.00074

Nie A, Zehnder A, Page RL, *et al.* DeepTag: inferring diagnoses from veterinary clinical notes. *npj Digital Medicine 2018 1:1* 2018;:1–8. doi:10.1038/s41746-018-0067-8

Nadkarni PM, Ohno-Machado L, Chapman WW. Natural language processing: an introduction. *Journal of the American Medical Informatics Association* 2011;**18**:544–51. doi:10.1136/amiajnl-2011-000464

Friedman C, Alderson PO, Austin JH, *et al.* A general natural-language text processor for clinical radiology. *J Am Med Inform Assoc* 1994;**1**:161–74.

Christensen LM, Haug PJ, Fiszman M. MPLUS: A Probabilistic Medical Language Understanding System. Morristown, NJ, USA: : Association for Computational Linguistics 2002. 29–36. doi:10.3115/1118149.1118154

Aronson AR. Effective mapping of biomedical text to the UMLS Metathesaurus: the MetaMap program. *Proc AMIA Symp* 2001;:17–21.

Denny JC, Irani PR, Wehbe FH, *et al.* The KnowledgeMap project: development of a concept-based medical school curriculum database. *AMIA Annu Symp Proc* 2003;:195–9.

Liu K, Mitchell KJ, Chapman WW, *et al.* Automating tissue bank annotation from pathology reports - comparison to a gold standard expert annotation set. *AMIA Annu Symp Proc* 2005;:460–4.

Zeng QT, Goryachev S, Weiss S, *et al.* Extracting principal diagnosis, co-morbidity and smoking status for asthma research: evaluation of a natural language processing system. *BMC Med Inform Decis Mak* 2006;**6**:30. doi:10.1186/1472-6947-6-30

Elkin PL, Brown SH, Husser CS, *et al.* Evaluation of the content coverage of SNOMED CT: ability of SNOMED clinical terms to represent clinical problem lists. *Mayo Clin Proc* 2006;**81**:741–8. doi:10.4065/81.6.741

Christensen LM, Harkema H, Haug PJ, *et al. ONYX: a system for the semantic analysis of clinical text*. Association for Computational Linguistics 2009.

Xu H, Stenner SP, Doan S, *et al.* MedEx: a medication information extraction system for clinical narratives. *J Am Med Inform Assoc* 2010;**17**:19–24. doi:10.1197/jamia.M3378

Savova GK, Masanz JJ, Ogren PV, *et al.* Mayo clinical Text Analysis and Knowledge Extraction System (cTAKES): architecture, component evaluation and applications. *J Am Med Inform Assoc* 2010;**17**:507–13. doi:10.1136/jamia.2009.001560

Chapman BE, Lee S, Kang HP, *et al.* Document-level classification of CT pulmonary angiography reports based on an extension of the ConText algorithm. *J Biomed Inform* 2011;**44**:728–37. doi:10.1016/j.jbi.2011.03.011

Wagner M, Tsui F, Cooper G, *et al.* Probabilistic, Decision-theoretic Disease Surveillance and Control. *Online J Public Health Inform* 2011;**3**. doi:10.5210/ojphi.v3i3.3798

Jackson RG, Ball M, Patel R, *et al.* TextHunter–A User Friendly Tool for Extracting Generic Concepts from Free Text in Clinical Research. 2014.

Tseytlin E, Mitchell K, Legowski E, *et al.* NOBLE - Flexible concept recognition for large-scale biomedical natural language processing. *BMC Bioinformatics* 2016;**17**:32. doi:10.1186/s12859-015-0871-y

Lee HJ, Zhang Y, Xu J, *et al.* UTHealth at SemEval-2016 Task 12: an End-to-End System for Temporal Information Extraction from Clinical Notes. 2016.

Koopman B, Karimi S, Nguyen A, *et al.* Automatic classification of diseases from free-text death certificates for real-time surveillance. *BMC Med Inform Decis Mak* 2015;**15**:53. doi:10.1186/s12911-015-0174-2

Berndorfer S, Henriksson A. Automated Diagnosis Coding with Combined Text Representations. *Stud Health Technol Inform* 2017;**235**:201–5.

Anholt RM, Berezowski J, Jamal I, *et al.* Mining free-text medical records for companion animal enteric syndrome surveillance. *Preventive Veterinary Medicine* 2014;**113**:417–22. doi:10.1016/j.prevetmed.2014.01.017

Wang Y, Sohn S, Liu S, *et al.* A clinical text classification paradigm using weak supervision and deep representation. *BMC Med Inform Decis Mak* 2019;**19**:1. doi:10.1186/s12911-018-0723-6

Goodfellow I, Bengio Y, Courville A, *et al. Deep learning*. 2016.

Agibetov A, Blagec K, Xu H, *et al.* Fast and scalable neural embedding models for biomedical sentence classification. *BMC Bioinformatics* 2018;**19**:541. doi:10.1186/s12859-018-2496-4

Du Y, Pan Y, Wang C, *et al.* Biomedical semantic indexing by deep neural network with multi-task learning. *BMC Bioinformatics* 2018;**19**:502. doi:10.1186/s12859-018-2534-2

Tran T, Kavuluru R. Predicting mental conditions based on "history of present illness" in psychiatric notes with deep neural networks. *J Biomed Inform* 2017;**75S**:S138–48. doi:10.1016/j.jbi.2017.06.010

Chen MC, Ball RL, Yang L, *et al.* Deep Learning to Classify Radiology Free-Text Reports. *Radiology* 2018;**286**:845–52. doi:10.1148/radiol.2017171115

Banerjee I, Ling Y, Chen MC, *et al.* Comparative effectiveness of convolutional neural network (CNN) and recurrent neural network (RNN) architectures for radiology text report classification. *Artif Intell Med* Published Online First: 23 November 2018. doi:10.1016/j.artmed.2018.11.004

Weng W-H, Wagholikar KB, McCray AT, *et al.* Medical subdomain classification of clinical notes using a machine learning-based natural language processing approach. *BMC Med Inform Decis Mak* 2017;**17**:155. doi:10.1186/s12911-017-0556-8

Gehrmann S, Dernoncourt F, Li Y, *et al.* Comparing deep learning and concept extraction based methods for patient phenotyping from clinical narratives. *PLoS One* 2018;**13**:e0192360. doi:10.1371/journal.pone.0192360

Rajkomar A, Oren E, Chen K, *et al.* Scalable and accurate deep learning with electronic health records. *npj Digital Medicine 2018 1:1* 2018;**1**:18. doi:10.1038/s41746-018-0029-1

Johnson AEW, Pollard TJ, Shen L, *et al.* MIMIC-III, a freely accessible critical care database. *Sci Data* 2016;**3**:160035. doi:10.1038/sdata.2016.35

Abadi M, Agarwal A, Barham P, *et al.* TensorFlow: Large-Scale Machine Learning on Heterogeneous Distributed Systems. arXiv. 2016;**cs.DC**.

Pham T, Tran T, Phung D, *et al.* DeepCare: A Deep Dynamic Memory Model for Predictive Medicine. In: *Advances in Knowledge Discovery and Data Mining*. Springer, Cham 2016. 30–41. doi:10.1007/978-3-319-31750-2_3

Pennington J, Socher R, Manning CD. Glove: Global vectors for word representation. Doha, Qatar: 2014. 1532–43.

Pascanu R, Mikolov T, Bengio Y. On the difficulty of training Recurrent Neural Networks. arXiv. 2012;**cs.LG**.

Segura-Bedmar I, Colón-Ruíz C, Tejedor-Alonso MÁ, *et al.* Predicting of anaphylaxis in big data EMR by exploring machine learning approaches. *J Biomed Inform* 2018;**87**:50–9. doi:10.1016/j.jbi.2018.09.012

Yu Z, Bernstam E, Cohen T, *et al.* Improving the utility of MeSH® terms using the TopicalMeSH representation. *J Biomed Inform* 2016;**61**:77–86. doi:10.1016/j.jbi.2016.03.013

Demner-Fushman D, Rogers WJ, Aronson AR. MetaMap Lite: an evaluation of a new Java implementation of MetaMap. *J Am Med Inform Assoc* 2017;**24**:841–4. doi:10.1093/jamia/ocw177

Barros JM, Duggan J, Rebholz-Schuhmann D. Disease mentions in airport and hospital geolocations expose dominance of news events for disease concerns. *J Biomed Semantics* 2018;**9**:18. doi:10.1186/s13326-018-0186-9

Hanauer DA, Saeed M, Zheng K, *et al.* Applying MetaMap to Medline for identifying novel associations in a large clinical dataset: a feasibility analysis. *J Am Med Inform Assoc* 2014;**21**:925–37. doi:10.1136/amiajnl-2014-002767

Harkema H, Dowling JN, Thornblade T, *et al.* ConText: an algorithm for determining negation, experiencer, and temporal status from clinical reports. *J Biomed Inform* 2009;**42**:839–51. doi:10.1016/j.jbi.2009.05.002

Ye Y, Wagner MM, Cooper GF, *et al.* A study of the transferability of influenza case detection systems between two large healthcare systems. *PLoS One* 2017;**12**:e0174970. doi:10.1371/journal.pone.0174970

Pedregosa F, Varoquaux G, Gramfort A, *et al.* Scikit-learn: Machine Learning in Python. *Journal of Machine Learning Research* 2011;**12**:2825–30.

Figure legends

Figure 1. Diagram of the training and evaluation design. Relevant acronyms: MIMIC: Medical Information Mart for Intensive Care; CSU: Colorado State University; MetaMap, a tool for recognizing medical concepts in text; LSTM: long-short term memory recurrent neural network classifier; RF: Random Forest classifier; DT: Decision Tree classifier

Figure 2. F_1 scores by category using various training configurations. Training with CSU data (green), MIMIC data (yellow) or MIMIC+CSU (purple); validating on CSU data (Panel A) or MIMIC data (Panel B). The color of the category text is darkened (black) and the box made bigger if it surpasses the threshold of at least 0.70 F_1 score (dotted horizontal line).

A CSU validation

B MIMIC validation

Training: CSU · MIMIC · MIMIC+CSU