Grant Final Report

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Improving Outpatient Medication Lists Using Temporal Reasoning and Clinical Texts

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Structured Abstract

Purpose: The goal is to pilot and test natural language processing (NLP) methods and tools to facilitate the use of electronic clinical texts to improve medication lists.

Scope: This study extracts and encodes medication information from clinical texts available in an ambulatory electronic health record (EHR) system.

Methods: We designed and developed a general NLP system, called "Medical Text Extraction, Reasoning and Mapping System (MTERMS)," to encode clinical text using different terminologies and establish dynamic mappings between them to improve data interoperability. Evaluators manually reviewed 30 free-text and 10 structured outpatient notes compared to MTERMS output. The mapping between RxNorm and a local medication terminology was also assessed. Requirements for integrating NLP output to the medication reconciliation process were studied.

Results: MTERMS achieved an overall F-measure of 90.6 and 94.0 for free-text and structured notes respectively for medication and temporal information. The local medication terminology had 83.0% coverage compared to RxNorm's 98.0% coverage for free-text notes. 61.6% of mappings between the terminologies are exact match. Capture of duration was significantly improved (91.7% vs. 52.5%) from systems in the third i2b2 challenge.

Key Words: natural language processing; terminology; medication systems; medication reconciliation

Final Report

Purpose

An accurate and complete medication list on a patient's electronic health record (EHR) is critical to prevent medication prescribing and administration errors. Medication reconciliation in the ambulatory setting is challenging. Clinicians may be unaware of errors due to episodic and often hurried interactions between clinicians and patients with little information exchange. Most prior research proposed to aggregate structured medication data from the EHR to generate and maintain a reconciled list. However, an important cause of errors of omission are clinical texts (e.g., clinic notes) where critical information may exist but not be available for medication reconciliation or decision support. Natural Language Processing (NLP) systems can automatically extract and encode medication information from free-text notes, creating a structured output useful for medication reconciliation systems.

One challenge for medication reconciliation is that the drug names from different EHR applications (e.g., Computerized Physician Order Entry) and NLP systems are usually coded using different terminologies (e.g., local or commercial) and therefore not interoperable. In addition, it is not clear how to organize and present NLP output in an appropriate way with information from other sources to effectively support a clinical workflow. In this study, we proposed a NLP-based approach to improve the medication reconciliation process.

Scope

A major goal of health IT is to use electronic clinical data and information technology to improve quality of health care and to support clinical research. Accurate and complete medication information at the point of care is crucial for delivery of high-quality care and prevention of adverse events. As the prevalence of chronic illness and the number of available pharmaceuticals grow, patients are taking a variety of brands and increasing quantity of medications. Physicians in the U.S. write more than three billion prescriptions per year in the ambulatory setting,[1] and 75% of office visits to family physicians and general internists are associated with the continuation or initiation of a drug.[2,3] The medication regimens may change frequently because of lack of efficacy, new indications, medication side effects, insurance requirements, etc. In addition, each patient may be cared for by multiple physicians, which make management of patients' treatment even more complicated.[4,5]

Patients' medical records are often not updated appropriately or in a timely manner. Outdated medications are frequently not deleted. One study[6] shows that 67.4% medications were still active one calendar day after their inactive status was document in the notes. Active medications are often not added timely in the structured medication list.[7-9] Lack of updated information is a major cause of medication errors. Adverse drug events and medication errors are estimated to cost the US health care system $177 billion annually.[10]

While medication errors are common and can cause injuries, they are often avoidable. Recent efforts strived to establish a reconciled medical regimen through the integration of electronic medical records with other information sources (e.g. claims, pharmacies, or patient). By comparing a patient's medication orders to all of the medications that the patient has been taking, the reconciliation aims to avoid medication errors such as omissions, duplications, dosing errors, or drug-drug interactions. However, most studies of medication reconciliation have taken place in the inpatient setting. In addition, the data sources necessary for reconciliation may not be accurate[11] or may not be available.[12] Information recording the observations and actions related to patient medications is commonly distributed in medical records and may cross multiple clinical information systems, and may also involve different documentation formats.[13] Most efforts to date proposed aggregate structured medication data from EMR and CPOE systems to generate and maintain a reconciled medication list. However, medications in non-structured narrative sources (such as discharge summaries or clinic notes) must also be reconciled.

Clinical narrative notes or reports can contain rich medication information. Clinicians frequently document the patient treatment history and plan, including changes in the medication regimen, through narrative notes. Many EHRs allow entry of free-texts (e.g. notes and comments) in digital format, making possible computation identification of medication information from clinical texts. If the medication information buried in clinical texts can be automatically identified and structured[14], this will dramatically increase the amount and quality of information available to physicians, patients and researchers.

In the past three decades, natural language processing (NLP) has been a fertile area of research in biomedical informatics. Many NLP methods and systems have been developed for automatically extracting and structuring clinical information (e.g., medical problems and medications) from clinical text. However, very few studies were proposed to use NLP as a complementary means to improve medication reconciliation. Cimino et al[15] combined NLP, a controlled terminology, and a medication classification system to create metrics to summarize the medication data in both structured and free-text data. Breydo et al[6] developed an algorithm for detection of documentation of inactive medication in the narrative medical documents.

Using NLP to pull information from textual records and then present that view alongside other data sources, such as structured medication list in EHR and prescription fill data in Pharmacy Information Systems, will make the medication reconciliation task more efficient. A stumbling block has always been that the information from these sources is usually coded using different medical terminologies and therefore not interoperable, making information integration a great challenge. For example, the medication list may be coded using an institutional terminology, pharmacy data may be coded by a commercial terminology, and most existing NLP systems encode clinical text using standard terminologies (e.g., the Unified Medical Language System (UMLS)). At present, the real-time translations between these diverse terminologies, especially local terminologies to standard terminologies, using automated methods (such as NLP) have not been well established. Another challenge is that it is not clear how to organize and present NLP output in an appropriate way with information from other sources to effectively support a clinical workflow.

We therefore developed a general NLP system, named Medical Text Extraction, Reasoning and Mapping System (MTERMS), which extracts clinical information from clinical text and encodes the extracted information using both local and standard terminologies (e.g., RxNorm). It also allows mapping between terminologies when appropriate. We also identified function requirements for designing a user interface to efficiently use NLP output for medication reconciliation.

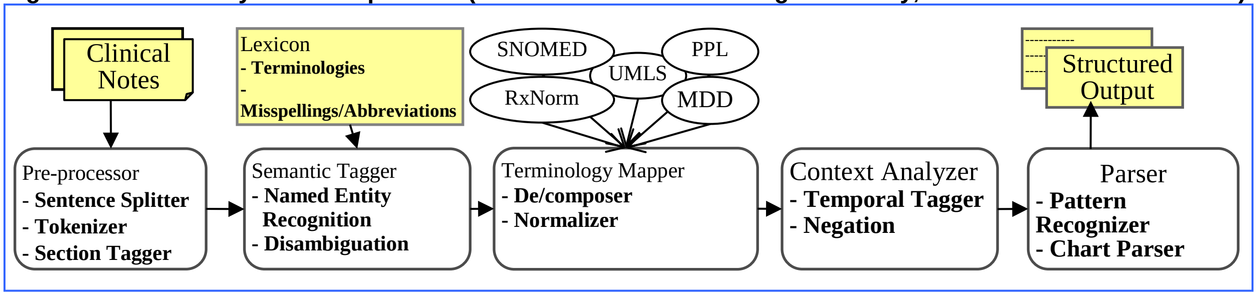
Methods

Our methods consist of the following steps: 1) Design and development of a NLP application which identifies medication names and drug signatures (e.g., dose amount) and other contextual information (e.g., status) from free-text clinical notes, encodes medication names using standard and local terminologies and conducts terminology mapping simultaneously, and structures the extracted information; 2) Evaluate the tool by verifying the NLP output against manual review; and 3) Identify requirements for a user interface (UI) to efficiently use NLP output for medication reconciliation.

NLP System Design and Development

We developed a general NLP system, called the Medical Text Extraction, Reasoning and Mapping System (MTERMS). MTERMS applies a modular, pipeline approach flowing from a Preprocessor, Semantic Tagger, Terminology Mapper, Context Analyzer, to a Parser in order to structure inputted clinical free-text documents. Figure 1 shows MTERMS system components. The output of MTERMS is a structured document in XML format. The preprocessor is used for cleaning, reformatting and tokenizing the text into individual sections, sentences, and word units. The semantic tagger uses lexicons to identify words or phrases to determine what categorical bucket they should be placed in (e.g. medication name and route). The terminology mapper translates concepts between different terminologies. The context analyzer looks for temporal context and other contextual information to further determine the meaning of a phrase in context with the rest of the text. The parser identifies the structure of phrases and sentences.

Figure 1. MTERMS System Components (MDD: Partners Master Drug Dictionary; PPL: Partners Problem List)



The Pre-processor contains a Sentence Splitter that uses a set of rules mainly based on punctuation and carriage return. The Section Tagger Uses the Partners Notes Concept Dictionary for structured notes to extract the Section headers. The list was manually reviewed by a physician and a nurse to exclude ambiguous terms and to add additional common sense headers.

The Semantic Tagger uses a lexicon that includes a subset of terms from standard terminologies (e.g., UMLS, RxNorm, and SNOMED CT), local terminologies (e.g., Partners Master Drug Dictionary (MDD), Partners Problem List (PPL)), HL7 value sets, regular expression rules, and manually collected terms from chart review, or literature review.

For the Context Analyzer, we adopted NegEx[16] and TimeText[17] algorithms to tag negated terms, temporal information, and other contextual information.

MTERMS' terminology mapper automatically translates Partners Master Drug Dictionary (MDD) to RxNorm. RxNorm, created and maintained by the National Library of Medicine (NLM), aims to provide a standardized nomenclature that relates itself to terms from commonly used source vocabularies, and to mediate messages between systems not using the same software and vocabulary. However, little research has been done to study the mapping between RxNorm and medication terminologies developed at local institutions or other organizations. Such studies are critical for the future adoption and integration of RxNorm in EHRs and data interoperability. The Partners' MDD is an enterprise-wide drug dictionary, primarily used in inpatient and outpatient CPOE systems. MDD was first developed in 1992 and is maintained by pharmacist knowledge engineers to meet requirements of different academic medical centers and outpatient users. Given the age of the local systems and the evolution that has taken place, the challenges in terminology mapping are apparent.The terminology mapper uses multiple levels of linguistic analyses and NLP techniques, including simple analysis (e.g., exact string match), morphological analysis (e.g., handling punctuation and other morphological variations), lexical analysis (e.g. handling abbreviations and acronyms), syntactic analysis (e.g. pattern recognition, phrase segmentation and recombination), and semantic analysis (e.g. identifying meaning and assigning the terms to an appropriate semantic group). The algorithm begins by identifying elements tagged by the Semantic Tagger of the same semantic type (e.g., DrugName) that are at the same or overlapping word position in the text. Next, if the drug name is tagged by both terminologies, the algorithm compares the names to see if an exact string match exists. If not an exact string match, then additional analyses are conducted on the MDD term, and RxNorm is used as the reference to match against. Rules are applied to normalize difficult strings. For example, specific symbols need to be handled, e.g. MDD uses the symbol "/" or "+" to connect ingredients in a multiple ingredient product while RxNorm uses "/".

The Parser is essentially a recognizer where a grammar verifies whether the structure of a particular sentence fits the grammar rules of the language. We adopted a semantic-based approach similar to MedLEE[18] and MedEx[19]with consideration of sequencing a Pattern Recognizer, a deep Chart Parser and a shallow Chunker in order to achieve an optimal system efficiency without affecting the semantic parsing performance

Evaluation

In order to evaluate the performance of MTERMS in processing medication information from clinical free-text documents, we focused on free-text outpatient clinical notes created mainly by patients' primary care physicians and medical specialists, such as cardiologists. Patients with chronic diseases usually have rich medication information in their EHRs and their medication lists are challenging to maintain. Five common chronic diseases were included in this study: diabetes, hypertension, congestive heart failure, chronic obstructive pulmonary diseases, and coronary artery disease. We retrieved 2 years of data (2009 and 2010) that meet above criteria from Partners Ambulatory EHR system, called the Longitudinal Medical Records (LMR), through the Partners Research Patient Data Registry. A test set was set aside by a non-study staff member consisting of 40 randomly selected clinical notes that were stratified by cohort to ensure that all diseases were represented within the sample. Free-text notes and structured notes were evaluated separately as the structure and content are different, thus the system performance may also be different. Structured clinical notes refer to instances where the medication list was copied directly from the Structured Medication List (SML) in a machine specified format that differs from natural language. LMR allows physicians to copy medications from the structured medication list and paste them into the notes for further editing. 10 of the 40 notes contain the “copy-paste” medications and another 30 notes only contain free-text medication entries. We assessed the system’s performance on processing these two types of the notes separately. All developers were blinded to the test set and only had access to the training set.

A physician and a clinical Informatician served as judges to manually review clinical notes and MTERMS annotations for medication names and drug signatures from MTERMS output for clinical notes in the test corpus, while a Doctor of Pharmacy candidate judged the corresponding temporal information related to medications. Raw agreement was used to compare the inter-rater reliability of reviewers for 10 randomly selected clinical notes from the test set. The two reviewers reached an agreement for the first 10 notes and then each assessed another 15 notes separately. The commonly used statistical metrics of Precision, Recall, and F-measure[20] were calculated for each type of data. The Doctor of Pharmacy candidate manually reviewed the terminology mapping under the supervision of a pharmacist. The performance of the term mapping is annotated using the following codes: Exact Match, Partial Match and Missing.

User Interface (UI) Requirements

We studied an existing medication reconciliation application at our institute and worked with a few healthcare providers to identify the requirements and use cases of using clinical notes and NLP in the medication reconciliation process.

Results

Overall, there were 1108 free-text note terms from 30 charts and 1035 structured note terms from 10 charts for a combination of findings types (medication names, drug signatures and temporal) analyzed with F-measures of 90.6 and 94.0 respectively. The raw agreement between the two evaluators was 86.3% for medication names and drug signatures on 10 charts. Table 1 further breaks down the total number of instances, precision, recall, and F-measure for the various findings types for the free-text notes and structured notes separately.

Table 1. MTERMS System Performance on Processing Medication Related Information

	Free-Text Notes (n=30)				Structured Notes (n=10)			
Findings Type	Total #	Precision (%)	Recall (%)	F-Measure (%)	Total #	Precision (%)	Recall (%)	F-Measure (%)
Drug Name	455	92.5	91.6	92.1	271	93.8	93.5	93.7
Dose	177	92.1	91.6	91.8	171	89.3	93.8	91.5
Frequency	174	91.4	91.4	91.4	139	97.1	97.1	97.1
Route	50	88.0	100	93.6	141	97.2	100	98.6
Strength	20	29.4	55.6	38.5	116	82.8	98.0	89.7
Necessity	27	100	100	100	16	100	87.5	93.3
Drug Form	13	77.8	63.6	70.0	11	100	90.9	95.2
Dispense Amount	1	0	-	-	97	97.8	93.8	95.8
Status	79	70.5	67.2	68.8	26	87.5	91.3	89.4
Duration	20	100	100	100	52	76.9	100	87.0
Date & Time	34	97.1	100	98.5	6	100	100	100
Relative Time	15	93.3	100	96.6	2	100	100	100
Temporal (Other)	43	100	100	100	19	100	100	100
Total	1108	90.3	90.9	90.6	1067	92.4	95.6	94.0

Table 2 shows the coverage of RxNorm source terminologies ordered by their inclusion within MTERMS search sequence. 98.0% and 83.0% of terms in free-text notes are covered by RxNorm and MDD respectively, whereas 93.4% and 94.3% of terms in structured notes are covered by RxNorm and MDD respectively.

Table 2. Coverage of RxNorm Source Terminologies Ordered By MTERMS Search Sequence and Coverage of local Master Drug Dictionary (MDD)

RxNorm Source (SAB)	(%) in Free-Text Notes	(%) in Structured Notes
RxNorm	88.1	93.1
SNOMED CT	9.4	5.9
MMX (Micromedex)	0	0
VANDF (Veterans Administration)	1.1	0
NDDF (First DataBank)	0.2	0
MMSL (Multum)	1.1	0.9
Misspelling (Drugs.com)	0	0
Overall RxNorm Coverage	98.0	93.4
Overall MDD Coverage	83.0	94.3

Table 3 presents an analysis of the terminology mapping between MDD and RxNorm, which shows that 63.0% and 58.7% of mappings in free-text notes and structured notes respectively are exact matches and 14.7% and 27.9% are partial matches respectively. Overall, 61.6% of mappings are exact matches.

Table 3. Mapping Medication Terms between local Master Drug Dictionary (MDD) and RxNorm

Type	% in Free-Text Notes	% in Structured Notes
Exact	63.0	58.7
Broader (Partial)*	2.3	6.3
Narrower (Partial)^	12.1	21.2
Incomplete (Partial)	0.2	0.5
Extraneous (Incorrect Match)	0.2	0
Missing	22.1	13.5

* Resulting MDD terms have more specific meaning than RxNorm terms.
^ Resulting MDD terms have a less specific meaning than RxNorm terms

Our initial design of the User Interface for presenting and using NLP output for medication reconciliation links a medication on the structured list to all the notes identified by MTERMS that contain this medication. It also presents recent medications that are not in the structured list and corresponding notes that contain them. Further evaluation of this approach is needed.

Discussion

MTERMS achieved 90.3% precision and 90.9% recall for free-text clinical notes, and 92.4% precision and 95.6% recall for structured clinical notes on processing medication names, drug signatures, and temporal information. These results seem consistent with previous studies but may not be directly comparable as this study focused on outpatient clinical notes, whereas previous studies focused on discharge summaries or applied more stringent annotation guidelines. Medication information in structured notes is formatted automatically by the EHR system, for example, “Lipitor (ATORVASTATIN) 20 MG (20MG TABLET Take 1) PO QD x 60 days #60 Tablet(s).” NLP tools can be trained to capture these specific structures. However, the format may vary in different systems or different versions of a system and can be modified by physicians when copied to a free-text field. Although structured notes, on average, contained more medications than free-text notes, one would argue that this information might not be that useful due to readability issues, and redundancy with the structured medication list.

MTERMS missed some medication abbreviations (e.g., INH) and vitamins (e.g., B12 which is Vitamin B12), which may have been on the exclusion list due to ambiguity concerns. MTERMS also incorrectly captured some non-drug terms such as “gel” which is from FDB NDDF as an ingredient and also misinterpreted “thymus” in “the patient has an enlarged thymus as “Thymus Extracts” which is from VANDF (Veterans Administration Nation Drug File). MTERMS is integrated with the Temporal Constraint Structure (TCS) tagger and achieved high precision and recall on capturing temporal information. The TCS structure allows MTERMS to conduct temporal reasoning of clinical events. It is more difficult to capture strength and drug form information in free-text notes than structured notes as these terms in free-texts have more variations. One challenging areas for strength is the presence of ambiguous fractions with missing units. For example, percocet 2.5mg/325mg may be represented as Percocet 2.5/325 in the free-text notes. Another example is that it is unclear if vancomycin 3/10 is a valid strength or a date. The challenges with drug form are in disambiguating equipment (e.g., pill organizer), brand name of drugs (e.g., Timolol eye drops), and where it represents a class of products instead of a form in context of the sentence (e.g., eye drops, nasal spray). Status is still a challenging area and needs an expanded lexicon and further investigation. We adopted HL7's value set to standardize the Route information. Standard structured output for frequency also needs further investigation.

Approximately 60% of mappings between MDD and RxNorm were exact match for both types of notes; however, 22.1% and 13.5% were missing for free-text notes and structured notes respectively (Table 3). A common reason for missing is abbreviations (e.g., MVI for multivitamin). Another reason for a missing match might be an obsolete name that is not maintained in RxNorm but is still in MDD (such as "pancreatic enzymes"). It is not surprising that MDD covered a greater percentage of terms in the structured notes than the free-text notes (Table 2) because MDD is used within the Computerized Physician Order Entry (CPOE) system.

Mapping medication terms from a local terminology source to a normalized standard requires a variety of simultaneously applied strategies in order to capture terms specified at various levels of complexity. The simplest and most effective strategy was a basic string match with no manipulation, indicating that terms were identical. In normalization, simpler sequenced strategies often yielded a greater volume of additional matched terms than more complex and targeted strategies. There is a difference in granularity across terminologies in terms of additional drug signature elements included within a drug name, which makes mapping of these terms difficult. A potential extension of MTERMS terminology mapper would be to apply N-grams or statistical or machine learning methods. In addition, dynamic, real-time mappings provide up-to-date maps between continually changing terminologies. However, an alternative to the dynamic mapping would be to use a static knowledge base approach updated on a regular basis to keep the mapping up-to-date. The tradeoff between dynamic and static mapping is the optimization of speed, storage, and maintenance.

The feasibility for real-time clinical use of NLP in assembling the medication reconciliation list is strong. However, a real-life application will require change management. For example, a terminology management process is needed to review how updates to terminologies will affect the mappings and to track retired concepts. A common occurrence in electronic order entry systems is free text medication entries. These represent something of a black box to the systems that process them. NLP could be used to extract coded medications from these entries and allow duplication alerts or drug interaction system to catch potential medication errors.

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List of Publications and Products

Journal Article

Zhou L, Plasek JM, Mahoney LM, et al. Mapping Partners Master Drug Dictionary to RxNorm Using an NLP-based Approach. *Journal of Biomedical Informatics*. 2011. Online first.

Conference Proceedings

Zhou L, Plasek JM, Mahoney LM, Karipineni N, Chang F, Yan X, Chang YJ, Dimaggio D, Goldman DS, Rocha RA. Using Medical Text Extraction, Reasoning and Mapping System (MTERMS) to Process Medication Information in Outpatient Clinical Notes. *AMIA Annu Symp Proc*. 2011 1639-48.

Conference Abstracts

Zhou L, Yan X, Chang YJ, Chang F, Rocha, RA. *Improving Completeness and Correctness of Medication Lists Using Temporal Reasoning and Clinical Narratives*. The AHRQ 2010 Health IT Grantee and Contractor Meeting, June 2-4, 2010. Washington, DC.

Zhou L, Plasek JM, Karipineni N, Mahoney LM, Chang F, Dimaggio D, Rocha, RA. *Improving Medication Reconciliation Using Natural Language Processing.* The 2011 AHRQ Annual Conference, September, 2011, Bethesda, MD