1st American Systems and Services LLC

NIST NCPDP Analysis – RxNorm Support Assessment

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A. Introduction

RxNorm is a medications terminology created, curated and sponsored by the National Library of Medicine. The goal of the RxNorm vocabulary is to associate a precise description with a drug name and to link the description to all of the names from all of the source vocabularies that are associated with the same description. Every unique description in RxNorm has a unique immutable identifier. It is designed to serve the purpose of mediating between the many propriety drug terminologies currently employed by electronic health record systems.

This report provides an overview of the RxNorm terminology system and resources publically available for its implementation. While not an implementation guide, it provides a bibliography, and pointers to technical resources provided by the National Library of Medicine for those participating in the Department of Health and Human Services' and Centers for Medicare and Medicaid Meaningful Use and Certification programs.

In addition, the document provides an analysis of the SCRIPT standard's support for RxNorm with respect to the needs of the medication reconciliation process—including the prescribing of new prescriptions and interaction checking. Identification of gaps, issues and opportunities for potential future analysis.

Document sections:

RxNorm Background. Overview of the RxNorm structures and intended usage from a general perspective—apart from SCRIPT or other particular messaging standards. Description of the key concepts and relationships within the RxNorm information model.

RxNorm Relationships to Other Knowledgebases. Overview of relationships between the RxNorm "native" concepts and external drug concepts to which they can be mapped (using the UMLS Metathesaurus). Description of how concepts are mapped between external knowledgebases and RxNorm, with examples for branded medications, generics, ingredients, and compounds (including identification of limitations or challenges).

RxNorm Implementation Overview. Overview of RxNorm resources available to implementers, including RxNav, RxTerm, and the RxNorm API.

SCRIPT 10.6 Support for RxNorm. Description of SCRIPT's support for RxNorm content, for the message types included in this project's test set. Identification of each element in which RxNorm concepts can be conveyed, including population rules and any limitations or challenges that exist.

HL7 C32 CCD Support for RxNorm. Description of the CDA Medications module's support for RxNorm content, as constrained by the HITSP C32 definition. Identification of each element in which RxNorm concepts can be conveyed, including population rules and any limitations or challenges that exist.

Summary of Support, Challenges and Opportunities. Summary identification of SCRIPT version 10.6's support for RxNorm, including any gaps in the information that can be conveyed, any implementation challenges (including mapping from external knowledgebases), and variances between SCRIPT's support and that in the C32 CCD document.

B. RxNorm Background

Created by the National Library of Medicine (NLM) in 2004, RxNorm:

> … provides normalized names for clinical drugs and links its names to many of the drug vocabularies commonly used in pharmacy management and drug interaction software, including those of First Databank, Micromedex, MediSpan, Gold Standard Alchemy, and Multum. By providing links between these vocabularies, RxNorm can mediate messages between systems not using the same software and vocabulary. *[source: http://www.usgovxml.com/DataService.aspx?ds=RxNorm]*

RxNorm is a database and also a vocabulary system within itself. Utilizing the methodology created by the NLM for the Unified Medical Language System (UMLS) and its Metathesaurus , RxNorm consists of approximately 11 "source concept" terminologies (e.g., First Databank as noted above) and then includes a "value add" by establishing relationships between the source vocabularies and creating a concept unique identifier (CUI) or entity description of a given clinical drug.

A CUI is defined by the NLM for the UMLS and hence for RxNorm as:

> a Metathesaurus concept to which strings with the same meaning are linked. One of the principles of the Metathesaurus is that meanings should be preserved over time regardless of what terms (atoms) are used to express those meanings. The CUI is an identifier that uniquely represents a meaning and (ideally) over time the meaning of a CUI does not change. As sources are updated and as Metathesaurus editors discover errors or find that the meanings of terms have shifted over time, the meaning corresponding to a CUI may be altered (merged or split) or may disappear. In such cases, the changes in the meaning of the CUIs involved are tracked in the CUI history table, so that any CUI from any previous release of the Metathesaurus may always be mapped to the equivalent concept in the current Metathesaurus (if any) or may be identified as having been deleted (in which case the closest similar concept will often be specified).
> *[source: http://www.nlm.nih.gov/research/umls/new_users/glossary.html]*

An RxNorm CUI reflects the general organization of the UMLS and:

> Like the UMLS Metathesaurus as a whole, RxNorm is organized by concept. A concept is a collection of names identical in meaning at a specified level of abstraction. It serves as a means whereby strings of characters from disparate sources may be taken to name things that are the same… In RxNorm, where a normalized form exists, it is designated as the preferred form of the name (by means of its association with the TS [Term Status] field in RXNCONSO). The concept is assigned an RxNorm concept unique identifier (RXCUI) of 575803. This RXCUI always designates the same concept, no matter the form of the name and no matter in what table it is found. Drugs whose names map to the same RXCUI are taken to be the same drug—identical as to ingredients, strengths, and dose forms. Conversely, drugs that differ in any of these particulars are conceptually distinct and will have different RXCUIs. *[source: http://www.nlm.nih.gov/research/umls/rxnorm/overview.html]*

Thus RxNorm can serve as a mediator between different health care electronic record systems and terminology systems. An RxNorm clinical drug name reflects all of the active ingredients, strengths, and dose form comprising a drug. When any of these elements vary, a new RxNorm drug name is created as a separate concept. Thus, an RxNorm name should exist for every strength and dose of every available combination of clinically significant ingredients .

The RxCUI yields a unique identifier. But also included within RxNorm are a set of relationships which serve to describe the relationships between and the composition of concepts. In the instance of RxNorm, a concept is composed of definitional attributes or relationships, described in the following section.

The Elements of a Normalized Form

RxNorm follows a standard format in the naming of clinical drugs. Drugs named in disparate ways in various other vocabularies are linked to a normalized name prepared according to RxNorm's naming conventions.

The normalized form of the name of a clinical drug may be thought of as being composed of a number of elements, each a concept in its own right. Each element of the normalized form can be identified by the value of the TTY [Term Type] field of RXNCONSO. The possible values are as follows:

TTY	Name	Definition	Example(s)
IN	Ingredient	A compound or moiety that gives the drug its distinctive clinical properties. The preferred name is usually the USAN name.	Fluoxetine, Insulin, Isophane, Human Gentamicin Sulfate (USP)
PIN	Precise Ingredient	A specified form of the ingredient that may or may not be clinically active. Most precise ingredients are salt or isomer forms.	Fluoxetine Hydrochloride
MIN	Multiple Ingredients	Two or more ingredients created from SCDF. In rare cases when IN/PIN or PIN/PIN combinations of the same base ingredient exist, created from SCD.	Fluoxetine / Olanzapine
DF	Dose Form	A complete list of Dose Forms can be found in Appendix 2 of the RxNorm Documentation.	Topical Solution, Oral Tablet
SCDC	Semantic Clinical Drug Component	Ingredient plus strength—see section on Rules and Conventions, below, for units of measurement and for rules pertaining to the calculation of	Fluoxetine 4 MG/ML

TTY	Name	Definition	Example(s)
		strengths.	
SCDF	Semantic Clinical Drug Form	Ingredient plus dose form.	Fluoxetine Oral Solution
SCD	Semantic Clinical Drug	Ingredient plus strength and dose form.	Fluoxetine 4 MG/ML Oral Solution
BN	Brand Name	A proprietary name for a family of products containing a specific active ingredient.	Prozac
SBDC	Semantic Branded Drug Component	Branded ingredient plus strength.	Fluoxetine 4 MG/ML [Prozac]
SBDF	Semantic Branded Drug Form	Branded ingredient plus dose form.	Fluoxetine Oral Solution [Prozac]
SBD	Semantic Branded Drug	Ingredient, strength, and dose form plus brand name.	Fluoxetine 4 MG/ML Oral Solution [Prozac]
SY	Synonym of another TTY	Given for clarity.	Prozac 4 MG/ML Oral Solution
BPCK	Brand Name Pack	Branded Drug Delivery Device.	{12 (Ethinyl Estradiol 0.035 MG / Norethindrone 0.5 MG Oral Tablet) / 9 (Ethinyl Estradiol 0.035 MG / Norethindrone 1 MG Oral Tablet) / 7 (Inert Ingredients 1 MG Oral Tablet) } Pack [Leena 28 Day]
GPCK	Generic Pack	Generic Drug Delivery Device.	{11 (varenicline 0.5 MG Oral Tablet) / 42 (varenicline 1 MG Oral Tablet) } Pack

C. RxNorm Relationships to Other Knowledgebases

As noted earlier, RxNorm is both a terminology itself as well as a bridge between proprietary and open source pharmaceutical resources. It is important to remember that RxNorm:

1. Provides the concept unique identifier for a concept;
2. Identifies that concept across the source vocabularies which are:

SAB	Source Name
GS	Gold Standard Alchemy
MDDB	Medi-Span Master Drug Data Base
MMSL	Multum MediSource Lexicon
MMX	Micromedex RED BOOK
MSH	Medical Subject Headings (MeSH)
MTHFDA	FDA National Drug Code Directory
MTHSPL	FDA Structured Product Labels
NDDF	First DataBank NDDF Plus Source Vocabulary
NDFRT	Veterans Health Administration National Drug File - Reference Terminology
SNOMEDCT	SNOMED Clinical Terms (drug information)
VANDF	Veterans Health Administration National Drug File

RxNorm also provides the most definitive list of National Drug Codes (NDC's) by virtue of its collection and coordination of those codes across the various knowledge vendors. Per a recent teleconference conducted with Dr. John Kilbourne of the National Library Of Medicine's RxNorm program and the First American and NIST teams.

D. RxNorm Implementation Overview

Given all of the above information, how does one actually use RxNorm ? Are there tools available to aid in the review and implementation of the terminology? The subsequent sections of this paper will address the NLM's specific tooling for RxNorm: RxNav, RxTerms, and the RxNorm API.

The reader is, however, encouraged to review the background information available on the NLM's website and the articles/presentations noted in Appendix A. The structure of both the UMLS and methodology behind RxNorm is highly complex. Section One of this document serves only as brief overview to familiarize the reader with the minimum amount of information needed to work with the RxNorm database.

RxNorm: Tooling: RxNav , RxTerms and the RxNorm API

As noted previously, RxNorm is considered a part of the Unified Medical Language System (UMLS). The UMLS comes with a suite of tools including the UMLS Terminology Service (UTS), MetaMorphoSys and a specific set of tools for use with RxNorm: RxNav which allows the user to browse RxNorm specific content directly from the UMLS; RxTerms the interface terminology for RxNorm and the RxNorm Applied Programming Interface (API). Knowledge of and utilization of these programs is critical for the understanding of and eventual use/deployment of RxNorm into a given system.

RxNav

RxNav is a browser for RxNorm content within the UMLS. Per the support documentation provided by the NLM, RxNav intended use is for those who wish to familiarize themselves with the entire content of RxNorm in detail in a graphical format.

RxNav is a browser for several drug information sources, including RxNorm, RxTerms and NDF-RT. RxNav finds drugs in RxNorm from the names and codes in its constituent vocabularies. RxNav displays links from clinical drugs, both branded and generic, to their active ingredients, drug components and related brand names. RxNav also provides lists of NDC codes and links to package inserts in DailyMed. http://rxnav.nlm.nih.gov/

Rx NAV Example:

The NLM Support documentation for RxNav walks a user through the steps of using RxNav. Example driven, it steps a developer or clinician through the processes needed to identify a specific drug within the RxNorm terminology and its source vocabularies. The documentation may be found at: http://rxnav.nlm.nih.gov/

Types of searching within RxNav:

Search By	Example	Details
String	Tylenol	the concept name strings
AMP ID	2050	the Alchemy Marketed Product Id (AMP ID) from Gold Standard Alchemy (SAB:GS)
GCN_SEQNO	009172	the Generic Code Sequence Number from First Databank Inc (SAB:NDDF)
GFC	108077	the Generic Formula Code (GFC) from Micromedex DRUGDEX (SAB:MMX)
GPPC	14559	the first five characters of the Generic Product Packaging Code from Master Drug Data Base (SAB:MDDB). Medi-Span,

Search By	Example	Details
		a division of Wolters Kluwer Health
HIC_SEQN	004489	the ingredient identifier from First Databank Inc (SAB:NDDF)
LISTING_SEQ_NO	284438	the FDA generated unique identification number for each product from FDA National Drug Code Directory (SAB:MTHFDA)
MESH	D000212	a Subject Medical Headings (MeSH) identifier from the National Library of Medicine (SAB:MSH).
MMSL_CODE	CD1001	a derived identifier that combines the Term type (TTY) and the Multum Mediasource Lexicon (SAB:MMSL) numeric code. First two letters represent the term type: BD, BN, CD, GN or IN.
NDC	00045018618	the National Drug Code (NDC) from the National Drug Code Directory
NUI	N0000170281	the National Drug File Reference Terminology (NDF-RT) Unique Identifier (SAB:NDFRT)
RXCUI	202433	the RxNorm concept unique identifier
SNOMED ID	1039008	the SNOMED CT concept identifier from SNOMED Clinical Terms drug information (SAB:SNOMEDCT). SNOMED International
SPL_SET_ID	1C5BC1DD-E9EC-44C1-9281-67AD482315D9	the FDA Structured Product Label Set Identifier
UMLS CUI	C0000266	the Unified Medical Language System (UMLS) Concept Unique Identifier

Search By	Example	Details
UNII_CODE	LVX8N1UT73	the FDA Unique Ingredient Identifier Code.
VUID Number	4021359	the Veterans Health Administration Unique Identifier from the Veterans Health Administration National Drug File (SAB:VANDF)

RxTerms

RxTerms is the user interface project being undertaken by the NLM to support the incorporation of RxNorm into applications.

RxTerms is a drug interface terminology derived from RxNorm. By reorganizing the drug information into two dimensions as prescribers do when writing prescriptions and by eliminating drug names that are less likely to be needed in a prescribing environment, RxTerms helps the user to efficiently enter complete prescription orders. Preliminary evaluation of RxTerms using a list of most commonly prescribed drugs showed that its coverage was very good (99% for both generic and branded drug names). There was significant efficiency gain compared to using the unprocessed RxNorm names. RxTerms fills the gap for a free, up-to-date drug interface terminology that is linked to RxNorm, the U.S. designated standard for clinical drugs.

Implementers may wish to consider RxTerms as a data entry option. RX Terms is, as noted previously concept based and has the following structure:

- Brand name
- Display name
- Display name synonym
- Full generic name
- Full name
- Generic RxCUI
- Dose form
- Route
- RxCUI
- RxNorm dose form
- Strength
- Suppress
- Term type

Queries can be run using RxTerms using the RxTerms API newly available from the NLM.

RxNorm API

The RxNorm API is a web service for accessing the current RxNorm data set. Below is a summary of operations that can be performed using the API.

Operation	Description
findRxcuiById	Search for an identifier from another vocabulary and return the RXCUIs of any concepts which have an RxNorm term as a synonym or have that identifier as an attribute.
findRxcuiByString	Search for a name in the RxNorm data set and return the RXCUIs of any concepts which have that name as an RxNorm term or as a synonym of an RxNorm term.
getAllRelatedInfo	Get all the related RxNorm concepts for a given RxNorm identifier. This includes concepts of term types "IN", "BN", "SBD", "SBDC", "SBDF", "SCD", "SCDC", "SCDF", "DF", "BPCK" and "GPCK".
getDrugs	Get the drug products associated with a specified name. The name can be an ingredient, brand name, clinical drug form, branded drug form, clinical drug component, or branded drug component.
getIdTypes	Get the valid identifier types of the RxNorm data set.
getMultiIngredBrand	Get the brands that contain all the specified ingredients. Note that the brands returned may contain other ingredients in addition to those specified.
getNDCs	Get the National Drug Codes (NDCs) for the RxNorm concept
getProprietaryInformation	Get the concept information associated with the concept for the specified sources. The user must have a valid UMLS license and be able to access the UMLSKS authority service to obtain proxy tickets to use this function.
getRelatedByRelationship	Get the related RxNorm identifiers of an RxNorm concept specified by a relational attribute.
getRelatedByType	Get the related RxNorm identifiers of an RxNorm concept

Operation	Description
	specified one or more term types.
getRelaTypes	Get the relationship names in the RxNorm data set.
getRxConceptProperties	Get the RxNorm Concept properties
getRxNormVersion	Get the version of the RxNorm data set
getSpellingSuggestions	Get spelling suggestions for a given term. The suggestions are RxNorm terms contained in the current version.
getTermTypes	Get the valid term types in the RxNorm data set
getUMLSVersion	Get Unified Medical Language System (UMLS) version

The above represents the service that allows queries to be made via the RxNorm API. The RxNorm API will query the RxNorm database which is updated on an as needed basis: be it daily, weekly or monthly.

Implementers may instantiate the UMLS into their applications and then update and then deploy the RxNorm API in order to map their proprietary data to the RxNorm standard.

The RxNorm API functions are detailed in by the NLM in:
http://mor.nlm.nih.gov/download/rxnav/RxNormAPI.html

E. SCRIPT 10.6 Incorporation of RxNorm

The SCRIPT standard enables medications to be identified using RxNorm codes in prescription messages (e.g., new prescription, prescription change) and in the medication history message. Four RxNorm concept types may be used to describe a prescribed, dispensed, or requested medication:

- RxNorm Semantic Clinical Drug (SCD)
- RxNorm Semantic Branded Drug (SBD)
- RxNorm Generic Package (GPCK)
- RxNorm Branded Package (BPCK)

When present in a SCRIPT message, the RxNorm code is to be used as the primary identification for the referenced drug. For example, NCPDP guidance directs the pharmacy receiving a new prescription message containing an RxNorm reference to use the RxNorm code to locate the drug to dispense, and to use the accompanying drug description to validate that drug selection.

It is expected that the use of RxNorm codes in SCRIPT will replace the current convention whereby a "representative NDC" is used to identify a prescribing-level medication (a medication at the drug name / strength / dose form level). When RxNorm codes are in use, the NDC code serves solely to identify a particular packaged product—for example a dispensed product in a prescription renewal request message or medication history message.

Relevant SCRIPT Elements. RxNorm codes are indicated using the DrugDBCode and DrugDBQualifier elements (DRU-010-I013-08-1154 Reference Number and DRU-010-I013-09-1153 Reference Qualifier in the EDIFACT version of SCRIPT). To identify an ingredient in a compound drug, the implementer should place the RxNorm reference in the ItemNumber and CompoundProductIDQualifier elements (Compound Ingredient Item Number CPD- 010-I017-03-7140 and Code List Responsibility Agency CPD-010-I017-04-3055 in the EDIFACT version).

Source: NCPDP. *SCRIPT Implementation Recommendations* document, section: RxNorm Guidance for SCRIPT.

F. HL7 C32 CCD Incorporation of RxNorm

As noted in previous discussions, RxNorm is the standard specified by several US Federal organizations and programs (e.g. CMS, Meaningful Use certification) for exchange of pharmaceutical related information. Primary among the artifacts that convey patient clinical information including medications is the HITSP C32 document, derived from the HL7 Continuity of Care/Clinical Data Architecture.

C32. The Summary Documents Using HL7 Continuity of Care Document (CCD) Component describes the document content summarizing a consumer's medical status for the purpose of information exchange. The content may include administrative (e.g., registration, demographics, insurance, etc.) and clinical (problem list, medication list, allergies, test results, etc) information. This Component defines content in order to promote interoperability between participating systems such as Personal Health Record Systems (PHRs), Electronic Health Record Systems (EHRs), Practice Management Applications and others

C32 specifies the "container" for the specific clinical information. C83 provides the payload within the container: the terminologies or standards by which an organization must report their data.

Within C83, RxNorm is cited for two clinical domains: Medication Lists and ePrescribing. Per Meaningful Use certification direction, one can utilize RxNorm or its source vocabularies to meet 2011 goals. However, by 2013, RxNorm alone must be used. Confusion as to what constituted a source for RxNorm has been noted in many venues. With the 2013 regulations now being finalized, the use of a single RxNorm code, not a bridge code (vendor-based proprietary information mapped to RxNorm), should eliminate much of the confusion around compliance. Unfortunately, so called road maps or transition guidance has not been specified by HHS. This gap could be addressed by three artifacts:

- an overall guide to RxNorm: what is it, how it was developed and what tools are available
- an implementation guide specifically designed for RxNorm including into NCPDP script
- maintenance of specifications within CCD/CDA2 within the medication domain.

G. Summary of Support, Challenges and Opportunities

There is a perceived need within the community for an RxNorm implementation guide. Olivier Bodenreider of the NLM cited several requests for such an activity specifically using the ONC/MU/Certification use cases.

The 1st American Systems and Services contract group would recommend the following next steps to NIST for their testing and implementation compliance suites:

1. The current RxNorm, RxNorm API and RxNav tools are useful and powerful, but the non-informed implementer could easily overlook these tools and mistakenly use the UMLS documentation to attempt to perform the same functions.

   Recommended action: Work with the National Library of Medicine to develop an overall guide to RxNorm with specific attention paid to the RxNorm API. This documentation could be made available for distribution by the Office of the National Coordinator for the vendor community and other standards development organizations (e.g. NCPDP), and could also serve as internal NIST process documentation.

2. Specific use cases can and should be developed to meet implementation guide needs. For example: How does one walk through First Data Bank to RxCUI to submit to NIST validation?" This would aid those meeting 2011 requirements (use of RxNorm source vocabularies) and provide direction on use of RxNorm to support 2013 compliance.

   Recommended action: Work closely with the National Library of Medicine and the HL7 and NCPDP communities in resource sharing. For example, in the context of HL7, this activity could include such recommendations as the use of the CD data type within C83 and the translation code to capture the current native proprietary codes and the internal mappings to RxNorm. This could be considered both a quality assurance exercise as well as development of validation of RxNorm mappings.

Appendix A – Bibliography

1. J Am Med Inform Assoc. 2010 Nov 1;17(6):714-9.

Comparing and evaluating terminology services application programming interfaces:

RxNav, UMLSKS and LexBIG.

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To facilitate the integration of terminologies into applications, various

terminology services application programming interfaces (API) have been developed

in the recent past. In this study, three publicly available terminology services

API, RxNav, UMLSKS and LexBIG, are compared and functionally evaluated with

respect to the retrieval of information from one biomedical terminology, RxNorm,

to which all three services provide access. A list of queries is established

covering a wide spectrum of terminology services functionalities such as finding

RxNorm concepts by their name, or navigating different types of relationships.

Test data were generated from the RxNorm dataset to evaluate the implementation

of the functionalities in the three API. The results revealed issues with various

aspects of the API implementation (e.g., handling of obsolete terms by LexBIG) and

documentation (e.g., navigational paths used in RxNav) that were subsequently

addressed by the development teams of the three API investigated. Knowledge about

such discrepancies helps inform the choice of an API for a given use case.

PMCID: PMC3000749 [Available on 2011/11/8]

PMID: 20962136 [PubMed - indexed for MEDLINE]

2. J Med Syst. 2010 Aug;34(4):651-7. Epub 2009 Apr 3.

Achieving standardized medication data in clinical research studies: two approaches and applications for implementing RxNorm.

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The National Institutes of Health has proposed a roadmap for clinical research.

Test projects of this roadmap include centralized data management for distributed

research, the harmonization of clinical and research data, and the use of data

standards throughout the research process. In 2003, RxNorm was named as a

standard for codifying clinical drugs. Clinical researchers looking to implement

RxNorm have few template implementation plans. Epidemiological studies and

clinical trials (types of clinical research) have different requirements for

model standards and best implementation tools. This paper highlights two

different (epidemiological and intervention) clinical research projects, their

unique requirements for a medication standard, the suitability of RxNorm as a

standard for each, and application and process requirements for implementation.

It is hoped that our experience of selecting and implementing the RxNorm standard

to address varying study requirements in both domestic and international settings

will be of value to other efforts.

3. J Am Med Inform Assoc. 2010 Jul-Aug;17(4):432-9.

Analyzing categorical information in two publicly available drug terminologies:

RxNorm and NDF-RT.

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BACKGROUND: The RxNorm and NDF-RT (National Drug File Reference Terminology) are a suite of terminology standards for clinical drugs designated for use in the US federal government systems for electronic exchange of clinical health information. Analyzing how different drug products described in these terminologies are categorized into drug classes will help in their better organization and classification of pharmaceutical information.

METHODS: Mappings between drug products in RxNorm and NDF-RT drug classes were extracted. Mappings were also extracted between drug products in RxNorm to five high-level NDF-RT categories: Chemical Structure; cellular or subcellular Mechanism of Action; organ-level or system-level Physiologic Effect; Therapeutic Intent; and Pharmacokinetics. Coverage for the mappings and the gaps were evaluated and analyzed algorithmically.

RESULTS: Approximately 54% of RxNorm drug products (Semantic Clinical Drugs) were found not to have a correspondence in NDF-RT. Similarly, approximately 45% of drug products in NDF-RT are missing from RxNorm, most of which can be attributed to differences in dosage, strength, and route form. Approximately 81% of Chemical Structure classes, 42% of Mechanism of Action classes, 75% of Physiologic Effect classes, 76% of Therapeutic Intent classes, and 88% of Pharmacokinetics classes were also found not to have any RxNorm drug products classified under them. Finally, various issues regarding inconsistent mappings between drug concepts were identified in both terminologies.

CONCLUSION: This investigation identified potential limitations of the existing

classification systems and various issues in specification of correspondences

between the concepts in RxNorm and NDF-RT. These proposals and methods provide

the preliminary steps in addressing some of the requirements.

PMCID: PMC2995643 [Available on 2011/7/8]

PMID: 20595311 [PubMed - indexed for MEDLINE]

4. J Biomed Inform. 2009 Jun;42(3):558-70. Epub 2009 Apr 24.

A graph-based approach to auditing RxNorm.

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OBJECTIVES: RxNorm is a standardized nomenclature for clinical drug entities

developed by the National Library of Medicine. In this paper, we audit relations

in RxNorm for consistency and completeness through the systematic analysis of the

graph of its concepts and relationships.

METHODS: The representation of multi-ingredient drugs is normalized in order to

make it compatible with that of single-ingredient drugs. All meaningful paths

between two nodes in the type graph are computed and instantiated. Alternate

paths are automatically compared and manually inspected in case of inconsistency.

RESULTS: The 115 meaningful paths identified in the type graph can be grouped

into 28 groups with respect to start and end nodes. Of the 19 groups of alternate

paths (i.e., with two or more paths) between the start and end nodes, 9 (47%)

exhibit inconsistencies. Overall, 28 (24%) of the 115 paths are inconsistent with

other alternate paths. A total of 348 inconsistencies were identified in the

April 2008 version of RxNorm and reported to the RxNorm team, of which 215 (62%)

had been corrected in the January 2009 version of RxNorm.

CONCLUSION: The inconsistencies identified involve missing nodes (93), missing

links (17), extraneous links (237) and one case of mix-up between two

ingredients. Our auditing method proved effective in identifying a limited number

of errors that had defeated the quality assurance mechanisms currently in place

in the RxNorm production system. Some recommendations for the development of

RxNorm are provided.

PMCID: PMC2722378

PMID: 19394440 [PubMed - indexed for MEDLINE]

5. AMIA Annu Symp Proc. 2009 Nov 14;2009:391-5.

STRIDE--An integrated standards-based translational research informatics platform.

Lowe HJ, Ferris TA, Hernandez PM, Weber SC.

Stanford Center for Clinical Informatics, Stanford University, Stanford CA, USA.

STRIDE (Stanford Translational Research Integrated Database Environment) is a

research and development project at Stanford University to create a

standards-based informatics platform supporting clinical and translational

research. STRIDE consists of three integrated components: a clinical data

warehouse, based on the HL7 Reference Information Model (RIM), containing

clinical information on over 1.3 million pediatric and adult patients cared for

at Stanford University Medical Center since 1995; an application development

framework for building research data management applications on the STRIDE

platform and a biospecimen data management system. STRIDE's semantic model uses

standardized terminologies, such as SNOMED, RxNorm, ICD and CPT, to represent

important biomedical concepts and their relationships. The system is in daily use

at Stanford and is an important component of Stanford University's CTSA (Clinical

and Translational Science Award) Informatics Program.

PMCID: PMC2815452

PMID: 20351886 [PubMed - in process]

6. AMIA Annu Symp Proc. 2009 Nov 14;2009:244-8.

Automated mapping of pharmacy orders from two electronic health record systems to RxNorm
within the STRIDE clinical data warehouse.

Hernandez P, Podchiyska T, Weber S, Ferris T, Lowe H.

Center for Clinical Informatics, Stanford University, Stanford, CA, USA.

The Stanford Translational Research Integrated Database Environment (STRIDE)

clinical data warehouse integrates medication information from two Stanford

hospitals that use different drug representation systems. To merge this pharmacy

data into a single, standards-based model supporting research we developed an

algorithm to map HL7 pharmacy orders to RxNorm concepts. A formal evaluation of

this algorithm on 1.5 million pharmacy orders showed that the system could

accurately assign pharmacy orders in over 96% of cases. This paper describes the

algorithm and discusses some of the causes of failures in mapping to RxNorm.

PMCID: PMC2815471

PMID: 20351858 [PubMed - in process]

7. AMIA Annu Symp Proc. 2008 Nov 6:46-50.

Evaluating the technical adequacy of electronic prescribing standards: Results of an expert panel process.

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To support more informed prescribing decisions, e-prescribing systems need data on patients' medication histories and their drug-specific insurance coverage. We used an expert panel process to evaluate the technical adequacy of two standards for delivering this information, the Medication History function of the NCPDP SCRIPT Standard and the NCPDP Formulary and Benefit Standard. Methods: We convened a panel representing 14 organizations that had experience with these standards. Experts within each organization submitted narrative responses and ratings assessing the standards in 6 domains, including data quality, completeness, usability, and interoperability. Areas of disagreement were discussed in recorded teleconferences. Narrative was analyzed using a grounded-theory approach. Results: Panelists agreed that the structure of the Medication History Standard was adequate for delivering accurate and complete information but implementation problems made the data difficult to use for decision support. The panel also agreed that the Formulary and Benefit Standard was adequate to deliver formulary status lists, but other parts of the standard were not used consistently and group-level variations in coverage were not represented. A common problem for both standards was the lack of unambiguous drug identifiers; panelists agreed that RxNorm deserves further evaluation as a solution to this problem. Conclusions: A panel of industry experts found the basic structure of these two standards to be technically adequate, but to enable benefits for

patient care, improvements are needed in the standards' implementation.

PMCID: PMC2656071

PMID: 18999287 [PubMed - indexed for MEDLINE]

8. AMIA Annu Symp Proc. 2008 Nov 6:86-90.

Medication and indication linkage: A practical therapy for the problem list?

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Background: Establishing a relationship between medications and diagnoses within a functioning electronic medical record system (EMR) has many valuable applications, such as improving the quality and utility of the problem list to support better decisions. Methods: 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 National Drug File Reference Terminology, and SNOMED-CT (SCT)standard terminologies and mappings we evaluated the linkage for local concept terms for medications and problems (diagnoses & complaints).Results: We were able to map 24,398 candidates as 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. Conclusions: Medications can be mapped by machine to a disease/ disorder using established terminology standards. This mapping may inform many knowledge management and decision support features in an EMR.

PMCID: PMC2655999

PMID: 18999215 [PubMed - indexed for MEDLINE]

9. AMIA Annu Symp Proc. 2008 Nov 6:1066.

Integrating information from disparate sources: the Walter Reed National Surgical Quality Improvement Program Data Transfer Project.

Nelson V, Li F, Green S, Tamura T, Liu JM, Class M.

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The Walter Reed National Surgical Quality Improvement Program Data Transfer web module integrates with medical and surgical information systems, and leverages outside standards, such as the National Library of Medicine's RxNorm, to process surgical and risk assessment data. Key components of the project included a needs assessment with nurse reviewers and a data analysis for federated (standards were locally controlled) data sources. The resulting interface streamlines nurse reviewer workflow by integrating related tasks and data.

PMID: 18999090 [PubMed - indexed for MEDLINE]

10. AMIA Annu Symp Proc. 2008 Nov 6:591-5.

Using the RxNorm web services API for quality assurance proposes.

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Auditing large, rapidly evolving terminological systems is still a challenge. In the case of RxNorm, a standardized nomenclature for clinical drugs, we argue that quality assurance processes can benefit from the recently released application programming interface (API) provided by RxNav. We demonstrate the usefulness of

the API by performing a systematic comparison of alternative paths in the RxNorm

graph, over several thousands of drug entities. This study revealed potential

errors in RxNorm, currently under review. The results also prompted us to modify

the implementation of RxNav to navigate the RxNorm graph more accurately. The

RxNav web services API used in this experiment is robust and fast.

PMCID: PMC2656097

PMID: 18999038 [PubMed - indexed for MEDLINE]

11. AMIA Annu Symp Proc. 2008 Nov 6:227-31.

RxTerms - a drug interface terminology derived from RxNorm.

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A good interface terminology is an essential component of any Computerized

Provider Order Entry system. RxTerms is a drug interface terminology derived from

RxNorm. By reorganizing the drug information into two dimensions as prescribers

do when writing prescriptions and by eliminating drug names that are less likely

to be needed in a prescribing environment, RxTerms helps the user to efficiently

enter complete prescription orders. Preliminary evaluation of RxTerms using a

list of most commonly prescribed drugs showed that its coverage was very good

(99% for both generic and branded drug names). There was significant efficiency

gain compared to using the unprocessed RxNorm names. RxTerms fills the gap for a

free, up-to-date drug interface terminology that is linked to RxNorm, the U.S.

designated standard for clinical drugs.

PMCID: PMC2655997

PMID: 18998891 [PubMed - indexed for MEDLINE]

12. Inform Health Soc Care. 2008 Sep;33(3):151-7.

The pharmaceutical management system at Shade Tree Family Clinic: a medical student-run free clinic's experience.

Rosenbaum BP, Patel SG, Guyer DL, Dunn SR, Herceg ME, Knox CK, Miller RF.

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The Shade Tree Family Clinic (STFC) is a student-run free walk-in health clinic

opened by Vanderbilt University medical students in October 2005 to address the

acute and chronic health needs of the underinsured community in East Nashville.

STFC founders decided that the clinic would provide complete medical care,

including dispensing commonly prescribed medications at no charge to patients.

After several months of managing the inventory in a log book, a medical student

author created a Web-based pharmaceutical tracking system to manage the

medication formulary. In the process, the authors found little literature

available addressing the logistics of setting up an electronic pharmacy system.

The system created uses the freely available RxNorm and US Department of Veterans

Affairs National Drug File Reference Terminology databases for medication and

classification data. Incorporation of these databases allows medical students to

dispense and restock medications with ease. The system ensures accurate data

entry, improves efficiency, and facilitates continuity of care at a clinic

staffed by hundreds of different students and physicians. The STFC pharmaceutical

tracking system has facilitated the acquisition and efficient management of

medications and consequently has had a great impact on the success of STFC.

PMID: 18850398 [PubMed - indexed for MEDLINE]

13. AMIA Annu Symp Proc. 2007 Oct 11:781-5.

Use of RxNorm to exchange codified drug allergy information between Department of Veterans Affairs (VA) and Department of Defense (DoD).

Warnekar PP, Bouhaddou O, Parrish F, Do N, Kilbourne J, Brown SH, Lincoln MJ.

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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.

PMCID: PMC2655912

PMID: 18693943 [PubMed - indexed for MEDLINE]

14. AMIA Annu Symp Proc. 2007 Oct 11:646-50.

Assessing the impact of HL7/FDA Structured Product Label (SPL) content for

medication knowledge management.

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The amount and quality of the SPL drug knowledge which has been released so far is assessed. All published labels were loaded into a relational database and classified to create vendor-independent descriptions. While SPL labels cover only 23% of RxNorm clinical drugs, they still describe 78% 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. In the interim, existing gaps can be temporarily closed with RxNorm or other sources.

Extraction and mapping of drug names from free text to a standardized nomenclature.

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Free text fields are often used to store clinical drug data in electronic health records. The use of free text facilitates rapid data entry by the clinician. Errors in spelling, abbreviations, and jargon, however, limit the utility of these data. We designed and implemented an algorithm, using open source tools and RxNorm, to extract and normalize drug data stored in free text fields of an anesthesia electronic health record. The algorithm was developed using a training set containing drug data from 49,518 cases, and validated using a validation set

containing data from 14,655 cases. Overall sensitivity and specificity for the

validation set were 92.2% and 95.7% respectively. The mains sources of error were

misspellings and unknown but valid drug names. These preliminary results

demonstrate that free text clinical drug data can be efficiently extracted and

mapped to a controlled drug nomenclature.

PMCID: PMC2655777

PMID: 18693874 [PubMed - indexed for MEDLINE]

16. Year Med Inform. 2008:67-79.

Biomedical ontologies in action: role in knowledge management, data integration and decision support.

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OBJECTIVES: To provide typical examples of biomedical ontologies in action,

emphasizing the role played by biomedical ontologies in knowledge management,

data integration and decision support.

METHODS: Biomedical ontologies selected for their practical impact are examined

from a functional perspective. Examples of applications are taken from

operational systems and the biomedical literature, with a bias towards recent

journal articles.

RESULTS: The ontologies under investigation in this survey include SNOMED CT, the

Logical Observation Identifiers, Names, and Codes (LOINC), the Foundational Model

of Anatomy, the Gene Ontology, RxNorm, the National Cancer Institute Thesaurus,

the International Classification of Diseases, the Medical Subject Headings (MeSH)

and the Unified Medical Language System (UMLS). The roles played by biomedical

ontologies are classified into three major categories: knowledge management

(indexing and retrieval of data and information, access to information, mapping

among ontologies); data integration, exchange and semantic interoperability; and

decision support and reasoning (data selection and aggregation, decision support,

natural language processing applications, knowledge discovery).

CONCLUSIONS: Ontologies play an important role in biomedical research through a

variety of applications. While ontologies are used primarily as a source of

vocabulary for standardization and integration purposes, many applications also

use them as a source of computable knowledge. Barriers to the use of ontologies

in biomedical applications are discussed.

PMCID: PMC2592252

PMID: 18660879 [PubMed - indexed for MEDLINE]

Exchange of computable patient data between the Department of Veterans Affairs (VA) and the Department of Defense (DoD): terminology mediation strategy.

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Complete patient health information that is available where and when it is needed

is essential to providers and patients and improves healthcare quality and

patient safety. VA and DoD have built on their previous experience in patient

data exchange to establish data standards and terminology services to enable

real-time bi-directional computable (i.e., encoded) data exchange and achieve

semantic interoperability in compliance with recommended national standards and the eGov initiative. The project uses RxNorm, UMLS, and SNOMED CT terminology standards to mediate codified pharmacy and allergy data with greater than 92 and 60 percent success rates respectively. Implementation of the project has been well received by users and is being expanded to multiple joint care sites. Stable and mature standards, mediation strategies, and a close relationship between healthcare institutions and Standards Development Organizations are recommended to achieve and maintain semantic interoperability in a clinical setting.

PMCID: PMC2274797

PMID: 18096911 [PubMed - indexed for MEDLINE]

Trans-Atlantic data harmonization in the classification of medicines and dietary supplements: a challenge for epidemiologic study and clinical research.

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OBJECTIVES: As international scientific collaboration increases, there is a growing requirement for research data to be comparable among countries. Despite the importance of medication and dietary supplement data in research, there are no international standards for the collection and storage of these data. In the absence of such standards, we needed to adopt a strategy for classification and coding of medications and dietary supplements to meet demands of our multi-national study.

METHODS: Given the inter-country variations in nomenclature that characterize

prescription, over-the-counter (OTC) medications, traditional herbal medicines,

and dietary supplements, we adopted RxNorm as a data standard for medication

data, and developed an independent system that extends this standard and allows

for flexible and scalable data collection for dietary supplements.

RESULTS: RxNorm was implemented in May 2005 and as of July 2006, coverage has

been 99%, at the level of active ingredients, of all the medications reported in

our study. Development of a dietary supplement database began in August 2005, and

has thus far coded some 1200 dietary supplements and 650 infant formula products

and forms from the four countries in our study.

CONCLUSION: The methods we have used to collect, store, and manage medication and

dietary supplement data serve as interim solutions until international standards

are developed. It is hoped that such standards will ultimately emerge, and that

our strategy and data model will be of value in other research environments in

the immediate future.

PMCID: PMC2259273

PMID: 17289429 [PubMed - indexed for MEDLINE]

19. AMIA Annu Symp Proc. 2006:1057.

Implementation of RxNorm as a terminology mediation standard for exchanging pharmacy medication between federal agencies.

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The federal government is working toward its goal of achieving interoperability

between health information systems through several multi-agency efforts. While

some interoperability partnerships exist between federal agencies, only a few

systems are involved and these projects have proven difficult to implement. This

paper describes the process of implementing an interoperable standard for

exchanging computable pharmacy data between the Department of Defense (DoD) and

the Department of Veterans Affairs (VA).

PMCID: PMC1839491

PMID: 17238676 [PubMed - indexed for MEDLINE]

20. Year Med Inform. 2006:124-35.

The practical impact of ontologies on biomedical informatics.

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OBJECTIVES: To examine recent research work in the development and evaluation of

controlled biomedical terminologies - especially, the representation of

structured, controlled definitional knowledge about the terms themselves; such

terminologies are often referred to as 'ontologies'.

METHODS: A review of the published literature using PubMed, as well as full-text

searches of recent Medinfo and American Medical Informatics Association (AMIA)

Symposia proceedings, searching for the terms 'ontology' and 'ontologies' and for

articles discussing specific, prominent ontological work.

RESULTS: We summaries the ontologic aspects of twelve current terminology

projects: Galen, the Unified Medical Language System (UMLS), the Medical Entities

Dictionary (MED), SNOMED-CT, LOINC, the Foundational Model of Anatomy (FMA), the

Gene Ontology (GO), ISO Reference Terminology Model for Nursing Diagnosis,

NDF-RT, RxNorm, the NCI Thesaurus, and DOLCE+. We discuss the origins, domain,

and ontologic representation of each of these and attempt to summarize the impact that each has had on terminologic work and biomedical applications. We also note the contributions of the Protégé tool to many of these efforts.

CONCLUSION: Terminologic research and development have advanced significantly in the past 20 years, especially since the recent orientation toward controlled biomedical ontologies. This work has had significant impact on the development of terminologies themselves, their acceptance and dissemination as standards, and their use in supporting biomedical information systems.

PMID: 17051306 [PubMed - indexed for MEDLINE]

21. Acad Emerg Med. 2004 Nov;11(11):1198-205.

Medical informatics standards applicable to emergency department information systems: making sense of the jumble.

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The adoption of medical informatics standards by emergency department information systems (EDISs) is not universal, despite obvious benefits. Clinicians and administrators looking to obtain an EDIS need to know exactly what the various standards can do for them and how the systems they depend on can be integrated and extended. In addition to the standard methods for systems to communicate (chiefly Health Level 7 [HL7]) and those required for submission of claims (Current Procedural Terminology [CPT]-4, International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM], and X12N), there are several other available standards that are clinically useful and can greatly

improve the ability to access and exchange patient information. Major advances in the Unified Medical Language System of the National Library of Medicine have made the patient medical record information standards (Systematized Nomenclature of Medicine [SNOMED], Logical Observation Identifiers, Names, and Codes [LOINC], RxNorm) easily accessible. Detailed knowledge of the arcana associated with the technical aspects of the standards is not needed (or desired) by clinicians to use standards-based systems. However, some knowledge about the commonly used standards is helpful in choosing an EDIS, interfacing the EDIS with the other hospital information systems, extending or upgrading systems, and adopting decision support technologies.

PMID: 15528585 [PubMed - indexed for MEDLINE]

Appendix B: UMLS Licensing Information

- https://uts.nlm.nih.gov//home.html

General information can be sought by emailing: custserv@nlm.nih.gov.

Appendix C: Other References

Help/Documentation:

- http://www.nlm.nih.gov/research/umls/rxnorm/docs/index.html

RxNorm API documentation:

- http://mor.nlm.nih.gov/download/rxnav/RxNormAPI.html

RxTerms API documentation:

- http://rxnav.nlm.nih.gov/RxTermssRestAPI.html

WSDL/Data Location:

- http://mor.nlm.nih.gov/download/rxnav/RxNormDBService.wsdl