Grant Final Report

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Value of New Drug Knowledge for e-Prescribing

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Abstract

Purpose: To assess the value of the HL7/FDA Structured Product Labeling (SPL) drug knowledge representation standard and its associated terminology sources for building and enhancing decision support-enabled computerized provider order entry (CPOE) systems for e-prescribing.

Scope: The Regenstrief Institute's CPOE system (Gopher) and a newly created application based on SPL HL7 standards, terminology and knowledge sources.

Methods: Mapping clinical decision support knowledge base content from and to the standard knowledge content terminologies and assessing their ability to enhance the way clinical decision support knowledge may be managed and whether the public knowledge can enhance in-house developed and maintained knowledge content.
Build a e-prescribing system on the foundation of the SPL/HL7 standard and its associated terminologies to determine how they may be used directly to build clinical decision support enhanced CPOE systems which would be used by small and rural practitioners.

Results: We developed terminology mapping methodologies to map between the in house created knowledge and public knowledge. We were able to show that local clinical decision support knowledge could be made to detect 2-4 times more adverse situations (here: drug allergy conflict). Although we could not move the new application into practice as planned, we were able to use the SPL knowledge sources directly for knowledge-driven e-prescribing functions and are working on deployment in the Indiana health information network setting.

Key Words: none provided

Final Report

Purpose

The objective of this project was to create new knowledge and evidence regarding the benefits of uniform standards for health information for the dissemination of computer-actionable knowledge that can improve patient safety and quality of care, and for the development and implementation of HIT in diverse health-care settings.

The FDA has been working for several years on a new prescribing information (package insert) format with improved usability to prescribing providers. In the most recent step, the FDA has contracted the PI of this proposal to design the next release of the electronic Structured Product Label (SPL) which is to include computer-interpretable prescribing information in an HL7 standard data structure. This knowledge will be distributed in real time through the FDA and NLM's joint "DailyMed" initiative. We propose to Study the value that the upcoming FDA mandated electronic drug labeling HL7 standard will bring to existing and emerging Computerized Provider Order Entry (CPOE) systems and e-prescribing tools on the example of the Regenstrief Medical Gopher CPOE system and on a newly developed completely HL7 standards-based open-source prescribing tool.

Scope

The project had two thrusts:

1) Investigate how SPL can help in knowledge management of existing CPOE systems such as the Regenstrief Medical Gopher system; and

2) Develop a standards-based e-prescribing system which would use SPL, the underlying HL7 standards and terminologies as a foundation.

Methods

The amount and quality of the SPL drug knowledge had been less than hoped in the beginning of the project, particularly as far as clinical decision support knowledge base content is concerned (e.g., drug-interactions, contraindications, dosing guidelines). All published SPL labels were loaded into our standards based data and knowledge systems.

We developed algorithms to extract the vendor-independent clinical drug descriptions from the vendor and product-centric labels and validated these against the RxNorm clinical drug terminology and knowledge base. While SPL labels still cover only 23% of RxNorm clinical drugs, they were found to describe 77% of actual community pharmacy dispenses records. SPL

descriptions agree well with RxNorm. SPL can be used as the primary source of drug information for e-prescribing systems once the upcoming FDA listing rule takes effect.

Notably we found here that the value of “generic names” and pre-formed trees of drug abstractions classes are significantly reduced if instead one has detailed knowledge of all ingredients of the drugs and the chemical and effect classes of each of those ingredients.

We also used RxNorm (and previously Multum) knowledge content as an interim remedy to cover existing gaps in the SPL content both in terms of breadth of coverage as well as clinical decision support relevant detail. Specifically we could use RxNorm to actually generate drug descriptions in the standard SPL format which we could load into the e-prescribing system to complete the catalog of available drugs.

We exported the Regenstrief Gopher knowledge base from its legacy database into an XML format and into a relational database for mapping to standard terminologies. We showed that standard relational database techniques can be used to map the meaning of drug classes between the Gopher system to drug classes in the VA National Drug File Reference Terminology (NDF-RT), which is the terminology selected by the federal medication terminology infrastructure for describing mechanism of action, physiologic effect, and chemical classes of drugs.

We further mapped the SPL content to NDF-RT in such a way that we could add clinical decision support relevant knowledge content into the published SPL labels using the standard format. These enhanced labels were loaded into the standards based data system upon which the e-prescribing system was built. The drug selection and drug-allergy and drug-interaction detection queries were implemented in this system based solely on this standard SPL knowledge content.

We evaluated the SPL knowledge using a large set of drug-intolerance, orders, and dispense records covering >50,000 patients over 30 years. Here we found that the more systematic nature of the public knowledge sources improved the sensitivity of the system to detect adverse situations such as drug-allergy conflicts and (preliminary) also drug-drug-interaction events by a factor of 2 to 4. The effect of this was mostly attributable to a more systematic organization of the public terminology (NDF-RT/MeSH) and a more reliable classification of drug formulations based on their ingredients (rather than on ad-hoc drug class hierarchies.)

We also analyzed other standard terminologies to be used with SPL and in increasing numbers of EHR systems and health information networks. The FDA has adopted the Veteran Administration and Kaiser Permanente (VA/KP) Problem List Subset of SNOMED as the terminology to represent indications in electronic labels. We evaluated the ability of this subset to represent the text phrases extracted from existing drug labels. We compiled a test set of 1265 distinct indication phrases and mapped them to all of UMLS, SNOMED and the VA/KP subset of SNOMED. We found that the post-coordination of SNOMED terms improved representation of text indications found in drug labels from 80% to over 90% and suggested that the VA/KP Subset of SNOMED may be has significant limitations for coding drug indications.

We were able to map SNOMED findings into the HL7 v3 representation formats and built this into the e-prescribing system such that patient problems may be encoded directly into SNOMED concepts by the user using auto-complete functions.

Further we investigated on the ability of SNOMED coded problems and indications and the NDF-RT drug-indication linkage to enhance e-prescribing by providing indication based suggested drug orders. We evaluated over 1.6 million de-identified patient records from the Regenstrief Medical Record System (RMRS) with over 90 million diagnoses and 20 million medications. Using RxNorm, the VA NDF-RT, and SNOMED standard terminologies and

mappings we evaluated the linkage of local concept terms for medications and problems. We were able to map 24,398 candidate medication and indication pairs. The overall sensitivity and specificity for term pairs was 67.5% and 86% respectively and 39.5% and 97.4 when adjusted for term pair occurrence within single patient records. We found that medications could be mapped by machine to a disease/ disorder using established terminology standards. While there were still some significant flaws due to imprecise or erroneous indication links in NDF-RT the mapping may inform many knowledge management and decision support features in an EMR.

We also sought to determine how well the HL7 / ASTM Continuity of Care Document (CCD) standard supports the requirements underlying JCAHO medication reconciliation recommendations. In particular, JCAHO emphasizes that transition points in the continuum of care are vulnerable to communication breakdowns, and that these breakdowns are a common source of medication errors. These transition points are the focus of communication standards, suggesting that CCD can support and enable medication related patient safety initiatives. Data elements needed to support JCAHO recommendations were identified and mapped to CCD, and a detailed clinical scenario was constructed. The mapping identified minor gaps, and identified fields present in CCD not specifically identified by JCAHO, but useful nonetheless when managing medications across transitions of care, suggesting that a closer collaboration between JCAHO and standards organizations will be mutually beneficial. The nationally recognized CCD specification provides a standards-based solution for enabling JCAHO medication reconciliation objectives.

In our standards-based e-prescribing system we could load both SPL and CCD documents into the same database and – provided the mapping to the same terminology exists – use CCD documents for adding prior patient data into the prescribing application so as to facilitate managing medication lists and providing interaction and contra-indication decision support functions.

The medication order entry application which we had created based on these standards includes an allergy list, problem list, a list of both historical medications and a managed "current" medication list. It promotes tracking indications with drug orders by allowing drag-and-drop relation between problems and prescriptions being written.

As planned, the system operates solely from standard public knowledge sources without any manual maintenance of order catalogs or decision support knowledge, so it suggests that one of the very costly steps of deploying EHR applications, the local creation of data dictionaries, may indeed be overcome using available format and content standards.

We did focus group end-user testing event and found that some of our more comprehensive interests, particularly the link of medications to managed problem-lists were found of lesser interest to our prospective adopters. On the other hand, we found that some significant basic administrative data management functions were important to make the system meaningful to use. Fragmentation of the environments in which this system was to be deployed made its actual deployment exceedingly challenging. For example, one site had an EMR system in which doctors would maintain allergies and problems, and hence the e-prescribing function would have to either interface with that (closed) system or force the user to enter data twice. In both of our adopter sites we had competing implementations of other software occur before the time that we were ready to deploy the application.

Our initial plan to deploy the system remotely on stand-alone server computers was therefore not enacted. Upon closer look at the needed connection of the e-prescribing application with the

other electronic health data environment it appears exceedingly challenging to deploy such applications in a drop-ship, turn-key, lights-out fashion.

Results

The standards based data and knowledge tools core has been made publicly available and was significantly improved through this project. Various industry and academic users have adopted all or parts of it. The ability to process any standard format HL7 data and particularly the ability of the HL7 Reference Information Model to represent a wide range of health care data and decision support knowledge has been useful to load SPL and other knowledge content as well as patient records in CCD format into the same system and provide decision support functions.

Our work has shown that standard data formats and terminology are both valuable for integrating health care data and knowledge for clinical decision support with minimal manual efforts and that the role of terminology is specifically for the purpose of mapping and for providing detailed knowledge content. Our software piloted a certain "late binding" approach to terminology, whereby terminology is a useful tool for data linkage, but is not a precondition for storing, querying, and operating with the data. This is shown best by our ability to use the SPL labels and their descriptions of drugs directly for medication data entry without requiring any "clinical drug" terminology: the user simply types the names of ingredients or brands into a simple entry box and auto-completion ensures that orders are for items that are available on the market. Thus we could easily use various drug data bases at different times (1) Multum, (2) SPL, (3) RxNorm content in SPL simply by loading this knowledge content into the system. Overall we found that the specific need for application terminology management was minimal using the standards based approach.

Specifically on SPL content we found that the initial coverage throughout the award years was not perfect, even though some SPL label covered the majority of kinds of currently prescribed drugs in outpatient settings. We could use RxNorm to bridge current coverage gaps of SPL, but any e-prescribing approach that operates purely on SPL would require the new FDA e-listing process as mandated by the FDA Amendment Act of 2007 be fully implemented, as it is expected for 2009. When FDA published product labels really do cover all of currently marketed drugs, as they should by law, then the need for other drug-terminologies that simply list and group drugs could be entirely replaced by SPL labels.

SPL had more detail on the drugs that are covered, but RxNorm and SPL have excellent agreement on the detail contained in both. The HL7 v3 SPL data is accessible with object-oriented software and relational database systems. User-defined abstraction from manufactured drugs can easily be created on the basis of detailed drug descriptions in the relational database.

We found that present public terminology including NDF-RT and SNOMED, though imperfect, can be mapped readily into the HL7 v3 framework in general and into SPL specifically. For instance, SNOMED allergy condition to allergen substance (class) linkage is exactly what it is in HL7 v3 (causative agent) and NDF-RT drug product, ingredient and substance-class structure also fits directly the format of SPL data structures. This means that SPL in its final intended form naturally serves as a hub to integrate all relevant drug knowledge and tag it with standard terminology. Before all the terminology content is delivered with standard SPL labels, our work has shown that this terminology can be added automatically (however, the

automatic augmentation process cannot avoid propagating imprecisions and errors in the underlying terminologies and knowledge bases.

We could shows that even with somewhat imprecise and incomplete terminology mapping and coverage, clinical decision support functions could be markedly improved in the laboratory over a successful in-house managed knowledge base. We showed this using drug-allergy checking in a published journal paper, and similarly with drug-interactions (not yet published). We implemented (and published) simple database query approaches to implement logically robust and fast decision support functions which we use in the e-prescribing system in the same form as in the data laboratory studies.

Our standards based methods finds 2-4 times more issues than the current production deployed method. While most of the additionally detected issues are logically justified, the increased sensitivity highlights the importance of both well-maintained chemical structure terminology and more accurate intolerance records in order to increase the overall effectiveness of this safety feature.

We found that mapping local terminology to standard terminology and SPL was possibly and that such mappings could provide value to improve the legacy application dictionaries. For example, we showed how RxNorm, NDFRT, and SNOMED-CT can be used to make inferences about the Problem List of a single patient record using the Medications List. While the sensitivity was much less than desirable, the specificity was reasonable, particularly in the context of term frequency. Furthermore, we have identified challenges and opportunities for these standards and in their utility as a knowledge base for clinical decision support.

List of Publications and Products

Papers

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