

Use of RxNorm to Exchange Codified Drug Allergy Information between Department of Veterans Affairs (VA) and Department of Defense (DoD)

Pradnya P. Warnekar, RPh, MS¹, Omar Bouhaddou, PhD¹, Fola Parrish, PharmD², Nhan Do, MD², John Kilbourne, MD³, Steven H. Brown, MD^{4,5}, Michael J. Lincoln, MD^{1,6}

¹Department of Veterans Affairs Office of Information, Salt Lake City, UT

²Department of Defense, Tricare Management Activity, Falls Church, VA

³National Library of Medicine, Bethesda, MD

⁴Department of Veterans Affairs, Nashville, TN

⁵Department of Biomedical Informatics, Vanderbilt University, Nashville TN

⁶Department of Biomedical Informatics, University of Utah, Salt Lake City, UT

Abstract

Under a congressional mandate, VA and DoD have built a framework to exchange standardized, codified patient drug allergy information through a mediation terminology. Initially, the Unified Medical Language System (UMLS) was deemed to be the most appropriate translator. After both agency files were mapped to UMLS, DoD could understand 45 percent of VA's mapped terms and VA could understand 26 percent of DoD's mapped terms. A significant portion of the non-mediated information was brand names in DoD with generic counterparts in VA. Recently, a Consolidated Health Informatics (CHI) group designated RxNorm as the standard for trade name allergies. An analysis was conducted to estimate mediation improvement using RxNorm. Both agency files were re-mapped to RxNorm. By utilizing the RxNorm defined relationships between brand names and generics and between variants of therapeutic moieties, DoD will understand 74 percent of VA terms and VA will understand 58 percent of DoD terms.

Introduction

An Executive Order from the United States President calls for all federal agencies to build and deploy interoperable electronic health record systems that are based on national standards.¹ Accordingly, VA and DoD have built a framework called the Clinical Health Data Repository (CHDR) interoperability project that allows patient data to be exchanged between the two agencies. In CHDR phase II, data within three clinical domains (drug allergies, pharmacy prescriptions, and laboratory results) is exchanged using mediation terminologies. When CHDR phase II began, there were no CHI-recommended terminology standards for the allergies domain, and UMLS was deemed to be the most suitable mediation terminology because of its wide coverage. When CHI recommended allergy standards after the start of CHDR phase II, both agencies had to plan to switch to the recommended terminologies.

This paper analyzes the required process and presents the results of switching from UMLS to RxNorm as a mediation terminology for drug allergies.

Background

Today, patient data is often distributed across disparate organizations. Fully interoperable patient information has the potential to significantly improve patient care quality and safety. Phase II of the CHDR project exchanges standardized, codified patient information between VA's Health Data Repository (HDR) and DoD's Clinical Data Repository (CDR). With no recommendations from CHI, we initially chose UMLS to be the mediation standard for the allergies domain. As the project progressed into the production phase, CHI recommended standards for the allergies domain that were endorsed by the National Committee on Vital and Health Statistics (NCVHS). RxNorm is the recommended standard for brand names. Upon further analysis, RxNorm, and particularly its built-in relationships, were found to provide considerable potential to improve the mediation success rates.

Methods

To achieve semantic interoperability between two or more systems that do not "speak the same language," data mapping needs to take place. One method to equate concepts across terminologies is direct mapping. However, this methodology is cumbersome to maintain, requiring a combinatorial explosion of mappings, and thus is not scalable. An alternative to direct mapping is mapping through mediation terminologies. Using this method, all participating systems map their content to the same standard and use that standard to exchange patient data. This process is a one-time effort, requires minimal maintenance, and is easily scalable. Thus, we chose to transfer patient information in CHDR phase II utilizing bilaterally agreed upon mediation terminologies.

Interoperability Framework

The CHDR framework consists of the components that are outlined in Table 1.² VistA is the Veterans Health Information Systems and Technology Architecture that is currently in place at VA. AHLTA is DoD's Armed Forces Health Longitudinal Technology Application.

Component	VA	DoD
EHR system	VistA	AHLTA
National patient database	HDR	CDR
Terminology mediation server	VETS*	TSB**

*VHA Enterprise Terminology Services

** Terminology Service Bureau

Table 1. CHDR framework components

VA and DoD electronic health record (EHR) systems are used extensively. For example, in VA alone, VistA runs at more than 1,400 sites of care and is used by over 75,000 providers. It is within these systems that native decision support systems operate. In each agency, standardized administrative and clinical data is aggregated in national repositories. Clinical information from these databases is translated by terminology servers and sent across the CHDR gateway service as standardized HL7 messages.

CHDR is designed to serve patients who are designated as Active Dual Consumers (ADC) (which means they can receive care at both VA and DoD facilities). When a patient becomes an ADC, all historical records pertaining to outpatient pharmacy prescriptions, allergies, and laboratory are pulled and transferred to the other agency. Subsequent care of an ADC patient results in a "push" to the partner agency as clinical transactions occur.

Content Creation

The primary purpose of this research was to compare the mediation rate of drug allergens in the two agencies using UMLS-based mediation versus RxNorm-based mediation. Our hypothesis was that RxNorm-based mediation would prove superior to UMLS-based mediation because of the rich inter-relationships in the RxNorm content.

UMLS-Based Mediation

The UMLS consists of concepts from disparate terminology systems that are integrated through common identifiers.³ UMLS version 2005 AA was selected to perform the initial mapping for drug allergies with subsequent semi-annual updates. UMLS contains the VA National Drug File

(VANDF), so most drug allergen mappings were already accomplished for VA. For allergy terms not already covered by the UMLS Metathesaurus, the command-line query tool was used. On the DoD side, an algorithm-based tool developed by Language & Computing, Inc. was used to map their allergy terms to UMLS concepts.

RxNorm-Based mediation

RxNorm is a standardized vocabulary for medications described at the prescription level. RxNorm maps equivalent concepts from various drug information sources to its standardized concepts, which are assigned concept unique identifiers (CUI). Distinct, named relationships link all concepts within RxNorm. For example, a clinical drug is linked to its ingredient, ingredient-strength, dose form, and ingredient-dose form concepts through explicit named relationships. RxNorm also includes branded counterparts, linked to its branded components.⁴ This was important for CHDR because DoD uses brand names in their drug file but VA uses generics. RxNorm's relationships between trade names and their generic equivalents and between therapeutic moiety variants promised to increase interoperability between the two agencies in the allergies domain.

The December 2006 release of RxNorm, which was synchronized with UMLS 2006 AD, was selected for the analysis. Each agency's file was first updated to the UMLS 2006 AD version and then mapped to RxNorm. (When RxNorm is synchronized with UMLS, every RxNorm concept is associated with a UMLS concept). The set of common and unique allergy concepts to each agency was determined based on the RxNorm CUIs in both files.

To build an expanded translation table, RxNorm relationships had to be leveraged. This required several queries to the RxNorm database. Initially, we focused on single ingredient trade names. A table of all single ingredient trade names with their generic counterparts was built. This list was matched with the DoD unique allergy list on the basis of trade names. The results were then matched with the VA mapping table on the basis of generic names. Thus, we obtained a table that contained all the DoD trade names that could be translated to a generic name in VA. An extract of the results of this process from the VA relationship table is shown in Table 2.

Next the investigators focused on the therapeutic moiety variant relationship. This was important because, for example, DoD has quinine hydrochloride in its file while VA has quinine. Both substances have the therapeutic moiety quinine and

neither of them should be prescribed if an allergy to either one was noted. However, they have different RxCUIs and so the quinine moiety relationship must be computable. To implement this, we undertook the following steps: Retrieve all ingredient concepts from RxNorm that participate in the “has_form” relationship. Match the ingredients with the DoD unique allergies list. Match the resulting table with the VA mapping file. Repeat the process so that ingredient concepts on either side of the relationship can be matched with the agency files. An extract of the results of this process from the VA relationship table is shown in Table 3.

Terminology Servers

VA has built VETS to store and deploy its standard terminologies. VETS includes a set of HL7 Common Terminology Services (CTS)-compliant services to support clinical applications including the CHDR framework.⁵ Every standard term in VA is assigned a VA Unique Identifier (VUID) within VETS. Unidirectional translation services translate codes between two coding systems.

Only one mapping table is currently loaded in VETS for all domains. This mapping table contains a one-to-one mapping between each VUID and a mediation terminology code. When several VUIDs are mapped

to a single mediation code, a preferred translation flag is assigned to one of the VUIDs to mark it as a preferred translation for VA inbound messages.

To support the enriched mediation strategy described above, there will be two tables: one will contain all exact mappings and will be searched first; and the second will contain related mappings and will be searched next. VETS will also communicate to CHDR whether a translation is exact or through a relationship. Accordingly, CHDR will process the HL7 message from DoD to store either textual data (brand name) and a coded triplet (equivalent generic name) or only a coded triplet. The changes will apply only to inbound messages. All outbound messages will function the same way as they do today.

Mediation Success

After mapping both agency files to RxNorm, we estimated the number of allergy terms common to both agencies that would mediate successfully. The frequency of use for these common terms in actual practice should also be taken into account. When frequency data is available, the formula to estimate the mediation success rate for an agency can be expressed as follows:

Mediation Success Rate = Sum of frequency of common concepts / Sum of frequency of all concepts

DoD Text	DoD RxCUI	Relationship	VA RxCUI	VA Text	VUID
PARLODEL	38	tradename_of	1760	BROMOCRIPTINE PREPARATION	4019639
TOPICYCLINE	211	tradename_of	10395	TETRACYCLINE PREPARATION	4017625
ADIPEX-P	332	tradename_of	8152	PHENTERMINE PREPARATION	4019891
ALFENTA	479	tradename_of	480	ALFENTANIL PREPARATION	4019597
SECTRAL	9631	tradename_of	149	ACEBUTOLOL PREPARATION	4019592
MENTAX	218315	tradename_of	47461	BUTENAFINE PREPARATION	4024054
TROVAN	220496	tradename_of	115552	TROVAFLOXACIN PREPARATION	4024108

Table 2. Examples of translation between DoD brand name allergens and equivalent VA generics through RxNorm relationships.

DoD Text	DoD RxCUI	Relationship	VA RxCUI	VA Text	VUID
TIMOLOL	10600	has_form	221172	TIMOLOL HEMIHYDRATE	4020919
TOLBUTAMIDE	10635	has_form	221173	TOLBUTAMIDE SODIUM	4017889
TRIMETHOPRIM	10829	has_form	221176	TRIMETHOPRIM SULFATE	4019528
CODEINE	2670	has_form	235412	CODEINE POLISTIREX	4019491
MEPHENTERMINE SULFATE	82042	has_form	6756	MEPHENTERMINE	4019814
ADEFOVIR DIPIVOXIL	141400	has_form	16521	ADEFOVIR	4024286
MILRINONE LACTATE	155120	has_form	52769	MILRINONE	4023601

Table 3. Examples of translation between therapeutic moiety variants utilizing RxNorm relationships

Results

UMLS-Based Mediation

The investigators found that the VA standard drug allergens list had 12,715 terms, of which 8,066 could be mapped to a UMLS concept. Thus, 37 percent of terms within the VA cannot be mapped or exchanged. The DoD file had 10,631 standard terms and all of these had maps in UMLS. Of the mapped terms, 2,735 allergy terms were shared by both agencies. As shown in Table 4, this result can be interpreted as 45 percent of VA mapped terms are understood by DoD and 26 percent of mapped terms within DoD are understood by VA.

	VA	DoD
Drug allergy terms	12715	10631
Terms mapped to UMLS	8,066 (63%)	10,631 (100%)
Unmapped terms	4,649 (37%)	0 (0%)
Distinct UMLS CUIs	6,013	10,631
Common (shared) terms	2,735 (45%)	2,735 (26%)
Unique (unshared) terms	3,278 (55%)	7,896 (74%)

Table 4. Common and unique allergy terms in VA and DoD using UMLS as the mediation terminology

RxNorm-Based Mediation

Subsequently both agency files were re-mapped to RxNorm. Of the total 6,013 UMLS CUIs in the VA mapping file, 5,204 (87 percent) could be converted to an RxNorm CUI. This is because RxNorm excludes drug classes and multi-ingredient generics as single concepts from its scope. DoD had a higher conversion rate of 97 percent. The analysis of common and unique allergy terms for the two agencies revealed that there were few overall numerical differences from UMLS, which was expected (2,687 common terms, 2,517 unique VA terms, and 7,635 unique DoD terms).

Despite these similar overall mapping numbers, by using the relationships modeled in RxNorm, there was a substantial increase in the quantity of information that could be exchanged. Thus using RxNorm, VA could understand 3,325 more concepts from DoD. This represents 32 percent increased mediation from DoD to VA. Similarly, DoD could understand 3,845 terms from the VA.

When compared to the original 2,687, this is a 22 percent gain for DoD. Figure 1 depicts the new numbers subdivided by type of relationship.

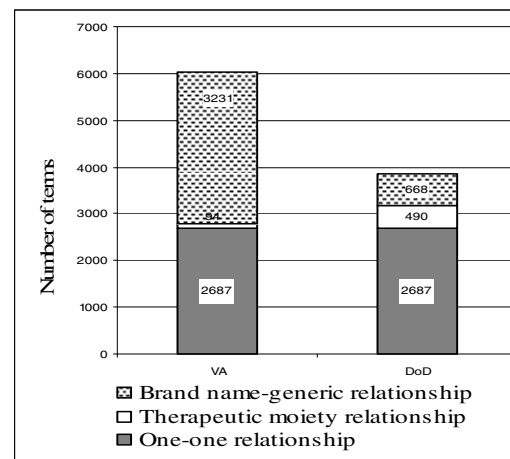


Figure 1. Increased number of mediated terms between VA and DoD by category of relationships

Discussion

Our goal in the CHDR phase II project is to achieve semantic interoperability in the allergies, pharmacy, and laboratory results domains. Given the current settings, the best way to achieve this is through data mediation. In the absence of a recommended national standard, UMLS was the obvious choice for drug allergens. There is plenty of prior research involving mapping to UMLS^{7,8}, but there is no published evidence to date of utilizing RxNorm to exchange computable patient allergy data (although CHDR has successfully utilized RxNorm for the mediation of pharmacy prescriptions⁹). Mapping to UMLS did present some challenges. First, working with UMLS requires powerful machines and database management systems. Second, there is no semantic type within UMLS that is specific to the drugs domain. Third, UMLS features duplicate synonymy for some concepts. For example, alcohol does not exist as an independent concept. But there are two other concepts in UMLS with identical semantic types that have alcohol as a synonym. So alcohol can be mapped to ethanol (C0001962) or alcohols (C0001975). Also, the release frequency of UMLS is quarterly. This is not fast enough for production systems that add new allergy terms every week.

The switch from UMLS to RxNorm as a mediation terminology for drug allergens

presents several advantages. First and foremost, RxNorm is designated as the national standard for exchanging allergies to branded drugs. The switch lets both agencies move closer to national terminology standards compliance. Second, RxNorm relationships provide additional drug information that can be used to significantly increase mediation success rates. The linkages are also vital for production systems that cannot easily change to accommodate recommended national standards. Third, RxNorm provides mappings between RxNorm CUIs and Food and Drug Administration's Unique Ingredient Identifier (FDA UNII)s, which makes the next migration simpler. Fourth, RxNorm publishes updates every month, as compared to quarterly UMLS releases.

There are some drawbacks to switching to RxNorm. First, it is not built to be a complete drug reference terminology. As a result, it does not model drug classes and multiple ingredient generics (which make up a portion of the drug allergies file in both agencies) as single terms. . This results in the need to continue using UMLS to mediate such terms. Second, both agencies will have to make the switch to RxNorm. A unilateral switch could be implemented, but this would require additional mappings, and the mediation rates would not improve in both directions. Third, in addition to content preparation, other components of the project will require modifications. VETS will have to accommodate a relationship table and change its APIs to read the table, and CHDR will have to change its HL7 messages. Similar changes must also take place on the DoD side. These changes will require resources that are always scarce.

In the current switch process, mapping between the native terminology files to RxNorm is only as good as the mapping to UMLS, because UMLS was used as the bridge to map to RxNorm. Ideally, each agency will submit its medication related terms to RxNorm and let them establish the mappings and relationships. Updated mappings can then be harvested from RxNorm every month.

After the switch to RxNorm, future plans for the project include determination of mediation rates with frequency counts, step wise migration to other CHI/HITSP allergy standards like FDA UNII)s and NDF-RT chemical drug classes.⁶ The

idea of using relationships between concepts for mediation can be extended to the pharmacy domain.

Conclusion

Interoperability through mediation is a step in the right direction if we are to build a national health information network. The switch to RxNorm as a mediation terminology is definitely beneficial for two primary reasons. First, the mediation rates improve significantly and second, both agencies are closer to compliance with national standards. It will also help in migrating to other national standards. Projects like CHDR have the potential to evaluate standards and provide feedback about their practicality, maturity, and sustainability. Endeavors of this nature should be encouraged and promoted.

References

1. <http://www.whitehouse.gov/news/releases/2004/04/20040427-4.html>
2. Bouhaddou O, Warnekar P et al. Exchange of computable patient data between the Department of Veterans Affairs (VA) and the Department of Defense (DoD): standards and terminology strategy (in preparation)
3. UMLS:<http://www.nlm.nih.gov/pubs/factsheets/umlsmeta.html>
4. RxNorm: <http://www.nlm.nih.gov/research/umls/rxnorm/index.html>
5. HL7 CTS specifications: <http://www.hl7.org>
6. HITSP_EHR Selected Standards June 2006_Final.doc
7. Zeng Q, Cimino JJ. Mapping medical vocabularies to the Unified Medical Language System. Proc AMIA Symp. 1996:105-109
8. Aronson AR. Effective mapping of biomedical text to the UMLS Metathesaurus: the MetaMap program. Proc AMIA Symp. 2001:17-21.
9. Parrish F, Do N, Bouhaddou O, Warnekar P. Implementation of RxNorm as a terminology mediation standard for exchanging pharmacy medication between federal agencies. Proc AMIA Symp. 2006:1057