# A FrameNet for Cancer Information in Clinical Narratives: Schema and Annotation

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#### Abstract

This paper presents a pilot project named Cancer FrameNet. The project's goal is a general-purpose natural language processing (NLP) resource for cancer-related information in clinical notes (i.e., patient records in an electronic health record system). While previous cancer NLP annotation projects have largely been ad hoc resources to address a specific and immediate information need, the frame semantic method employed here emphasizes the information presented in the notes themselves and its linguistic structure. To this end, three semantic frames (targeting the high-level tasks of cancer diagnoses, cancer therapeutic procedures, and tumor descriptions) are created and annotated on a clinical text corpus. Prior to annotation, candidate sentences are extracted from a clinical data warehouse and de-identified to remove any private information. The frames are then annotated with the three frames totaling over thirty frame elements. This paper describes these steps in the pilot project and discusses issues encountered to evaluate the feasibility of general-purpose linguistic resources for extracting cancer-related information.

Keywords: clinical information extraction, cancer, frame semantics

# 1 Introduction

Important medical information about cancer patients is often only available in free text (natural language) notes in electronic health records (EHRs). This information is frequently needed for research, quality improvement, surveillance, and other important functions. However, the manual abstraction of this information can be incredibly timeconsuming and expensive, often making it infeasible for both early-stage research and clinical quality improvement projects. Thus, natural language processing (NLP) approaches can offer a tremendous service in oncology.

Existing NLP systems for cancer-related information generally fall under a type of biomedical NLP task known as *phenotyping*, which is the task of identifying patients that meet a certain set of criteria. Phenotyping specifications are often highly task-specific, which frequently yields one-off NLP datasets and algorithms that do not generalize to similar phenotyping tasks. For example, one phenotype method may identify lung cancer patients with a tumor of at least 2cm in diameter, while another method may identify lung cancer patients with at least two tumors that are 1cm in diameter. Such methods are quite similar, yet often produce incompatible annotations and algorithms.

The key insight is that phenotyping methods often conflate extraction (identifying relevant portions of text) and reasoning (determining if the extracted text fulfills the task's needs). By separating these steps and focusing on generalpurpose extraction, it will be possible to easily and rapidly develop phenotyping methods. This is because the bulk of the effort is typically spent in the extraction step (annotating data and developing NLP algorithms), while the reasoning step is often a straightforward set of rules. Continuing the example above, an NLP system capable of extracting all tumor references and their sizes from text would easily meet the needs of both phenotyping methods (along with potentially many others).

The challenge then becomes how to develop generalpurpose extraction algorithms for clinical text, especially when it isn't necessarily clear a priori what information needs to be extracted. Luckily, *frame semantics* provides a useful framework for developing such a resource. In frame semantics, a word or phrase evokes a frame of semantic knowledge that describes the characteristic attributes associated with a concept. For example, for *tumor*, the frame would likely contain elements that describe the size, location, and morphology of the tumor. The set of frame elements can either be defined a priori by a subject expert or added iteratively based on the data (this work combines both approaches).

The specification of a set of frames combined with annotated examples is referred to as a FrameNet, the best known being Berkeley FrameNet (Baker et al., 1998). But other FrameNets exist as well, notably domain-specific FrameNets. This paper describes a pilot project to build such a domain-specific resource—referred to hereafter as Cancer FrameNet—that focuses on cancer-related information. The goal of the pilot is to test the feasibility of a much larger resource covering the depth and breadth of cancer information in patient records. Even as a pilot, however, this resource is still sizable, covering three important frames, 22 lexical units, and nearly 8 thousand annotated sentences.

There are several potential pitfalls for frame annotation in clinical notes, thus the need for a feasibility pilot. These issues include the consistency of cancer-related information in clinical notes: is cancer too complex with too many variables to be reliably annotated (both manually and by an automatic NLP system)? Another issue is the overlapping information of frames: are there really semantically distinct concepts that can be formed into different frames? Finally, frame annotation is typically limited to sentence and clause context (excluding implicit information), but does this apply to cancer-related information in clinical notes?

It should be noted that there is a second major challenge in the generalizability of clinical NLP systems. This involves the portability of algorithms from one institution's clinical notes to another, as oftentimes these can be drastically different. While we acknowledge the critical importance of this problem, we make no attempt to solve it here. All data described in this paper come from a single institution. It is our hope, however, that upon establishing a generalpurpose resource, annotated frames from additional institutions can be added in order to improve inter-institutional generalizability.

The rest of this paper is structured as follows: Section 2 outlines previous work in both domain-specific FrameNets and cancer-related information extraction. Section 3 describes the pre-annotation process: where the data came from, how it is extracted and prepared for annotation, including how it is de-identified to protect patient privacy. Section 4 lays out the frames covered in the pilot project: what they are, why they were chosen, and the current frame elements. Section 5 details the annotation process. Finally, Section 6 discusses the potential ramifications of Cancer FrameNet on cancer information extraction, including its strengths and weaknesses, and how it might or might not overcome some of the aforementioned pitfalls.

# 2 Background

The theory of frame semantics has spawned many practical natural language resources. Most prominent is the Berkeley FrameNet project (Baker et al., 1998; Baker et al., 2015). which is intended to be an open-domain encoding of common knowledge (commercial transactions, transportation, crime, international affairs, etc.). The FrameNet construction methodology has been ported to many other languages (Heppin and Gronostaj, 2014; Lin et al., 2015; Rezhake and Kuerban, 2015; Ohara, 2016). More interesting, many domain-specific FrameNets exist, ranging from soccer (Schmidt, 2006; Torrent et al., 2014) to sentiment (Ruppenhofer, 2013) to disability (Savova et al., 2005) to cellular pathways (Dolbey et al., 2006; Dolbey, 2009). No such resource targets the types of cancer-related information found in EHR notes.

While not explicitly based on a FrameNet-style approach, a significant amount of work has focused on NLP systems for extracting cancer-related information from EHRs. A sampling of the types of information extracted include: a frame-like representation of radiological findings (Taira et al., 2001); procedures, tumor stages, and various biomarker scores (Xu et al., 2004); tumor and node staging (Mc-Cowan et al., 2007); Gleason score, tumor stages, and margin status (D'Avolio et al., 2008); histology, site, dimension, and various tumor types (Coden et al., 2009); tumor progression (Cheng et al., 2010); colonoscopy status (Denny et al., 2010); colonoscopy quality measures (Harkema et al., 2010); Gleason score, Clark level, and Breslow depth (Napolitano et al., 2010); cancer history (Wilson et al., 2010); counts of examined and positive tumors and nodes (Martinez and Li, 2011); pancreatic cancer predictors (Zhao and Weng, 2011); tumor staging and biomarkers (Segagni et al., 2012); pain in prostate cancer patients (Heintzelman et al., 2013); highest level of pathology, number of removed adenomas (Imler et al., 2013); tumor, node, metastases, and ACPS stages (Martinez et al., 2013); liver cancer status (Ping et al., 2013); change of event state (Vanderwende et al., 2013); twenty-two staging indicators (Ashish et al., 2014); volume, size, and location (Wang et al., 2014); and diagnosis, hormone receptor status, tumor size, and number of positive nodes (Napolitano et al., 2016). This synopsis understates the number of extracted information types, but it is still clear that there is a significant breadth of information as well as consistent areas of overlap.

A more direct comparison to our work is the recent work in the DeepPhe project (Savova et al., 2017). DeepPhe takes a document-level approach to extracting cancer information, which is more appropriate for certain data types than the sentence-based approach proposed below. Most crucially, it is unknown how well their document-level approach generalizes to other institution's data. On the other hand, while the pilot project discussed in this paper focuses on a single institution as well, we hypothesize that a framebased method targeting information at the sentence level will result in greater potential for generalization across institutions.

# **3** Preparing Clinical Narratives

Several steps are necessary to prepare clinical narratives for frame annotation: clinical notes must be retrieved from the clinical data warehouse, lexical units (see Section 4) and their proper context must be extracted, then private patient information must be de-identified. All of this must be done within a secure HIPAA-compliant environment.

The clinical notes are derived from the UT Physicians clinics, a chain of outpatient clinics in the Houston area. The snapshot available from the data warehouse contains more than 260,000 notes with more than 175 million tokens. While by no means a large corpus by EHR standards, it contains sufficient data for a pilot evaluation. This project was deemed exempt by the Committee for the Protection of Human Subjects, the UTHealth Institutional Review Board, under protocol number HSC-SBMI-13-0549.

For each lexical unit (see Section 4), every sentence containing the lexical unit is extracted from the note corpus. Sentence segmentation is by no means a simple task in clinical data (Miller et al., 2015; Zweigenbaum et al., 2016). Stanford CoreNLP (Manning et al., 2014) was used to identify initial sentences, but due to the lack of punctuation in clinical notes, these often constituted multiple (sometimes dozens) of sentences (newlines are often used as end-ofsentence markers, but frequently newlines do not end sentences). As a result, several high-precision rules were used to prune down sentence length. Ultimately, a human annotator was required to remove words not part of the lexical unit's proper sentence boundary. This was done in conjunction with the de-identification stage below.

Clinical notes contain significant amounts of copy-pasting and templated sentences, so a random sample of sentences might contain substantial numbers of duplicates and nearduplicates. To maximize the diversity of the annotations, the sentences were sorted by TF-IDF cosine distance.

The final preparation step is to de-identify the notes, removing any protected health information (PHI) and replacing it with a placeholder. In the United States, the Health Insurance Portability and Accountability Act (HIPAA) mandates the de-identification of 18 categories of information:

- (1) names
- (2) geographic localities smaller than a state
- (3) dates and ages over 89
- (4) telephone numbers
- (5) fax numbers
- (6) e-mail addresses
- (7) Social Security numbers
- (8) medical record numbers
- (9) health plan numbers
- (10) account numbers
- (11) certificate/license numbers
- (12) vehicle & license numbers
- (13) device identifiers
- (14) web URLs
- (15) IP addresses
- (16) biometric identifiers
- (17) full face photographic images
- (18) any other identifying number/characteristic/code

We expanded on this to cover all ages and geographic localities, as well as other types of identifying information as described in Stubbs and Uzuner (2015). Furthermore, one of our lexical units is frequently a surname in the data: these sentences are completely discarded. Both human annotation and an in-house automatic system (Lee et al., 2017) were used. To reduce bias, the human de-identification occurred first, then the automatic system provided additional suggestions that the human may have missed. The automatic de-identifications were all manually verified to reduce the proliferation of false positives common with deidentification systems. Finally, at future stages of the annotation, as detailed below, annotators always have the option of identifying further PHI missed by this process.

## 4 Initial Frame Schemas

Based on the existing literature, three common phenotyping tasks were selected: (1) identification of patients with a particular cancer diagnosis, (2) identification of patients with a particular cancer treatment, and (3) identification of patients with particular tumor characteristics. To reduce the complexity of the second task, and to focus on data more likely to be found in outpatient notes, treatments are limited to surgical procedures (i.e., excluding medications, chemotherapy, etc.). These three tasks yield three frames (i) CANCER\_DIAGNOSIS, (ii) CANCER\_THERAPEUTIC\_PROCEDURE, and (iii) TUMOR\_DESCRIPTION. We also define an abstract root frame, CANCER\_MASTER\_FRAME, from which all three inherit elements. This enables frame elements (attributes) that are universal, such as negation and certainty. For each of these frames, an expert in cancer informatics (EVB) helped devise a list of lexical units:

<u>CANCER\_DIAGNOSIS</u>: adenocarcinoma, cancer, carcinoma, leukemia, lymphoma, malignancy, malignant, melanoma, myeloma, sarcoma

<u>CANCER\_THERAPEUTIC\_PROCEDURE</u>: colectomy, hysterectomy, lymphadenectomy, mastectomy, palliative, pancreatectomy, prostatectomy, radiation, whipple

#### TUMOR\_DESCRIPTION: lesion, mass, tumor

For each of these lexical units, the process described in Section 3 was followed until up to 500 de-identified sentences were available for each lexical unit. Five of the lexical units (*lymphadenectomy, myeloma, pancreatectomy, sarcoma*, and *whipple*) had fewer than 500 sentences in the corpus.

The elements (attributes) of each frame were determined by an iterative process. First, an initial set of elements was proposed by the cancer expert. During the course of the annotation, new elements were frequently proposed by the annotators. Elements with sufficient frequency and importance-as determined by the cancer expert-were added to the frame schema. For example, FAMILY-HISTORY (for the CANCER\_DIAGNOSIS frame), EXTENT (for CANCER\_THERAPEUTIC\_PROCEDURE), and RECUR-RENCE (for TUMOR\_DESCRIPTION) were added after the start of annotation. It is expected that further annotation will yield additional changes to the schema. The set of frame elements, including brief definitions, is shown in Table 1. Note that some elements (e.g., STATUS, PA-TIENT) are part of all three frames, but not the CAN-CER\_MASTER\_FRAME as these are not expected to necessarily apply to future frames.

# **5** Annotation

The annotation process largely followed standard linguistic annotation practices (Pustejovsky and Stubbs, 2013). Notably, the sentences containing candidate lexical units were double-annotated then reconciled with the help of a third individual. All frame annotation was performed in Brat (Stenetorp et al., 2012). See Figure 1 for examples.

Two special annotations, whose functionality was briefly mentioned earlier, deserve more attention here. First, as shown in Table 1, there is a special "???" element that annotators can use to indicate potentially useful information that may later result in the creation of a new element. (see Figure 1 for an example). As the disease is so complex, there is simply too much information associated with cancer to include elements for all possible types of information. So the ??? element allows for the prioritization of information based on the actual frequency in the clinical notes. Second, the annotation denoted as ERROR is used by

Frame Element	Description
CANCER_MASTER_FR	RAME
CERTAINTY	Certainty/hedging of frame (e.g., <i>possible</i> , <i>likely</i> )
DATETIME	Temporal information for the frame (often reference to PHI element)
POLARITY	Existence/negation of frame (e.g., no, positive)
???	Used for other phrases in the text the annotator feels is important, but do not have a corresponding frame
	element
CANCER_DIAGNOSIS	
DESCRIPTION	Other frame with further information (e.g., TUMOR_DESCRIPTION)
FAMILYHISTORY	Specifies a family member with the diagnosis (as opposed to the PATIENT)
HISTOLOGY	Histological description (e.g., <i>carcinoma</i> ), can be lexical unit
LOCATION	Part of body associated with the cancer
PATIENT	Reference to the patient (e.g., <i>patient</i> , <i>female</i> )
QUANTITY	Some quantitative measure of the cancer
STATUS	Diagnostic status (e.g., <i>history</i> , <i>ongoing</i> )
CANCER_THERAPEUT	
AGENT	Agent performing the procedure (e.g., <i>surgeon</i> )
COMPLICATION	Unexpected, undesirable outcome of procedure (e.g., <i>nausea</i> )
EXTENT	Extent of the procedure, often how much of the mass is removed (e.g., <i>complete</i> )
LOCATION	Part of body procedure targets
PATIENT	Reference to the patient (e.g., <i>patient</i> , <i>female</i> )
RESULT	Result of the procedure (e.g., <i>successful</i> , <i>negative</i> )
STATUS	Procedure status (e.g., <i>planned</i> , <i>postoperative</i> )
TUMOR_DESCRIPTION	
LOCATION	Part of body tumor is located in, often ambiguous (e.g., lymph nodes)
MALIGNANCY	Whether the tumor is benign or malignant
MARGINSTATUS	Description of tumor margin (e.g., <i>superficial edge</i> )
METASTATIS	Whether the tumor has metastasized
PATIENT	Reference to the patient (e.g., <i>patient</i> , <i>female</i> )
QUANTITY	Some quantitative measure of the tumor
RECURRENCE	Whether the tumor has recurred
RESECTABILITY	Indicator of whether tumor is resectable
MORPHOLOGY	Morphology of tumor
Size	Diameter/volume of tumor, including unit (e.g., 3-4 mm)
SIZETREND	Trend in tumor size over time (e.g., increasing, decreasing, stable)
STAGE	Stage number (e.g., <i>stage IV</i> )
STATUS	Tumor status (e.g., <i>present</i> , <i>active</i> )
SUBTUMOR	Link to another TUMOR_DESCRIPTION that further describes this tumor, especially if this is describing a
	group of tumors

Table 1: Cancer FrameNet pilot frames and their elements.



Figure 1: Example annotations.

Information Type	Frequency
Sentences	7,961
Frame Instances	7,163
Average Sentence Length	18
CANCER_DIAGNOSIS	3577
adenocarcinoma	474
cancer	419
carcinoma	495
leukemia	364
lymphoma	473
malignancy	487
melanoma	450
myeloma	191
sarcoma	200
CANCER_THERAPEUTIC_PROCEDURE	2204
colectomy	281
hysterectomy	428
lymphadenectomy	68
mastectomy	459
palliative	133
pancreatectomy	34
prostatectomy	276
radiation	470
whipple	55
TUMOR_DESCRIPTION	1382
lesion	524
mass	352
tumor	506

Table 2: Frequencies of frame instances in the corpus.

annotators to mark both PHI that was missed (thankfully a rare occurrence) and sentence boundaries that should have been removed by the process described in Section 3. Thus ERRORs indicate "sentences" that must be altered before the annotations can be considered final.

Annotation Statistics The annotation was completely performed in 90 hours, taking approximately one minute per sentence, and additional time for reconciliation. Descriptive statistics of the annotated corpus are provided A total of 7,961 sentences are annoin Table 2. tated with 7,163 frame-evoking lexical units (out of a total of 8,206 candidate lexical units). Specifically, there are 3,577 CANCER\_DIAGNOSIS frames, 2,204 CAN-CER\_THERAPEUTIC\_PROCEDURE frames, and 1,382 TU-MOR\_DESCRIPTION frames. In terms of frame elements (e.g., LOCATION, PATIENT, HISTOLOGY), CAN-CER\_DIAGNOSIS had an average of 3.2 elements per frame instance, CANCER\_THERAPEUTIC\_PROCEDURE had an average of 1.7, and TUMOR\_DESCRIPTION had an average of 1.1 elements. The most common elements which are shared across frames are PATIENT (2,749 instances), STA-TUS (2,214), LOCATION (2,190), CERTAINTY (999), and POLARITY (638). See Table 3 for more frame element details.

Annotation Agreement Inter-annotator agreement results are shown in Table 4. While observed agreement for frames-shown in Table 4(a)-is high (around 90%) for all three frames, the fairly high levels of expected agreement (73-77%) result in at best moderate  $\kappa$  agreement for CANCER\_THERAPEUTIC\_PROCEDURE and TU-MOR\_DESCRIPTION (0.46 and 0.58, respectively). How-

	(a) Frame	Agreeme	nt		
		Observed	E	xpected	
Frame	A	Agreement		reement	$\kappa$
CANCER_DIAG		0.96		0.73	0.84
CANCER_THERAPEUTIC_		0.00		0.77	0.46
PROCEDURE		0.88		0.77	0.46
TUMOR_DESC	RIPTION	0.89		0.74	0.58
	(b) Frame Elen	nent Agre	ement		
-	Frame	0	erall		
	Element		$F_1$		
-	Agent	(	0.30		
	CERTAINTY	0	).69		
	COMPLICATIO	ON (	).33		
	DATETIME	0	).69		
	Extent	0	).87		
	FAMILYHISTO	ORY (	).84		
	HISTOLOGY	0	).66		
	LOCATION	0	0.82		
	MALIGNANC	Y (	).87		
	MARGINSTAT	rus (	.61		
	METASTASIS	(	).57		
	MORPHOLOG	у (	).56		
	PATIENT	0	).83		
	POLARITY	0	).77		
	QUANTITY	0	).41		
	RECURRENCE	E (	0.70		
	RESECTABILI	тү (	.88		
	RESULT	0	).34		
	Size	0	).83		
	SizeTrend	0	0.60		
	STAGE	0	0.80		
	STATUS	(	).75		

Table 4: Annotator agreement.

ever,  $\kappa$  agreement for CANCER\_DIAGNOSIS is excellent (0.84). The reason for the high expected agreements is the lack of ambiguity in many of the lexical units (e.g., *adenocarcinoma* is almost always used to indicate a diagnosis), but each of the frames have at least one lexical unit that has high levels of ambiguity (e.g., *cancer*, *radiation*, and *mass*). Table 4(b) shows the F<sub>1</sub> agreement for frame elements. It is unsurprising to see a wide range of agreements, from the very high (e.g., RESULT, COMPLICATION, AGENT). Notably, the elements with lowest agreement tend to be relatively rare in the corpus (e.g., 6 AGENTs and 71 COM-PLICATIONs), so low agreement was likely due to a lack of data for calibration.

### 6 Discussion & Conclusion

In this paper, we presented Cancer FrameNet, a pilot project focuses on building a cancer-related clinical narrative resource for developing NLP systems. We introduced an annotation schema consisting of three frames (CAN-CER\_DIAGNOSIS, CANCER\_THERAPEUTIC\_PROCEDURE, and TUMOR\_DESCRIPTION), as well as a corpus annotated according to the schema which consists of almost eight thousand sentences. Our primary goal is to inform the developmental process for an extended Cancer FrameNet resource, with the secondary goal of informing the develop-

			(a) CAN	ICER_DIA	AGNOSIS ele	ements					
Lexical Unit	CERTAINTY	DATETIME	POLARITY	Family History	HISTOLOGY	LOCATION	PATIENT	STAGE	QUANTIT	'Y STATUS	_
adenocarcinoma	112	10	16	46	91	376	119	134	1	84	-
cancer	61	8	30	85	12	335	197	25	0	101	
carcinoma	98	0	24	15	49	419	176	63	5	92	
leukemia	37	7	15	167	6	4	96	1	0	91	
lymphoma	87	16	28	56	41	77	202	22	0	142	
malignancy	192	5	209	9	2	122	195	6	1	46	
malignant	6	1	3	0	0	5	3	0	0	1	
melanoma	55	17	43	96	19	197	181	49	9	156	
myeloma	38	4	18	46	0	10	73	2	0	44	
sarcoma	20	3	5	34	2	101	69	3	0	63	
Lexical Unit	CERTAINTY	<b>DATETIME</b>	POLARITY	Agent	COMPLICATIO	n Extent	LOCATIO	n Patien	NT RESU	ILT STATU	S
				r_Thera	PEUTIC_PR	OCEDURE					
Lexical Unit	CERTAINTY	DATETIME	POLARITY	AGENI	COMPLICATIO	N EXIENI	LOCATIO	N PAHER	VI KESU	LI SIAIU	
aalaatamuu	7	7	4	0	4	107	56	77	1	104	_
colectomy	7	7 14	4	0	4	197 53	56 40	77	1	194 237	_
hysterectomy	21	14	13	1	9	53	40	183	1	237	
hysterectomy lymphadenectomy	21 3	14 7	13 2	1 0		53 3	40 48	183 20	1 1 0	237 38	
hysterectomy lymphadenectomy mastectomy	21 3 15	14 7 15	13 2 5	1 0 2	9 0 7	53 3 191	40 48 188	183 20 223	16	237 38 306	<u> </u>
hysterectomy lymphadenectomy mastectomy palliative	21 3 15 18	14 7 15 6	13 2 5 0	1 0 2 1	9 0 7 0	53 3 191 0	40 48 188 3	183 20 223 72	16 6	237 38 306 64	<u> </u>
hysterectomy lymphadenectomy mastectomy palliative pancreatectomy	21 3 15 18 1	14 7 15 6 2	13 2 5 0 0	1 0 2 1 0	9 0 7 0 3	53 3 191 0 15	40 48 188 3 25	183 20 223 72 8	16 6 2	237 38 306 64 24	<u> </u>
hysterectomy lymphadenectomy mastectomy palliative pancreatectomy prostatectomy	21 3 15 18 1 9	14 7 15 6 2 12	13 2 5 0 0 5	1 0 2 1 0 0	9 0 7 0 3 34	53 3 191 0 15 89	40 48 188 3 25 65	183 20 223 72 8 109	16 6 2 6	237 38 306 64 24 208	<u> </u>
hysterectomy lymphadenectomy mastectomy palliative pancreatectomy radiation	21 3 15 18 1	14 7 15 6 2	13 2 5 0 0	1 0 2 1 0	9 0 7 0 3	53 3 191 0 15	40 48 188 3 25 65 117	183 20 223 72 8	16 6 2	237 38 306 64 24 208 149	<u> </u>
hysterectomy lymphadenectomy mastectomy palliative pancreatectomy prostatectomy	21 3 15 18 1 9 25	14 7 15 6 2 12 11	13 2 5 0 0 5 90	1 0 2 1 0 0 2	9 0 7 0 3 34 10	53 3 191 0 15 89 5	40 48 188 3 25 65	183 20 223 72 8 109 253	16 6 2 6 3	237 38 306 64 24 208	
hysterectomy lymphadenectomy mastectomy palliative pancreatectomy radiation	21 3 15 18 1 9 25	14 7 15 6 2 12 11	13 2 5 0 0 5 90 1	1 0 2 1 0 0 2 0	9 0 7 0 3 34 10	53 3 191 0 15 89 5 0	40 48 188 3 25 65 117	183 20 223 72 8 109 253	16 6 2 6 3	237 38 306 64 24 208 149	
hysterectomy lymphadenectomy palliative pancreatectomy prostatectomy radiation whipple	21 3 15 18 1 9 25 3	14 7 15 6 2 12 11 5	13 2 5 0 0 5 90 1	1 0 2 1 0 0 2 0 0 0 0 0 0 0 0 0 0 0	9 0 7 0 3 34 10 4 CRIPTION el	53 3 191 0 15 89 5 0 ements	40 48 188 3 25 65 117	183 20 223 72 8 109 253	16 6 2 6 3 2	237 38 306 64 24 208 149 41	
hysterectomy lymphadenectomy mastectomy palliative pancreatectomy prostatectomy radiation whipple	21 3 15 18 1 9 25 3	14 7 15 6 2 12 11 5 MALIG- MA	13 2 5 0 0 5 90 1 (c) TUM	1 0 2 1 0 0 2 0 0 OR_DESC AS- MORP	9 0 7 0 3 34 10 4 CRIPTION el H- PATIENT	53 3 191 0 15 89 5 0	40 48 188 3 25 65 117 2	183 20 223 72 8 109 253 27	16 6 2 6 3 2	237 38 306 64 24 208 149 41	AGE S1
hysterectomy lymphadenectomy mastectomy palitative pancreatectomy radiation whipple DATE	21 3 15 18 1 9 25 3	14 7 15 6 2 12 11 5 MALIG- MA NANCY ST	13 2 5 0 0 5 90 1 (c) TUM RET.	1 0 2 1 0 0 2 0 0 OR_DESC AS- MORP	9 0 7 0 3 34 10 4 CRIPTION el H- PATIENT	53 3 191 0 15 89 5 0 ements	40 48 188 3 25 65 117 2 RECUR-	183 20 223 72 8 109 253 27 RESECT-	16 6 2 6 3 2	237 38 306 64 24 208 149 41 SIZE ST	 Age St
hysterectomy lymphadenectomy palliative pancreatectomy prostatectomy radiation whipple RTAINTY DATE TIME	21 3 15 18 1 9 25 3 POLARITY	14 7 15 6 2 12 11 5 MALIG- MA NANCY ST	13 2 5 0 0 5 90 1 (c) TUM (c) TUM (RGIN MET. ATUS TAS	1 0 2 1 0 2 0 2 0 0 <b>OR_DESC</b> AS- MORP IS OLOG 60	9 0 7 0 3 34 10 4 CRIPTION el H- PATIENT	53 3 191 0 15 89 5 0 ements QUANTITY	40 48 188 3 25 65 117 2 RECUR- RENCE	183 20 223 72 8 109 253 27 RESECT- ABILITY	16 6 2 6 3 2 SIZE 1	237 38 306 64 24 208 149 41 <u>SIZE</u> REND STA 36	 Age St

Table 3: Frequencies of frame elements in the corpus.

ment of further such corpora in other clinical domains. Additionally, we plan to utilize the corpus as training data for a future NLP system. However, due to the large variety of information types in cancer, and the restriction to a single institution, this corpus is of limited utility in developing complete and robust cancer information extraction methods. For example, important textual information such as post-treatment status, medication, and genomic & molecular testing results are critically important in the "precision medicine" era of cancer treatment.

Lexical

Unit lesion mass tumor

Apart from the limitations related to the corpus and missing elements in the schema, another complex issue is the granularity of the frames. For example, a reasonable phenotyping task might be to find cases of cancer of any original that have metastasized to the lymph nodes. However, a common phrase used to describe biopsy results is "with lymph node involvement", which does not necessarily specify directly whether it is a lymph node cancer (e.g., non-Hodgkin lymphoma) or a metastasis, even if it is likely the latter. Further, encoding hypothetical phrases such as "if tumor untreated" presents schematic difficulties, though these could likely be overcome given sufficient data for initial exploration.

On the whole, however, frame semantics provides a flexible means of encoding important cancer information without getting bogged down in the minute details of standardizing clinical representations (a major barrier to interoperability in structured clinical data). Rules can be developed on top of the extracted frames (the "reasoning" step we describe in the Introduction) that make the necessary assumptions to utilize imperfect data. For instance, in the lymph node example, the phenotyping algorithm could exclude patients who only have a diagnosis related to the lymph node, thus likely excluding the non-metastasis cases. It is also important to recognize that, given the presence of structured data in the EHR, NLP is often seen as an (imperfect) means of supplementing (also imperfect) structured data. In this context, given that the vast majority of sentences were represented quite well using the proposed frames, this approach appears quite promising.

Another potential pitfall of using frame semantics for cancer involves the ability of organizing information into compact frames. Put another way, if almost all cancer frames shared the exact same frame elements, then a frame-based schema would be a poor fit. Instead, we found frames to work quite well in this regard. First, three frame elements were used in the CANCER\_MASTER\_FRAME (CER-TAINTY, POLARITY, and DATETIME), but these actually generalize to just about all frames, well beyond cancer. Second, two frame elements were used in all three frames, PATIENT and STATUS. The former might ultimately be a better fit for CANCER\_MASTER\_FRAME, but the STATUS element has different semantics for each frame (e.g., the status of someone's cancer versus the status of the surgery to remove a tumor). Third, two elements, LOCATION and STAGE, were in two frames (CANCER\_DIAGNOSIS and TUMOR\_DESCRIPTION), but given the inter-relatedness of having a tumor and being diagnosed with cancer, this is not particularly surprising. Finally, beyond these cases, the remaining 16 elements were unique to a single frame, suggesting that frame-based representations are a good fit for cancer-related EHR text.

A common problem with clinical text is the mixture of structured data and true natural language prose. Commonly, structured descriptions are automatically or semiautomatically integrated with the clinical narrative. While frame semantics can handle such cases (often trivially), they are of limited value given the likely duplication of that same information in the structured part of the EHR data. However, in this pilot project we limited ourselves to just the sentence-level scope for frame annotation, so determining better ways to handle this kind of data in future projects will be important.

On the other hand, our limitation to sentences provides a useful starting point for cross-institutional data sharing. The privacy concerns surrounding sharing of complete records largely goes away when individual sentences are manually stripped of their PHI and any potential linking information back to the original record. The ability to gather multiple institutions' data, all organized according to the same frame semantic schema, into a single FrameNet would be highly valuable to the clinical NLP community. These frames could then be mapped to existing structured clinical data standards, such as FHIR and OHDSI.

The one notable exception to sentence-based annotation, and something we would strongly consider changing in a future such project, is the use of sentences at the frame identification stage. While individual frame elements can easily be annotated at the sentence level, the word sense disambiguation task of determining whether a phrase invokes a particular frame is sometimes difficult. This is usually limited to cases where the sentence is in fact a fragment (e.g., a single item in a bulleted list), but this is a common phenomenon in EHR text and therefore worth taking careful consideration in how to handle. It may be sufficient to provide a human annotator with the extra-sentential context, but limit the machine to simply the sentence itself for classification. Alternatively, we could relax the notion of sentences in the case of fragments to provide more context. These compromise strategies could overcome one of the primary issues the annotators struggled with, while likely not having that significant an impact on the resource for training NLP systems.

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