RAND HEALTH

The RAND Corporation is a nonprofit institution that helps improve policy and decisionmaking through research and analysis.

This electronic document was made available from www.rand.org as a public service of the RAND Corporation.

Support RAND

Browse Reports & Bookstore

Make a charitable contribution

For More Information
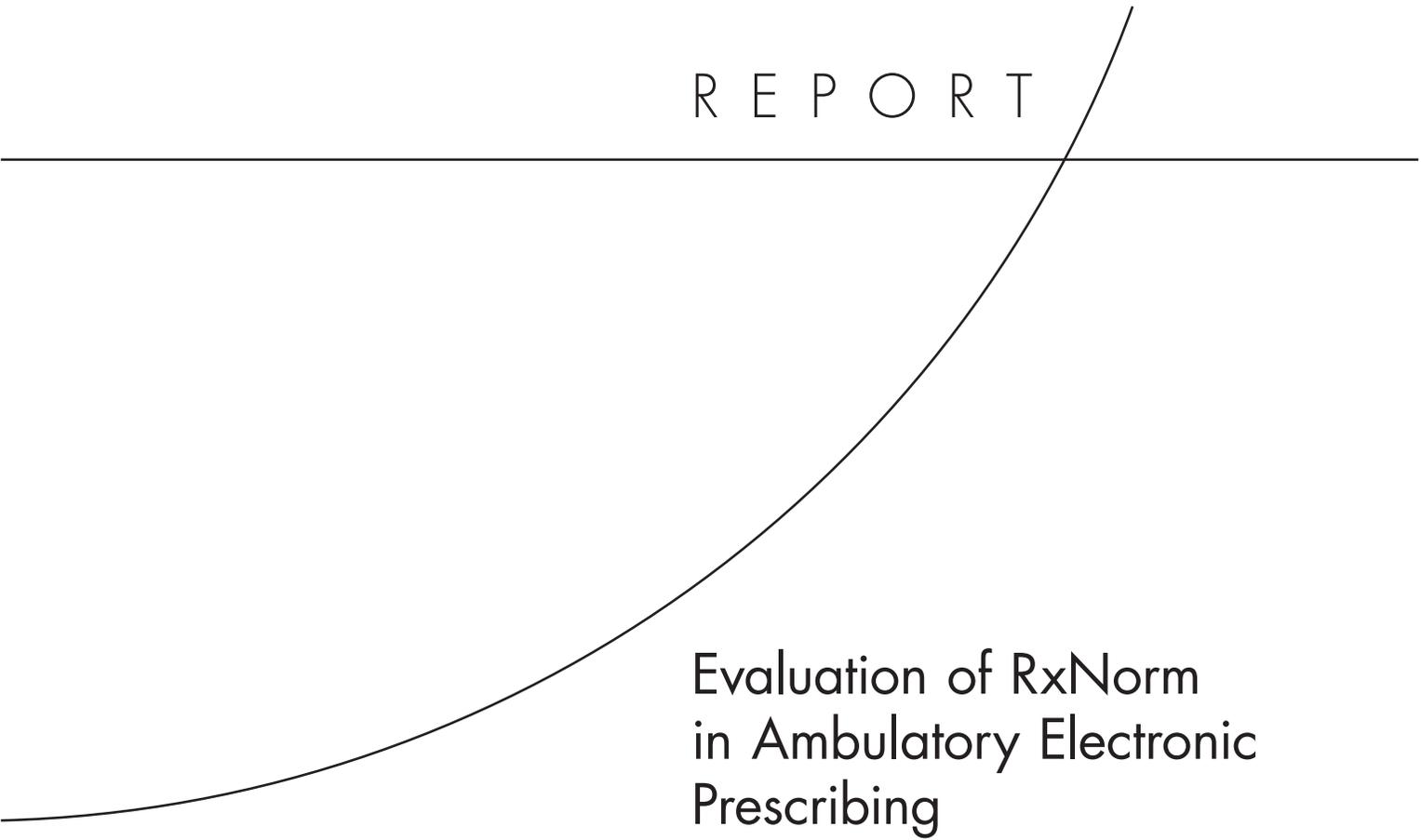
Visit RAND at www.rand.org

Explore RAND Health

View document details

R E P O R T

Evaluation of RxNorm in Ambulatory Electronic Prescribing

Douglas S. Bell, Sean M. O'Neill,

Kerry A. Reynolds, Diane Schoeff

RAND HEALTH

The RAND Corporation is a nonprofit institution that helps improve policy and decisionmaking through research and analysis. RAND's publications do not necessarily reflect the opinions of its research clients and sponsors.

RAND® is a registered trademark.

Preface

The Centers for Medicare & Medicaid Services (CMS), an agency within the U.S. Department of Health and Human Services, was mandated in Section 1860(D)-4 of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 to establish standards for a voluntary electronic prescribing (e-prescribing) program for physicians and pharmacies participating in Medicare Part D. In September 2008, CMS contracted with the RAND Corporation to evaluate two e-prescribing standards—the RxNorm drug nomenclature system and the Structured and Codified Sig Format for the patient instructions portion of prescriptions—that had not been ready for adoption when initial standards for e-prescribing were proposed in 2007.

This report summarizes RAND's evaluation of RxNorm. RAND's evaluation of the Structured and Codified Sig Format is being published separately (see Liu, 2011). The study was conducted in partnership with a coalition of leading corporations involved in creating and processing electronic prescriptions, including Surescripts, DrFirst, Allscripts, QS/1, Medco, and with Point of Care Partners, First Databank, and Medispan. Research collaborators included the University of Southern California and the University of California, Los Angeles. The study involved initial "laboratory" testing of RxNorm's technical adequacy for encoding de-identified prescription samples. It then proceeded to field testing in which RxNorm codes were added to live e-prescription transactions between participating prescribers and pharmacies. The implications of the study results for future e-prescribing policy are discussed in this report, and suggestions for future rule-making are presented. This report will be of interest to national and state policymakers, corporations involved in health information technology, and health care provider organizations concerned with addressing the need for improved drug identification.

The authors would like to acknowledge special contributions from Sherry Newman at Point of Care Partners; Rosa Garcia and Scot Hickey at RAND; and the pharmacists, physicians, and staff at sites that participated in pilot testing.

Contents

Figure and Tables

Figure

Tables

Summary

All drug prescriptions need to accurately identify medications that the prescriber intends for the pharmacist to dispense. In e-prescribing, the use of unambiguous, computer-interpretable drug identifiers offers the possibility of computer assistance to prevent errors, both in prescribing and dispensing (Bell, 2004). Currently, the Food and Drug Administration's National Drug Code Directory is the standard source for computer-interpretable drug identifiers in e-prescribing transactions. However, the National Drug Code Directory has not been accurately maintained (Levinson, 2006). Furthermore, it was designed to distinguish among drug packages from different sources rather than to represent the intent of prescribers, who are rarely concerned about the drug source or packaging. Thus, the National Drug Code identifiers used in e-prescriptions sometimes misrepresent the prescriber's intent, potentially creating both new kinds of errors and the need for inefficient manual checks to ensure accurate interpretation.

The ideal system of drug identifiers for e-prescribing would have one unique identifier for every clinically distinct medication available, where *clinically distinct* refers to differences that matter when the drug is administered to a patient (as opposed to differences that matter in production and distribution). The identifier system would be complete if it included every drug that is currently available for prescribing, and it would be semantically precise if each clinically distinct medication were represented by only one identifier. In the context of e-prescribing, this semantic precision would enable each party to the prescription transaction to interpret without ambiguity the clinical drug that the prescriber intended. An ideal system of drug identifiers would also be easily managed by its users and have features that enable the maintenance of precise meaning as corrections are made and as the availability of drugs changes over time. Finally, it would cover other, more-abstract concepts. For example, it would represent the concept of a tablet that contains a particular ingredient (regardless of strength), and this would enable precise reference to this class of medications for decision support purposes, such as formulary checking or allergy checking.

RxNorm is a drug nomenclature from the National Library of Medicine (NLM) that is designed to fulfill the criteria outlined above by assigning a rigorously derived, centrally maintained, and publicly available unique identifier to each clinically distinct drug. Thus, RxNorm has the potential to greatly improve drug identification in e-prescribing transactions. In 2006, we found that RxNorm covered 99.0 percent of medications represented in a sample of 19,824 ambulatory e-prescriptions, but, for 5.2 percent of these prescriptions, independent users of RxNorm had not selected the same RxNorm concept to represent the prescription. About half of these disagreements were attributable to the existence of duplicate, clinically synonymous drug concepts in RxNorm. These duplications represent semantic errors because, as just noted, one goal of RxNorm is to have only one unique identifier for each clinically distinct drug concept. Since 2006, the NLM has expanded RxNorm's coverage by adding a new concept type for drug-device packages, and it has continued to improve its concept maintenance methods.

RxNorm could also be used to address technical problems that have impaired the functioning of the Formulary and Benefit (F&B) standard from the National Council for Prescription Drug Programs (NCPDP). The F&B information available to prescribers is often missing or inaccurate (Grossman, 2007; Wang, 2008), due in part to the challenge of maintaining sufficiently detailed and accurate files using National Drug Code numbers (NDCs). This is challenging because, for each prescribable drug, many F&B entries are needed to cover all of the NDCs that might be used (Bell, 2008).

The study described in this report evaluated RxNorm's potential to improve how medications are represented within the transactions that are currently used in ambulatory prescribing. These are the new prescription (NEWRX) transaction and the refill request (REFREQ) transactions within the NCPDP SCRIPT standard and the prescription drug insurance coverage information represented in the NCPDP F&B standard. In Part I of the study, we evaluated the use of RxNorm in a "laboratory" environment, using historical prescription data samples. In Part II, we evaluated the usability and interoperability of RxNorm within live prescriptions being transmitted between participating physician offices and pharmacies. We also evaluated the perceptions of participating pharmacists and prescribers regarding the medication management process both before and during the inclusion of RxNorm identifiers with transactions between pilot participants. However, RxNorm identifiers were added to new prescriptions *after* the medication had been selected, so RxNorm affected only pharmacy fulfillment, not the prescribing interface. (This decision enabled e-prescribing vendors to continue using their existing prescribing interfaces. They considered this important from a safety standpoint to ensure that user errors in drug selection would be no greater during the pilot than they are in general.)

Laboratory Testing

The Completeness and Reliability of RxNorm for e-Prescription Transmissions

Using a sample of 19,743 e-prescriptions, we estimated the coverage rate of RxNorm for representing clinical drugs, measured the six-month replacement rate of the RxNorm concepts used, assessed the consistency of two independent concept mappings, and investigated inconsistent mappings.

The April and October 2009 releases of RxNorm contained clinical drug concepts for all but one prescription in the sample (99.995 percent). Of the concepts used in the April release, 8.1 percent were superseded by new concepts in the October 2009 release. Two independent mappings produced different concepts for 676 e-prescriptions (3.4 percent), including differences in extended-release dose forms, salts, and metered-dose inhalers, but the differences had relatively low clinical significance.

Thus, RxNorm provides standardized concepts covering nearly all ambulatory e-prescriptions in a large sample derived mostly from primary care settings. The level of agreement among independent uses of RxNorm was relatively high, and the cases of disagreement had low clinical relevance. Nonetheless, mechanisms are needed to resolve potential ambiguities that remain in the use of some concept types, particularly extended-release dose forms and metered-dose inhalers. In this report, we propose an algorithm that could be used to identify potentially ambiguous extended-release concepts and to flag them for exclusion from use in e-prescribing.

The Efficiency of RxNorm in Representing Formulary and Benefit Information

Using the formulary status list (FSL) from a large pharmacy benefit manager, we automatically matched each FSL entry to its corresponding prescribable concept (i.e., Semantic Branded Drug, Branded Pack, Semantic Clinical Drug, or Generic Pack) and drug–dose form concept (i.e., Semantic Branded Dose Form or Semantic Clinical Dose Form). Drug–dose form concepts are concepts that aggregate all of the strengths for a given drug–dose form pairing. We then determined the extent to which the drug–dose form concepts, prescribable concepts, and NDCs could be used to most parsimoniously represent the set of formulary entries while still preserving the formulary status expressed for each entry.

We found that 52 percent of FSL entries (27,483 of 52,913) matched an RxNorm concept. Of those, 26,810 (97.6 percent) could be represented by an RxNorm concept instead of an NDC without loss of formulary status information. The other 673 entries (2.4 percent) were NDCs that represented different formulary statuses within the same RxNorm concept (e.g., ranitidine 150-mg tablets from some manufacturers are covered, and others are not). The 26,810 formulary entries could be represented by 8,911 prescribable RxNorm concepts. Thus, using RxNorm, the same formulary information could be expressed with about one-third the number of entries. If these could in turn be aggregated to higher-level drug–dose form concepts, file sizes could be further reduced to one-quarter the number of entries. Among the formulary entries that did not match to RxNorm, 67 percent were out of scope for RxNorm (one example is equipment), and the reminder represented NDC numbers that could not be interpreted using the available drug databases.

In conclusion, we found that RxNorm offers substantial efficiency and parsimony gains for formulary entries that are within its scope, potentially enabling greater accuracy through easier maintenance and greater simplicity of presentation. The 2.4 percent of entries that represented different formulary statuses within the same clinical drug concept should not need to be represented because the drugs represented are clinically equivalent and therefore interchangeable at the pharmacy. Trying to present these formulary differences to prescribers probably creates unnecessary complexity, especially in comparison with the very substantial inaccuracies that are currently prevalent in F&B information (Grossman, 2007; Wang, 2008). Thus, F&B files would be more usable and probably more effective if NDCs were completely replaced by RxNorm concept unique identifiers (RxCUIs). If RxNorm could be modified to include diabetes care supplies, it would substantially increase the proportion of F&B concepts that could be represented more parsimoniously in the F&B standard.

Live Pilot Testing

The Use of RxNorm in Live New Prescription and Refill Request Transactions

Five ambulatory physician practices (using two e-prescribing software systems), two retail pharmacies (both using the same pharmacy management software system), and one mail order pharmacy participated in our live pilot program. The software used at each site was modified to add RxNorm identifiers to outgoing transactions and to process RxNorm identifiers from incoming transactions. De-identified data from all transactions were collected for analysis. The retail pharmacy software vendor implemented an alert triggered when the RxCUI of the drug selected to represent an incoming prescription did not match the RxCUI received with the prescription. We also examined the potential for e-prescribing systems to use RxNorm in reconciling refill requests. At the mail order pharmacy, pharmacists flagged incoming new prescriptions if, based on the NDC and drug name string received, they considered prescriber's intent ambiguous. The pharmacist then

judged whether the RxCUI received with the prescription was useful in disambiguating the prescription.

During a live pilot period of about 20 weeks, 3,829 new-prescription transactions were transmitted from participating prescriber offices to participating pharmacies. An RxCUI had been added to 96.3 percent of the 3,687 prescriptions that contained an NDC and for which complete data were retrieved. Among new prescriptions sent between partners that used different drug knowledge bases (e.g., sent from a MediSpan client to a First DataBank client), 4.5 percent (76 of 1,603) contained a representative NDC that could not be resolved in the pharmacy's drug knowledge base; 61 of these transactions (80 percent) had included an RxCUI, and, for 100 percent of these, the RxCUI accurately represented the drug prescribed. At the retail pharmacies, RxNorm mismatch alerts were recorded for 349 of 2,157 new prescriptions received (16 percent). Most of these were due to the fact that a pharmacy technician selected alternatives that would be expected to have a different RxCUI (e.g., he or she selected a tablet when the prescription was for a capsule or entered a branded concept, such as Keflex, when the prescription was for a generic concept, such as cephalexin). Some were due to differences in the versions of RxNorm used by the parties, including the use of some concepts that had been retired and one partner's choice not to use pack concepts.

Due to the short history of e-prescribing use among the prescribers involved, only two of the 893 refill request transactions conducted during the pilot could be mapped to a prior electronic prescription for the same patient within the previous ten months. Thus, there were insufficient historical data to test a proposed alert based on reconciling new refill requests with prior prescriptions.

At the mail order pharmacy (which used both MediSpan and First Databank to resolve NDCs), an RxCUI was sent with 1,444 of 1,495 prescriptions (96.6 percent). Of these, 28 (1.94 percent) were flagged as needing drug identity clarification, but the RxCUI received was considered helpful for only three of these (11 percent), due in part to the use of underspecified RxNorm terms, such as extended-release dosage forms that did not include a specific time interval.

In conclusion, we found that RxNorm could disambiguate most prescriptions when the representative NDC was not found in the recipient's drug knowledge base. However, use of RxNorm to alert for pharmacy data-entry errors resulted in a high rate of false alarms. This rate would have been lower had both parties regularly updated their RxNorm content and had pharmacy technicians regularly entered the precise drug name prescribed rather than making brand-name substitutions. RxNorm would be more useful for disambiguating prescriptions if underspecified terms, such as extended-release dose forms without a specific duration of action, were not used in prescriptions. RxNorm did not prove to be useful in reconciling refill requests because, at the time of the study, most patients had few prior e-prescriptions to be matched.

The Effects of RxNorm Use in Live Pilot Testing

Trained field researchers conducted site visits at each participating pharmacy and physician office at baseline and again after the switch to including RxNorm identifiers in transactions. Data were collected using multimethod observations and interviews. In addition to documenting changes that might be directly attributable to the use of RxNorm in the pilot, we also sought to elicit providers' views of the primary challenges associated with e-prescribing and drug identification.

At baseline, both prescribers and pharmacists perceived that, compared with handwritten prescriptions, e-prescribing systems often force prescriptions to be overspecified. Areas of overspecification included the drug itself (e.g., specifying a particular salt when other salts would be

equivalent from the prescriber's standpoint), the dose form (e.g., specifying a capsule when a tablet would be fine), and brand-name versus generic drugs. Overspecification caused confusion among prescribers and required pharmacies to recontact prescribers in order to clarify intent. After RxNorm implementation, the intended RxNorm-based alerting feature was working for only one of the two retail pharmacies at the time of our site visit. Pharmacy technicians expressed annoyance at the alerts because most were false positives (i.e., the prescribed drug or its equivalent had in fact been accurately selected), but the pharmacists expressed satisfaction with the potential to prevent drug-selection errors.

In conclusion, live pilot testing revealed that RxNorm could potentially reduce the need for pharmacy callbacks to resolve ambiguous prescriptions, thereby improving efficiency both for prescribers and pharmacies. However, the problem of prescription overspecification will not be addressed as long as the National Drug Code remains the primary system for drug identification. RxNorm could improve pharmacies' ability to automatically check the accuracy of medication selections, either upon initial data entry (the use case we tested) or when a drug is selected from stock for dispensing.

The Readiness of RxNorm for Use in Ambulatory e-Prescribing

Overall, RxNorm appears ready for use to represent ambulatory prescriptions from primary care physicians. Its completeness was extremely high for the sample we examined, and unresolved synonyms in RxNorm were rare. Most important, errors in mapping NDCs to RxNorm, although not rare (they occurred in 3.4 percent of the sample), were of low clinical significance (e.g., involving minor differences in dose forms, salts, or inhaler canister sizes). Further, many of these errors would be preventable if potentially ambiguous dose forms and salts were flagged for exclusion from use in e-prescribing.

E-prescribing vendors and pharmacy vendors proved capable of adding accurate RxCUIs to the vast majority of prescriptions in a live pilot test, and RxCUIs had potential value in clarifying the 4.5 percent of prescriptions containing an NDC from one of the e-prescribing systems that could not be resolved in the pharmacy's drug knowledge base. However, RxNorm would have been more useful in accurately representing the prescriber's intent and in preventing calls for clarification if prescribers could have directly selected RxNorm concepts rather than products specified at the National Drug Code level. Overall, for prescribing, RxNorm appears to provide more-accurate drug identifiers than the National Drug Code. We recommend that NCPDP consider switching from the National Drug Code to RxNorm as the primary drug identifier in prescriptions.

RxNorm also appears ready to enable a substantially more parsimonious representation of the data in FSLs of the F&B standard. The formulary status distinctions that could not be reproduced with RxNorm represent supplier-level coverage differences that prescribers should not need to be concerned about. Thus, RxNorm offers promise of more-manageable FSLs, which could then be more easily expanded to represent the group-level variations in coverage that are currently a source of inaccuracy. However, given that the e-prescribing industry has not yet developed experience with using RxNorm in the F&B standard, live pilot testing of this approach is recommended.

Abbreviations

BPCK	Brand Name Pack
CMS	Centers for Medicare & Medicaid Services
CUI	concept unique identifier
e-prescribing	electronic prescribing
F&B	Formulary and Benefit
FDA	Food and Drug Administration
FS	formulary status
FSL	formulary status list
g/mol	grams per mole
GPCK	Generic Pack
MDI	metered-dose inhaler
MEQ	milliequivalent
mg	milligram
MIN	multiple ingredient concept type
ml	milliliter
mol/l	moles per liter
NCPDP	National Council for Prescription Drug Programs
NDC	National Drug Code number
NEWRX	new prescription
NLM	National Library of Medicine
PBM	pharmacy benefit manager
REFREQ	refill request
RxCUI	RxNorm generic concept unique identifier
SBD	Semantic Branded Drug
SBDF	Semantic Branded Drug Form
SCD	Semantic Clinical Drug
SCDC	Semantic Clinical Drug Component
SCDF	Semantic Clinical Drug Form
SKU	stock-keeping unit
XR	extended release

Introduction

The Need for a Universal Drug Identifier System

Ambulatory electronic prescribing (e-prescribing) is expected to deliver improvements in the quality and safety of prescribing (Donyai, 2008; Eslami, 2007; Jani, 2008; Wolfstadt, 2008), but, to deliver these benefits, the systems must communicate unambiguous drug identities that can be interpreted both by pharmacists and by computerized decision support tools. Thus, a standard terminology system is needed for representing each prescribable drug (Brailer, 2004, 2005; Hammond, 2004).

More than a decade ago, Cimino described a set of 12 desiderata for controlled vocabulary systems (Cimino, 1998; Lau, 1999):

- comprehensive content
- concept permanence
- nonambiguity of concepts
- formal definitions
- multiple hierarchies
- meaningless concept identifiers
- do not use "not elsewhere classified"
- multiple granularities
- multiple consistent views
- context specific information
- graceful evolution
- support composition-decomposition.

The desiderata that are particularly relevant to drug identifiers in prescribing are comprehensiveness (i.e., up-to-date inclusion of all available drugs at the level of granularity required for prescribing[1]), concept permanence (i.e., the meaning of an identifier never changes), nonambiguity (i.e., each meaning has only one identifier, and vice versa), multiple granularities (i.e., representing classes, ingredients, brand names, dosage forms, etc. in a computable manner), graceful evolution (i.e., historical data using retired identifiers can still be unambiguously interpreted), and context-specific information (i.e., links to key knowledge sources, such as the Drug Enforcement Agency Schedule of Controlled Substances, drug classes, and commercial knowledge bases, are available).

---

[1] Section 3(a) of the August 2010 National Association of Boards of Pharmacy Model State Pharmacy Act and Model Rules suggests a general regulatory requirement for prescriptions to include the "name, strength, dosage form, and quantity of drug prescribed" (National Association of Boards of Pharmacy, 2010).

The only computable identifiers that are currently being used in e-prescribing transactions come from the National Drug Code Directory, which attempts to track every commercial prescription drug product. National Drug Code numbers (NDCs) could potentially meet some of the desiderata, given that the directory attempts to comprehensively document all prescribable drugs at a level of granularity that is acceptable for prescribing. (It specifies name, strength, and dosage form.) However, NDCs also specify the manufacturer and package size, which makes their meaning narrower than the clinician's intent, in most cases. Thus, forcing the selection of NDCs makes prescriptions overspecified, and this in some cases limits the pharmacist's ability to select the optimal manufacturer and package size for the patient. Concept permanence is also violated by NDCs because each drug packager generates its own NDCs and is allowed to reuse them, potentially creating substantial changes an identifier's meaning over time. This problem is compounded by incomplete and unreliable maintenance of the National Drug Code Directory. One study found that 27 percent of the 123,856 codes in the directory were erroneous and that 14,337 commercial prescription drug products lacked codes (Levinson, 2006). In a small minority of instances, the Food and Drug Administration (FDA) had failed to enter a manufacturer's report, but the most common reason for these errors was that the manufacturer had not reported changes to the FDA.

The RxNorm standard, developed by the National Library of Medicine (NLM), is the first standardized nomenclature of prescribable clinical drugs (NLM, 2006, 2009). It includes a hierarchy of related concept types that can be used to express fully specified prescriptions as well as broader concepts that can be used to aggregate multiple related prescribable entities.

The study described in this report sought to evaluate the completeness of RxNorm in representing a real-world sample of e-prescriptions by calculating the proportion of prescriptions that could be accurately mapped to RxNorm concept unique identifiers (CUIs). We also assessed the stability of RxNorm CUIs (RxCUIs) by calculating the rate of concept replacement occurring over a six-month period. Finally, we assessed the consistency of two separate NDC-to-CUI mappings used for matching prescriptions to RxNorm concepts. E-prescriptions that match to different but synonymous RxCUIs suggest the existence of an error in RxNorm because one goal of RxNorm is to map all clinically equivalent synonyms to a single RxCUI. E-prescriptions that match to more than one nonsynonymous RxCUI indicate areas of ambiguity that need to be resolved.

The Formulary and Benefit Standard

The National Council for Prescription Drug Program's (NCPDP's) Formulary and Benefit (F&B) standard is intended to allow for the interoperability of prescription drug insurance coverage information. The standard defines specific variables and values that must be listed to represent the coverage offered by a given health plan or prescription drug benefit provider. This standard represents a unique potential application of RxNorm for organizing a flat, nonsystematically indexed list of prescription drugs into a standardized, hierarchical format that may afford improved efficiency and streamlined decisionmaking.

Complete representation of a drug's coverage in the standard requires several files. The central file is the formulary status list (FSL), which contains the level-of-preference value (the formulary status [FS]) of prescribable products on the market. (An FS value of 0 indicates off formulary, which means no coverage.) FSL entries are currently indexed by NDC. Additional files in the F&B standard, including the Benefit Coverage List and the Formulary Alternatives List, serve additional, complementary roles.

A robust standard providing accurate formulary information for specific drugs at the point of care would save time for prescribers and reduce costs for patients. However, the F&B information currently available to prescribers through the standard is often missing or inaccurate. FSL files are large (often 5 megabytes or more), are difficult to manage, and have a great deal of redundancy, as they must anticipate all of the NDCs that might be used to represent a drug. The representation is made more inaccurate by the fact that, in practice, health plans typically maintain numerous subformularies, each specific to a given employer group or region (Bell, 2008). These subformularies are enforced at the time of fulfillment in the pharmacy, but these differences are not usually represented in the FSL due to the potential for added complexity. Consequently, the FSLs available under the standard do not reflect all of the variations in actual coverage policy, making the information available to prescribers inherently inaccurate.

RxNorm creates an opportunity to represent prescribable drugs more accurately and parsimoniously in the F&B standard. Greater simplicity should make these files easier to maintain, leading to more capacity to represent the complex subformularies that are actually in force. For example, a pharmacy benefit manager (PBM) may decide to cover all amitriptyline oral tablets, a distinction that encompasses many individual products with different NDCs. Making it unnecessary to account for each possible NDC for amitriptyline oral tablets allows a layer of complexity and many rows in the FSL to be removed.

Thus the goal of our analysis was to explore the potential benefits of representing medications in F&B lists using RxNorm instead of NDCs. To do this, we examined how often all of the NDCs for a given RxCUI shared the same FS. We compared two approaches, one using only prescribable RxNorm terms and another that permitted aggregation using the broader term types (see Table 1.1).

Table 1.1
Overview of Key RxNorm Term Types

Level of Specificity	Term Type	Name	Definition	Example
Prescribable	SBD	Semantic Branded Drug	Ingredient, strength, and dose form, plus brand name	"cefdinir 300 MG Oral Capsule [Omnicef]"
Prescribable	BPCK	Brand Name Pack	Branded drug delivery device	"{10 (cefdinir 300 MG Oral Capsule [Omnicef])} Pack [Omni-Pac]"
Prescribable	SCD	Semantic Clinical Drug	Ingredient, plus strength and dose form	"cefdinir 300 MG Oral Capsule"
Prescribable	GPCK	Generic Pack	Generic drug delivery device	"{10 (cefdinir 300 MG Oral Capsule) } Pack"
Broader	SBDF	Semantic Branded Drug Form	Branded ingredient, plus dose form	"cefdinir Oral Capsule [Omnicef]"
Broader	SCDF	Semantic Clinical Drug Form	Ingredient, plus dose form	"cefdinir Oral Capsule"

NOTES: SBD = Semantic Branded Drug. BPCK = Brand Name Pack. SCD = Semantic Clinical Drug. GPCK = Generic Pack. SBDF = Semantic Branded Drug Form. SCDF = Semantic Clinical Drug Form.

The Need for Live Pilot Testing

Although "laboratory" testing based on historical data can provide a good indication of potential benefits and issues associated with a new technology, ultimately, the technology needs to be tested in a live environment to ensure that it can meet standards of safety and accuracy under the demands of real-world, real-time transactions. The specific goals of our live pilot evaluation were (1) to assess the ability of vendors and pharmacies to accurately incorporate and use RxNorm identifiers in e-prescribing transactions and (2) to analyze physicians' and pharmacists' perceptions of the benefits (or risks) created by features that use RxNorm identifiers within their systems.

Because RxNorm had not previously been used in live prescription transactions, and because the vendor partners had no prior experience with RxNorm, we tested RxNorm as an add on to—rather than a replacement for—NDCs. Furthermore, the project was also constrained to a one-year time frame, which did not allow time for reengineering the medication selection process in e-prescription user interfaces.

Methods

Part I. Laboratory Testing

Completeness and Reliability

Overview

We collected a sample of 20,135 de-identified ambulatory e-prescriptions from two e-prescribing system vendors. First, using a series of automated and manual matches, we determined the overall coverage of RxNorm (in terms of percentage of e-prescriptions mappable to RxCUIs) in this sample. Second, we assessed the concept archiving and replacement rate over a six-month period and the ability to track these instances of archiving and replacement using RxNorm's forward-mapping mechanism. Finally, we assessed the consistency of two different NDC-to-CUI mappings: one derived from the RxNorm distribution and one proprietary product from a medical knowledge database vendor. In cases where e-prescriptions matched to different RxCUIs in each mapping, we ascertained the nature of the mismatch, classified mismatches according to common types, and used our results to identify the areas of RxNorm that require further refinement.

Data Sources

We obtained samples of de-identified e-prescriptions that had been transmitted from ambulatory physician practices to retail pharmacies using either of two point-of-care prescribing systems. A total of 82 providers, practicing at 48 sites in Kansas, Michigan, and Maryland, contributed to the sample. Provider specialties included internal medicine, family practice, pediatrics, and general surgery. Data fields provided in the sample included NDC, drug name, strength, form, and patient instructions. Prescribers and patients were identified in the data only by code numbers; no patient clinical or demographic data, including diagnosis or age, were provided.

E-prescriptions either out of scope for RxNorm or inadequately specified were excluded. E-prescriptions considered out of scope included messages that were not valid prescriptions (i.e., notes to the pharmacy or test orders), nondrug items (e.g., supplies and equipment), and multivitamins (which are officially out of scope for RxNorm and only partially represented). An inadequately specified e-prescription was one for which the specific drug being prescribed could not be determined from either the drug description or the representative NDC. Examples include e-prescriptions missing the drug component (e.g., "Artificial tears. Gel"), the form (e.g., "Indocin 50MG"), or the strength (e.g., "K-Dur") and e-prescriptions with significant errors in spelling, pack size, or units of measurement. Because it would not be possible to resolve these into specific prescribable entities, we excluded them as erroneous.

Overall Coverage

We defined *generic RxCUI* as an RxNorm SCD or GPCK. We then attempted to automatically match e-prescriptions to generic RxCUIs by using an NDC-to-CUI mapping that we derived from the RxNorm distribution. We conducted a second round of automated matching using a proprietary NDC-to-CUI mapping obtained from a medical knowledge database vendor. The remaining unmatched prescriptions, particularly those missing a representative NDC, were matched via manual searches of the RxCUI database. In cases of uncertainty about the equivalence of drug concepts being prescribed and those represented in RxNorm, we sought specific product information about the drugs in question from a variety of sources, including the drug manufacturer, wholesaler and retailer websites, and published drug reference compendia.

The Stability of RxNorm Concept Unique Identifiers over Time

The RxNorm distribution is updated weekly with new RxCUIs, some of which represent corrections intended to replace existing RxCUIs. Our primary analyses and NDC-to-CUI mapping used the version of RxNorm from October 21, 2009, which contained 18,775 generic RxCUIs. To measure RxNorm's concept archiving and replacement rate, we obtained a distribution of RxNorm from April 20, 2009, which contained 18,398 generic RxCUIs. We developed an NDC-to-CUI mapping from this older distribution and then used it to automatically match our sample. We then checked whether the RxCUIs that had been used in the April 2009 mapping were present in the October 2009 RxCUI database. For RxCUIs that were present only in the older distribution, we determined whether each could be forward mapped to a current (i.e., October 2009) RxCUI using RxNorm's archival tables.

The Consistency of RxNorm and Vendor Mappings

We directly compared the performance of the RxNorm-derived NDC-to-CUI mapping with the performance of the vendor NDC-to-CUI mapping in order to assess their consistency and also to highlight possible cases of synonymy or ambiguity in RxNorm. Mismatches occurred when an e-prescription matched to two different RxCUIs; we classified these cases into distinct types and then ordered the types according to the clinical significance of the dispensing error that would result if a prescription for one were filled with the other. We looked for both synonymy errors, which result when two distinct RxCUIs identify the exact same clinical drug, and ambiguous mappings, which result when two RxCUIs are distinct from each other but, for a given clinical drug, it is impossible to determine which of the two RxCUIs is "correct."

RxNorm's Potential Use in the Formulary and Benefit Standard

In addition to fully specified prescribable concepts, RxNorm includes broader concepts that can serve to aggregate the prescribable concepts. Thus, in our analysis, we distinguished between RxCUIs at two different levels of abstraction. *Prescribable concepts* are the lowest level of abstraction in RxNorm and comprise four different types of RxCUI: SBD, BPCK, SCD, and GPCK. *Drug–dose form concepts* represent a higher level of abstraction and do not contain information on the strength of the prescribable drug, just the active ingredient and form. Drug–dose form concepts are the SBDF and SCDF types.

The prescribable concept "Sertraline 100 MG Oral Tablet [Zoloft]" is represented by RxCUI 208149, an SBD. The corresponding drug–dose form concept "Sertraline Oral Tablet [Zoloft]" is represented by RxCUI 368413, an SBDF. Nonbranded products are represented with SCDs and SCDFs. In the case of generic sertraline, the corresponding concepts are "Sertraline 100 MG Oral Tablet" (CUI 312938, an SCD) and "Sertraline Oral Tablet" (CUI 373868, an SCDF).

It is important to note that, although each branded concept (SBD, BPCK, and SBDF) is associated with a corresponding generic concept (SCD, GPCK, and SCDF), generic concepts in RxNorm are intended only to represent generic prescribable drugs, not their branded equivalents. Therefore, the NDC-to-CUI mapping we derived gives precedence to branded concepts when both branded and generic concepts are available. Additionally, although they are prescribable concepts, the pack concepts (BPCK and GPCK) have no higher-level abstraction (i.e., no corresponding drug–dose form concept) in RxNorm.

There thus exists an opportunity to apply this hierarchical concept structure to flat, NDC-indexed lists of prescribable drugs, such as the FSL used by PBMs to track insurance coverage status. The streamlining achievable through implementing such a hierarchy to the flat FSL could allow for a higher degree of consistency in decisionmaking.

Mapping the FSL to RxNorm Concepts

We obtained FSLs from two independent PBMs (referred to in this report as PBM 1 and PBM 2). As defined in the F&B standard, the FS variable can assume values between 0 and 99, where 0 indicates "Non Formulary," 1 indicates "On Formulary, but Not Preferred," and 2 through 99 indicate "On Formulary," with larger values indicating a higher relative preference level. We explored the ability of RxNorm to faithfully represent prescribable drugs at higher levels of abstraction while preserving each formulary entry's FS.

For both FSLs, we automatically matched entries to both prescribable and drug–dose form concepts by using an NDC-to-CUI mapping that we derived from the RxNorm distribution. Our analysis included an assessment of the coverage rate, or what percentage of NDC-indexed entries in the FSL could be mapped to an RxCUI. The additional analyses described in the remainder of this section were carried out using only the FSL from PBM 1.

We randomly sampled 100 entries from PBM 1's FSL that failed to automatically match to an RxCUI in RxNorm, and we characterized them according to the categories (in scope, out of scope, underspecified, etc.) described earlier in this chapter. We attempted to match these entries using mappings from the same drug knowledge base vendor used to assess consistency, using both the NDC-to-CUI mapping used before and a proprietary NDC-indexed non-RxNorm concordance that yielded brief descriptions of each prescribable product. We used information from both of these mappings, supplemented with Internet searches (as we did for the coverage assessment) to characterize these products as either in scope or out of scope.

Applying a Hierarchical Structure to the FSL

RxNorm's hierarchical (prescribable and drug–dose form) nomenclature represents an opportunity to streamline the representation of FS. If, for instance, a PBM covers only generic sertraline and not brand-name Zoloft, the PBM could simply represent two statuses (CUI 373868 being on formulary and RxCUI 368413 off formulary) instead of needing to represent separately each of the 154 sertraline oral tablet FS entries encompassing all sertraline NDCs.

Most RxCUIs represent more than one NDC (i.e., more than one unique prescribable product) and, consequently, more than one formulary entry. However, because each formulary entry has its own FS, there is a possibility that a given CUI will represent two or more formulary entries with differing FSs. We therefore determined how well RxCUIs would be able to faithfully represent the original FS of each formulary entry at both the prescribable concept and drug–dose form concept levels.

To determine this, we first mapped each entry from PBM 1's FSL to its appropriate prescribable concept (i.e., SBD, BPCK, SCD, or GPCK). A formulary entry was considered faithfully

representable by a prescribable concept if and only if all formulary entries that mapped to that concept had the same FS. When possible, formulary entries were represented by prescribable concepts; otherwise they were represented by the original NDC. For each type of prescribable concept (i.e., SBD, BPCK, SCD, or GPCK), we counted the number of formulary entries aggregating to that level and the number of RxCUIs used to represent those formulary entries. Because representing formulary entries with higher-level concepts allows us to convey the same information in fewer rows of the FSL, we calculated the percentage reduction in the number of rows used as follows: (original number of rows – collapsed number of rows) / original number of rows.

We then attempted to represent formulary entries by using drug–dose form concepts (i.e., SBDF or SCDF) when possible. A formulary entry was considered faithfully representable by a drug–dose form concept if and only if all formulary entries that mapped to that concept had the same FS. In order of preference, formulary entries were represented by drug–dose form concepts, prescribable concepts, or the original NDC.

Part II. Live Pilot Testing

Use Cases and Pilot Software Development

The live pilot testing evaluation was guided by a set of use cases that described how each participating partner would take advantage of RxNorm in e-prescribing transactions. The partners agreed to the plan described in the next paragraph.

For new prescription (NEWRX) transactions, the e-prescribing system vendors would incorporate an RxCUI to represent the selected medication (i.e., BPCK, GPCK, SBD, or SCD) by looking up the most specific RxCUI associated with the NDC selected by the prescriber. The RxCUI was added to the transaction in the "Reference Number" field, along with the term type for the RxCUI, entered in the "Reference Qualifier" field. E-prescribing vendors did not change their medication selection user interfaces, so the "Item Description" for the prescription remained based on the original drug database name that had been selected, and the "Item Number" field was populated with the NDC number. The pharmacy system received and parsed out this RxCUI, using the RxCUI to improve its drug selection process. However, each pharmacy used markedly different work processes. The retail pharmacy vendor, QS/1, did not make use of the incoming NDC; this is because of the nonmatches and inaccurate matches that can take place when using NDCs across knowledge base vendors (see Chapter One). Thus, the QS/1 prescription work process involved the pharmacist or pharmacy technician keying in part of the drug name received and then selecting it from the pharmacy's drug knowledge base, even for electronic prescriptions. Having selected the exact drug prescribed, the pharmacist could then select the specific NDC-level medication to dispense, substituting a preferred alternative, if appropriate. QS/1's use case for RxNorm was to use the RxCUI as a way to check the selection of the prescribed medication from the initial pick list. However, Medco, the mail order pharmacy, did use the incoming NDC to match the prescription to a proprietary drug concept. Using that concept, it then suggested to the pharmacist available medications and appropriate alternatives. Medco offered to display the RxCUI and its associated string as an additional field in the e-prescription fulfillment application to help disambiguate unclear prescriptions that might otherwise require a callback to the prescriber.

For refill transactions, the pharmacy systems used the most specific RxCUI to represent the medication in outgoing refill request (REFREQ) transactions, and the e-prescribing system vendors received and parsed this RxCUI and reflected it back on their outgoing refill response transaction. The vendors also agreed to use the RxCUI received on refill requests to streamline the approval

workflow within the end-user application (by, for example, flagging instances of the requested medication not matching the originally prescribed medication).

Surescripts, the largest e-prescribing intermediary company in the United States, developed a separate portal for routing the RxNorm-containing pilot transactions to retail pharmacies, and it developed a different mechanism for routing the RxNorm-containing pilot transactions destined for mail order pharmacies through the existing mail order system. To conduct this special routing for pilot test transactions, each partner developed software modules, destined for deployment to pilot sites, that could detect transactions bound for other participating partner sites and route them with the modified transaction content (including the added RxCUI) via the appropriate server. Each partner conducted certification testing with Surescripts for each module before deployment.

Site Selection

We identified physician office–pharmacy pairs according to the following criteria: Both members of the pair were using the appropriate software from one of our pharmacy or prescribing-system partners and they had exchanged at least 120 e-prescriptions (including new and renewal transactions) with each other in the previous six months. Surescripts queried e-prescribing transmission data for eight states (California, Illinois, Kansas, Maryland, Massachusetts, Michigan, Ohio, and North Carolina) where each partner was expected to have a strong presence. Because our retail pharmacy partner required participating pharmacies to have upgraded to the latest version of its software, and because this upgrade involved substantial work process changes, only a small minority of the partner's customers were eligible in each state. With this additional requirement, we found no eligible dyads in California or Maryland and one to five eligible dyads in the other six states.

Five physician offices and three linked pharmacies (two retail and one mail order) participated in the study (two pharmacies were linked to multiple physician offices). All physician practices employed stand-alone electronic prescribing systems (i.e., the systems were not integrated with an electronic medical records system). The retail pharmacies that participated were privately owned, independent businesses. The mail order pharmacy was a large corporation and a subcontracted partner in the study.

Site Visits

Each participating pharmacy and physician site was visited by a team of one to three researchers. These initial "Time 1" site visits typically lasted for one to one-and-a-half days. During this time, the research team conducted formal qualitative interviews with key staff members, observations of organizational functioning and prescription-related processes, informal interviews with additional staff members, and time-motion workflow observations. In the case of individuals selected to participate in the formal interviews, the purpose of the interview was explained, and oral consent was obtained. These interviews lasted approximately one hour and covered a variety of topics related to electronic prescribing; they were also audio-recorded and transcribed. Participants did not receive individual compensation for their interviews, but the site was paid $1,000 in recognition of the time required from the staff as a whole. No potential participants who were approached declined to participate.

A "Time 2" visit was conducted at each site one to two months after the initiation of pilot transactions (i.e., two to three months after the initial visit). When possible, the same individuals were interviewed. When this was not possible, another person with a similar role was asked to participate instead (e.g., a prescriber would replace another prescriber). Because of a technical

problem with electronic prescribing that developed between one pharmacy–physician office pair, four physician offices and two pharmacies participated in the Time 2 site visit, and 14 individuals at these sites participated.

Interview Protocol

In both the initial and subsequent site visits, semistructured interviews were used to elicit information on a variety of topics relevant to electronic prescribing, including the overall experience with electronic prescribing as well as detailed information about e-prescribing roles and specific features of the e-prescribing system. Interviewers had a variety of expertise: Two had previous experience conducting qualitative interviews, and one had not previously conducted qualitative interviews but was a substantive expert (a pharmacist). All interviewers participated in an interactive two-day training session designed to enhance interviewing skills and help them become familiar with the interview protocol.

Different semistructured interview guides were created for each type of respondent; these guides included suggested questions, topics, and probes. Interviewers also exercised flexibility in probing and in following up on topics raised by interviewees. The interviews elicited information about general satisfaction with e-prescribing systems, processes, and transactions and also collected more-focused information on features identified as potentially problematic. Interview guides for physician offices and pharmacies covered some overlapping material but were tailored according to the uses and features of e-prescribing in each setting.

Interview Coding

Interviews were digitally recorded and transcribed. Transcripts were inspected, and information that identified individuals or the site was removed. Transcripts were uploaded into Atlas.ti for coding.

The coding scheme developed was based on both themes addressed in the structured interview and themes that frequently emerged during interviews. Once the coding scheme was complete, coder training and reliability testing began. One of the authors of this report served as the primary coder, and a research assistant participated as a reliability coder. Before coding began, the research assistant received training about the overall structure of e-prescribing systems, the general purpose of the project, and the anticipated coding scheme and code definitions. Next, the two coders jointly examined and coded two interviews, making adjustments to code definitions as necessary.

During the reliability phase, the primary coder chunked text into meaningful blocks, then applied codes. The second coder received documents that had been chunked into sections and applied codes to these preselected sections of text. Twenty-five percent of the Time 1 interviews were semirandomly selected, with the constraint that coded interviews included all interviewers, interviewee roles (e.g., pharmacist, pharmacy technician), and a variety of geographic locations. Interviews were coded in sets of two, and the coders met to examine the coded text, discuss the coding scheme and make any necessary adjustments after each set. Reliability was calculated using Cohen's Kappa by calculating reliability for each code within an interview and then aggregating across codes to represent reliability for each interview. The average reliability across interviews was good (Cohen's Kappa = 0.69).

The study was approved by the RAND institutional review board.

Results

Part I. Laboratory Testing

The Completeness and Reliability of RxNorm in Representing Ambulatory Prescriptions

After out-of-scope and invalid e-prescriptions were excluded, the final sample for the evaluation based on historical transactions included 19,743 e-prescriptions. Table 3.1 shows details of the excluded prescriptions. Of note, 297 of the 336 valid prescriptions that were excluded as out of scope for RxNorm (88 percent) were prescriptions for supplies primarily used in the management of diabetes.

Overall Coverage

The coverage of RxNorm for in-scope and properly specified prescriptions is shown in Table 3.1 in the rows below the "Included" category. Overall, 98.8 percent of the final sample matched using automatic mapping from a representative NDC: 94.4 percent with the RxNorm-derived mapping and an additional 4.4 percent when the commercial knowledge base mapping was applied to the remaining unmatched e-prescriptions. Of the 1.2 percent that did not match automatically, we were able to manually find an appropriate RxCUI for 236 of 237 e-prescriptions. A representative NDC had been transmitted in 98 of these 237 prescriptions, and no NDC had been used in the other 139. Of the 98 with an NDC, 97 could be matched manually, and all 139 with a missing NDC could be matched manually.

No adequate RxCUI could be found for only one in-scope e-prescription, resulting in an overall concept coverage rate of 99.995 percent for RxNorm. The one e-prescription that could not be precisely represented by an RxNorm concept was a combination pack containing three different strengths of nicotine patches (NDC 00067503956). RxNorm did contain SCD concepts for each separate patch strength, but, in the case of this particular product—a box of patches at each strength shrink-wrapped into one package—the expected pack concept did not exist in RxNorm. We confirmed with the manufacturer that the missing combination package is still available on the market.

Table 3.2 shows the total number of distinct prescribable concepts available in RxNorm, comparing the October 2009 version with one from six months earlier. Our ambulatory prescription sample required the use of only 1,901 of the 34,443 total "prescribable" RxCUIs available in the October 2009 RxNorm distribution (5.5 percent). Of note, the sample did include many instances of controlled substance prescriptions, including oxycodone, hydrocodone, and fentanyl patches, although Drug Enforcement Administration regulations require pharmacies to reject these prescriptions when they are transmitted electronically.

Table 3.1
Data Sample/Coverage Rate

Description	No. of e-Prescriptions	% of All e-Prescriptions	% Within Category of e-Prescriptions[a]
Total sample	20,135	100.0	n/a
Excluded: out of scope	336	1.67	100
Nondrug prescription	319	1.58	94.9
Equipment	3	0.01	0.9
Supplies (e.g., lancets, syringes, alcohol pads)	297	1.48	88.4
Proprietary formulation	7	0.03	2.1
Compound	12	0.06	3.6
Multivitamin prescription[b]	17	0.08	5.1
Excluded: invalid prescription	56	0.28	100
Nonprescription	14	0.07	25.0
Lab test order	5	0.02	8.9
Message to pharmacist	4	0.02	7.1
Patient instructions in drug field; no drug specified	5	0.02	8.9
Underspecified or misspecified (i.e., invalid) prescription	42	0.21	75.0
Drug underspecified	5	0.02	8.9
Form underspecified	7	0.03	12.5
Strength underspecified	15	0.07	26.8
Ambiguous spelling of drug name	10	0.05	17.9
Product off market[c]	2	0.01	3.6
Pack size nonexistent	2	0.01	3.6
Units misspecified	1	0.005	1.8
Included: in scope and properly specified	19,743	98.05	100
RxCUI found via automated mapping from NDC	19,506	96.88	98.8
Using NDC mapping provided with RxNorm	18,642	92.59	94.4
Using drug knowledge base vendor mapping[d]	864	4.29	4.4
RxCUI found via manual search of RxNorm	236	1.17	1.2
No representative NDC with original prescription	139	0.69	0.7
NDC present, but did not auto-match	97	0.48	0.5
RxCUI not found	1	0.005	0.005

[a] Percentages are based on the totals within each major category (e.g., 19,743 for the "included" prescriptions).
[b] Officially, the scope of RxNorm is limited to medications with four or fewer components, making multivitamins out of scope. In fact, many concepts with more than four components appear in RxNorm (including multivitamins with as many as 18 components), but RxNorm is not yet representing these comprehensively.
[c] These were for "Saliva Substitute" (NDC 00054376950). This product appeared to have been taken off the market by the manufacturer.
[d] We used a commercial vendor's NDC-to-CUI mapping as a supplement for those not mapped with the RxNorm mapping.

Table 3.2
Total Number of RxCUIs, by Distribution Release Date

	April 2009	October 2009
Total	33,507	34,443
Generic	18,398	18,775
SCD	18,162	18,520
GPCK	236	255
Branded	15,109	15,668
SBD	14,807	15,339
BPCK	302	329

NOTE: The listed quantities are from the official RxNorm distribution release in the particular month.

The Stability of RxNorm CUIs over a Six-Month Interval

Among the 19,604 e-prescriptions in the final laboratory testing sample that contained a representative NDC, 18,526 (94.5 percent) automatically matched to an RxCUI from the April 2009 RxNorm distribution. Of the 1,419 RxCUIs comprising those matches, 115 (8.1 percent)—which represented 1,065 e-prescriptions (5.7 percent of the sample)—had been replaced in RxNorm six months later (see Table 3.3). Forward mapping to an updated RxCUI was achieved for all 115 (100 percent) of these RxCUIs using appropriate records from RxNorm's archive/tracking table for retired concepts in the October 2009 RxNorm distribution.

Table 3.3
Change in RxNorm Concepts, April 2009 to October 2009

Status of RxCUIs Used in the April 2009 RxNorm Distribution	E-Prescriptions (No.)	E-Prescriptions (%)	Distinct NDCs (No.)	Distinct NDCs (%)	Distinct RxCUIs (No.)	Distinct RxCUIs (%)	% of Total April 2009 RxCUIs[a]
Present in October 2009	17,461	94.3	2,860	92.6	1,304	91.9	7.1
Obsolete or absent in October 2009	1,065	5.7	230	7.4	115[b]	8.1	0.6
Total	18,526	100.0	3,090	100.0	1,419	100.0	7.7

NOTE: Status is based on the NDC-to-CUI mapping derived from RxNorm April 2009 distribution. Using this mapping, 18,526 of 19,604 (94.5 percent) of the e-prescriptions auto-matched to an RxCUI.
[a] Percentages are based on the 18,398 generic RxCUIs in the April 2009 distribution.
[b] 100 percent of these were forward mapped to a replacement RxCUI in the October 2009 RxNorm archive/tracking table.

The Consistency of Two RxNorm Concept Mappings

Table 3.4 describes the two NDC-to-CUI mapping tables we used in terms of the total number of NDC-to–generic RxCUI linkages available. The RxNorm-derived mapping tables used 65.7 percent of the 18,775 distinct generic RxCUIs that existed in the October 2009 release. (The remaining RxCUIs were not associated with any NDC.) The RxNorm mapping product provided by our commercial drug knowledge base partner used 50.1 percent of the generic RxCUIs available.

Table 3.4
NDC-to-CUI Mappings in the Two Sources Used

	RxNorm Distribution	Commercial Vendor Product
No. of NDCs mapped	330,521	244,247
No. of distinct SCDs or GPCKs mapped to	12,329	9,411

Figure 3.1 tallies the outcomes when each of these mapping tables was applied to our sample. This double application provided two independent RxCUI lookups for each prescription. Of the 19,604 prescriptions with an NDC, 93.9 percent matched in both mappings, 1.2 percent matched only in the RxNorm-derived mapping, 4.4 percent matched only in the drug knowledge base vendor mapping, and 0.5 percent did not match in either mapping.

Figure 3.1
RxNorm and Vendor Match Rates

	Matched in Vendor Table	Not Matched in Vendor Table	Total
Matched in RxNorm	n = 18,408 (93.9%)	n = 234 (1.2%)	n = 18,642 (95.1%)
Not Matched in RxNorm	n = 864 (4.4%)	n = 98 (0.5%)	n = 962 (4.9%)
Total	n = 19,272 (98.3%)	n = 332 (1.7%)	n = 19,604 (100.0%)

RAND *TR941-3.1*

For 676 e-prescriptions (3.4 percent), the two mappings produced nonidentical RxCUIs at the generic level. The mismatches involved 106 distinct NDCs and represented only 67 distinct clinical drugs. Because there should be only one unique RxCUI to represent each generic prescribable drug concept, each mismatch implies the existence of an error, either in one of the NDC-to-CUI mappings or in RxNorm itself.

Table 3.5 categorizes the mismatches. Only one mismatch was categorized as having more than minor clinical significance if the NDC-to-CUI link had been relied on during drug dispensing. This prescription was linked by one match to a topical betamethasone cream and by the other match to an augmented topical betamethasone cream. Relying on one of these interpretations could have resulted in the patient receiving either a stronger or a weaker steroid cream than the prescriber intended. We classified the clinical significance of this difference as moderate, however, because it would be unusual for this difference in strength to result in patient harm. Other mismatches included more-minor form differences, the use of general rather than time-specific extended-release forms, and differences in inhaler canister sizes and salts.

Some mismatches appeared to be due to errors in RxNorm. For instance, the inactive ingredient strength issue example shown in Table 3.5's second-to-last row is most likely due to the fact that RxNorm included two concepts that actually represent the same sodium fluoride solution: One included only the weight of the fluoride ion (19 g/mol) in the concentration, and the other also included the weight of the sodium ion (23 g/mol). Assuming this is true, the actual concentration represented by both concepts would be 0.026 mol/l. RxNorm editorial policy dictates that the

correct, normalized representation of strength should be based on the active ingredients only, so we flagged the "1.1 MG/ML" concept as a likely error in RxNorm.

The Efficiency of RxNorm in Representing Formulary and Benefit Information

Mapping the FSL to RxNorm Concepts

For PBM 1, of 52,913 FSL entries, 27,483 (51.9 percent) automatically matched to an RxCUI (see Table 3.6). For PBM 2, 37,484 (70.8 percent) of 52,778 formulary entries automatically matched to an RxCUI. Sixty-four percent of formulary entries from PBM 1 and 39 percent of formulary entries from PBM 2 were off formulary.

Table 3.5
Classification of Mismatches Between Two Mappings to Generic RxNorm Concepts

Mismatch Type	No. of E-Prescriptions (%)	No. of NDCs (%)	No. of Unique Medications (%)	RxCUI Match Example	Vendor RxCUI Match Example
Form difference of moderate significance	3 (0.4)	2 (1.9)	1 (1.5)	"Betamethasone 0.5 MG/ML Augmented Topical Cream"	"Betamethasone 0.5 MG/ML Topical Cream"
Form difference of minor significance	9 (1.3)	6 (5.7)	5 (7.5)	"chlorhexidine gluconate 40 MG/ML Medicated Liquid Soap"	"chlorhexidine gluconate 40 MG/ML Topical Solution"
Use of general XR dose form when more than one specific duration exists[b]	6 (0.9)	3 (2.8)	2 (3.0)	"Verapamil 240 MG Extended Release Tablet"	"24 HR Verapamil 240 MG Extended Release Tablet"
Use of general XR dose form when only one specific duration exists[c]	113 (16.7)	17 (16.0)	12 (17.9)	"24 HR Potassium Chloride 20 MEQ Extended Release Tablet"	"Potassium Chloride 20 MEQ Extended Release Tablet"
Salt specified vs. unspecified	249 (36.8)	44 (41.5)	16 (23.9)	"Metoprolol 100 MG Oral Tablet"	"Metoprolol Tartrate 100 MG Oral Tablet"
MDI differing in canister size	54 (8.0)	5 (4.7)	4 (6.0)	"60 ACTUAT Albuterol 0.09 MG/ACTUAT Metered Dose Inhaler"	"200 ACTUAT Albuterol 0.09 MG/ACTUAT Metered Dose Inhaler"
MDI vs. its contents	213 (31.5)	22 (20.8)	21 (31.3)	"120 ACTUAT fluticasone 0.22 MG/ACTUAT Metered Dose Inhaler"	"fluticasone 0.22 MG/ACTUAT Inhalant Solution"
Prefilled syringe vs. its contents	7 (1.0)	2 (1.9)	1 (1.5)	"0.3 ML Epinephrine 1 MG/ML Prefilled Syringe"	"Epinephrine 1 MG/ML Injectable Solution"
Strength rounding difference	19 (2.8)	3 (2.8)	3 (4.5)	"Azithromycin 16.7 MG/ML Oral Suspension"	"Azithromycin 20 MG/ML Oral Suspension"[a]
Units difference	2 (0.3)	1 (0.9)	1 (1.5)	"Nicotine 10 MG/ML Inhalant Solution"	"Nicotine 4 MG/ACTUAT Inhalant Solution"[a]
Inactive ingredient strength issue	1 (0.1)	1 (0.9)	1 (1.5)	"Sodium Fluoride 1.1 MG/ML Oral Solution"[a]	"Sodium Fluoride 0.5 MG/ML Oral Solution"
Total	676 (100)	106 (100)	67 (100)	—	—

NOTES: MDI = metered-dose inhaler; XR = extended release.
[a] Probably an erroneous RxNorm concept.
[b] For example, there are both 12-hour and 24-hour extended-release forms available for verapamil. Thus, a prescription using the concept "Verapamil 240 MG Extended Release Tablet" would not contain sufficient information to distinguish the intended drug.
[c] For example, the only available extended release form of Potassium Chloride 20 MEQ is the 24-hour form. Therefore, a prescription using the nonspecific concept could be interpreted to indicate the 24-hour form, and thus the concept could be considered adequately specified.

Table 3.6
Automatic Matching of Formulary Entries to RxCUIs

	PBM 1 (No.)	PBM 1 (%)	PBM 2 (No.)	PBM 2 (%)
Entries in FSL	52,913	100.0	52,778	100.0
Formulary status				
1	33,937	64.1	20,502	38.8
2	18,976	35.9	532	1.0
3	n/a	n/a	31,744	60.1
Entries matched to an RxCUI	27,483	51.9	37,384	70.8

NOTE: Percentages may not sum to 100 due to rounding.

For PBM 1, we randomly sampled 100 of the 25,430 entries that did not match to an RxCUI (48.1 percent) and then characterized each one according to the categories described earlier in this chapter. As Table 3.7 shows, 31 were deemed to be within scope for RxNorm; these were successfully matched to an RxCUI using the vendor's proprietary NDC-to-CUI mapping, or they were sufficiently specified as to allow manual searches for the corresponding RxCUI. A total of 67 formulary entries were out of scope for RxNorm. After both secondary mappings (the vendor's non-RxNorm concordance and the NDC-to-CUI mapping) were completed, two formulary entries still had insufficient information to allow manual matching.

Table 3.7
Characteristics of a Random Sample of Formulary Entries That Failed to Automatically Match to an RxCUI

Category	No.
Total	100
In scope/expected to match	31
Matched via secondary mapping	24
Likely to be matchable via manual search	7
Out of scope	67
Equipment	3
Supply	35
Proprietary formulation	9
Compounding Ingredient	18
Multivitamin	2
Underspecified/no information	2

Applying a Hierarchical Structure to the FSL

The results of our attempt to map the FSL into a hierarchical structure while preserving the original FS of each entry are shown in Tables 3.8 and 3.9. Table 3.8 contains the results of our abstraction to prescribable concepts. The 27,483 formulary entries from PBM 1 that matched to an RxCUI were faithfully represented by 9,584 concepts, implying an effective row reduction of 65 percent. A total of 673 entries (2.4 percent) represented different formulary statuses within a single RxNorm prescribable concept and therefore would not be replaceable if these differences needed to be represented for the prescriber. Assuming that all rows not matching to any RxNorm concept would need to be retained, the overall row reduction would be 34 percent.

Table 3.8
Representation of Formulary Status List Entries with Aggregation, Where Possible, to RxNorm Prescribable Concepts

Abstraction Level	Entries Matched to an RxCUI?	No. of Entries Aggregated	% of Matched Entries	% of All Entries	No. of Concepts Used	% Reduction in Rows Used
Prescribable concepts	Yes	26,810	97.6	50.7	8,911	67
SBD	n/a	9,731	35.4	18.4	5,959	39
BPCK	n/a	214	0.8	0.4	198	7
SCD	n/a	16,831	61.2	31.8	2,736	84
GPCK	n/a	34	0.1	0.1	18	47
NDCs	Yes	673	2.4	1.3	673	0
Total (of matched entries)	Yes	27,483	100.0	51.9	9,584	65

Table 3.9
Representation of Formulary Status List Entries with Aggregation, Where Possible, to RxNorm Drug–Dose Form Concepts or Prescribable Concepts

Abstraction Level	Entries Matched to an RxCUI?	No. of Entries Aggregated	% of Matched Entries	% of All Entries	No. of Concepts Used	% Reduction in Rows Used
Drug–dose form concepts	Yes	25,529	92.9	48.2	5,876	77
SBDF	n/a	9,620	35.0	18.2	4,417	54
SCDF	n/a	15,909	57.9	30.1	1,459	91
Prescribable concepts	Yes	1,281	4.7	2.4	424	67
SBD	n/a	111	0.4	0.2	56	50
BPCK	n/a	214	0.8	0.4	198	7
SCD	n/a	922	3.4	1.7	152	84
GPCK	n/a	34	0.1	0.1	18	47
NDCs	Yes	673	2.4	1.3	673	0
Total (of matched entries)	Yes	27,483	100.0	51.9	6,973	75

Table 3.9 shows the results of our abstraction to drug–dose form concepts. Of the 27,483 formulary entries from PBM 1 that matched to an RxCUI, 25,529 (92.9 percent) could be faithfully represented using drug–dose form concepts (i.e., SBDF or SCDF) with no loss of FS information. A total of 1,281 formulary entries (4.7 percent) could be represented using prescribable concepts (i.e., SBD, BPCK, SCD, or GPCK) with no loss of FS information. Because the 27,483 matched formulary entries were faithfully represented by 6,973 RxCUIs, the effective row reduction was 75 percent; the overall row reduction (including noncompressible formulary entries that did not match to an RxCUI) was 39 percent.

Examples that illustrate the utility of these compressions are provided in Table 3.10. The first two columns list the NDC from a sample formulary entry and its corresponding FS. The "Prescribable Concept" subcolumns and the "Drug–Dose Form Concept" subcolumns list the prescribable concept (CUI, type, and name) and drug–dose form concept (CUI, type, and name), respectively, that correspond to the formulary entry. The final column lists the number of formulary entries with the same FS that fall under the same prescribable concept. Row headings in bold present the highest level of abstraction at which the sample formulary entry (and all others similar to it) can be represented with no loss of FS information.

Table 3.10
Examples of RxNorm Concepts Faithfully Representing Formulary Status Entries with Preservation of Original Formulary Status

Sample NDC	FS	Prescribable Concept CUI	Prescribable Concept Type	Prescribable Concept Name	Drug–Dose Form Concept CUI	Drug–Dose Form Concept Type	Drug–Dose Form Concept Name	No. of Similar Entries
Highest Level: SBDF								
00186013501	1	106530	SBD	"Lidocaine 5 MG/ML Injectable Solution [Xylocaine]"	94618	SBDF	"Lidocaine Injectable Solution [Xylocaine]"	2
00186011001	1	106532	SBD	"Lidocaine 10 MG/ML Injectable Solution [Xylocaine]"	94618	SBDF	"Lidocaine Injectable Solution [Xylocaine]"	11
00186024444	1	107707	SBD	"Lidocaine 15 MG/ML Injectable Solution [Xylocaine]"	94618	SBDF	"Lidocaine Injectable Solution [Xylocaine]"	2
00186012001	1	106534	SBD	"Lidocaine 20 MG/ML Injectable Solution [Xylocaine]"	94618	SBDF	"Lidocaine Injectable Solution [Xylocaine]"	8
Highest Level: SCDF								
00832004209	2	308136	SCD	"Amlodipine 2.5 MG Oral Tablet"	370573	SCDF	"Amlodipine Oral Tablet"	44
55111027090	2	197361	SCD	"Amlodipine 5 MG Oral Tablet"	370573	SCDF	"Amlodipine Oral Tablet"	56

Sample NDC	FS	Prescribable Concept CUI	Prescribable Concept Type	Prescribable Concept Name	Drug–Dose Form Concept CUI	Drug–Dose Form Concept Type	Drug–Dose Form Concept Name	No. of Similar Entries
43547023211	2	308135	SCD	"Amlodipine 10 MG Oral Tablet"	370573	SCDF	"Amlodipine Oral Tablet"	56
Highest Level: SBD								
00245004001	2	832718	SBD	"Potassium Chloride 8 MEQ Extended Release Tablet [Klor-Con]"	628957	SBDF	"Potassium Chloride Extended Release Tablet [Klor-Con]"	5
68645020254	2	628958	SBD	"Potassium Chloride 10 MEQ Extended Release Tablet [Klor-Con]"	628957	SBDF	"Potassium Chloride Extended Release Tablet [Klor-Con]"	9
00245015001	1	832731	SBD	"Potassium Chloride 15 MEQ Extended Release Tablet [Klor-Con]"	628957	SBDF	"Potassium Chloride Extended Release Tablet [Klor-Con]"	3
00245005810	2	833525	SBD	"24 HR Potassium Chloride 20 MEQ Extended Release Tablet [Klor-Con]"	628957	SBDF	"Potassium Chloride Extended Release Tablet [Klor-Con]"	6
Highest Level: BPCK								
00007326201	1	798210	BPCK	"{2 (16.1 ML tositumomab 14 MG/ML Injectable Solution) / 1 (2.5 ML tositumomab 14 MG/ML Injectable Solution) / 2 (20 ML iodine-131-tositumomab 1.1 MG/ML Injectable Solution) } Pack [Bexxar Therapeutic Packaging]"	—	—	—	2
Highest Level: SCD								
00904791451	1	310965	SCD	"Ibuprofen 200 MG Oral Tablet"	370674	SCDF	"Ibuprofen Oral Tablet"	78
53746046400	2	197805	SCD	"Ibuprofen 400 MG Oral Tablet"	370674	SCDF	"Ibuprofen Oral Tablet"	26
63739044310	2	197806	SCD	"Ibuprofen 600 MG Oral Tablet"	370674	SCDF	"Ibuprofen Oral Tablet"	39
68645022254	2	197807	SCD	"Ibuprofen 800 MG Oral Tablet"	370674	SCDF	"Ibuprofen Oral Tablet"	39

Sample NDC	FS	Prescribable Concept CUI	Prescribable Concept Type	Prescribable Concept Name	Drug–Dose Form Concept CUI	Drug–Dose Form Concept Type	Drug–Dose Form Concept Name	No. of Similar Entries
Highest Level: GPCK								
59762307001	2	749780	GPCK	"{3 (Azithromycin 500 MG Oral Tablet) } Pack"	—	—	—	7
Highest Level: NDC								
00904539946	1	312773	SCD	"Ranitidine 75 MG Oral Tablet"	373752	SCDF	"Ranitidine Oral Tablet"	4
00781188431	2	198193	SCD	"Ranitidine 300 MG Oral Tablet"	373752	SCDF	"Ranitidine Oral Tablet"	42
00904583224	1	198191	SCD	"Ranitidine 150 MG Oral Tablet"	373752	SCDF	"Ranitidine Oral Tablet"	2
49884054401	2	198191	SCD	"Ranitidine 150 MG Oral Tablet"	373752	SCDF	"Ranitidine Oral Tablet"	59

NOTE: — = no high-level abstraction is possible.

The potential streamlining benefits of implementing RxNorm in the F&B standard are evident in the case of amlodipine oral tablets. There are 156 distinct formulary entries for amlodipine oral tablets that can be faithfully represented by one drug–dose form concept, "Amlodipine Oral Tablet" (CUI 370573). An example of a prescribable concept being the highest level of abstraction is found in the case of ibuprofen oral tablets: There are 182 distinct formulary entries for ibuprofen oral tablets of four different strengths (200, 400, 600, and 800 mg). All of these entries are represented in RxNorm by one drug–dose form concept, "Ibuprofen Oral Tablet" (RxCUI 370674), but, because the 200-mg tablets have a different FS than the 400-, 600-, and 800-mg tablets, the drug–dose form concept cannot be used without the loss of FS information. However, the four prescribable concept RxCUIs that represent the 200-, 400-, 600-, and 800-mg tablets separately can indeed be used without loss of FS information. Therefore, using prescribable concepts in this case would allow us to faithfully represent 182 formulary entries with four RxCUIs instead of 182 NDCs.

The four rows under "Highest Level: NDC" illustrate a case in which no RxCUIs can be used to faithfully represent formulary entries without loss of FS information. "Ranitidine 150 MG Oral Tablet" (CUI 198191) represents 61 formulary entries, but 59 of those have one FS, and two have a different FS. Therefore, the 61 original NDCs are the only concept specific enough to represent those 61 formulary entries.

Part II. The e-Prescribing Live Pilot

The Use of RxNorm in Live Prescription Transactions

Tables 3.11 and 3.12 summarize all transactions that were exchanged during the pilot testing period, which encompassed about 20 weeks for the retail pharmacy transactions and nine weeks for the major source of mail order transactions. Of the NEWRX transactions, only 44 were sent without a representative NDC, indicating that they were write-in prescriptions that had not been generated from menu selections. These would not be mappable to an RxCUI and were therefore

excluded from the analysis. We also excluded 98 transactions sent to the mail order pharmacy from one site because the field showing RxCUI received had not been retrieved for these transactions. Among the remaining 3,687 transactions, an RxCUI had been successfully resolved and added to 3,549 (96.3 percent). (Note that, in Part I of the study, 2 percent of prescriptions were out of scope for RxNorm, and the RxCUI for an additional 1.5 percent of prescriptions could only be resolved through a manual search due to missing NDCs or incomplete NDC mappings.)

Only one retail pharmacy was making substantial use of the REFREQ transaction. The other pharmacy had decided to revert to faxing refill requests to e-prescribers (thus avoiding the transaction fees associated with electronic refill requests). The mail order pharmacy could not send refill requests to either vendor because neither had yet developed and certified systems to handle refill transactions with mail order pharmacies. Although both vendors had initially planned to develop the necessary systems during the pilot period, they both cancelled these plans due to an expectation that mail order transactions would eventually migrate from the legacy RxHub platform to the Surescripts platform, thus making the development efforts unneeded.

Table 3.11
Data Sources for the RxNorm Live Pilot Test

Partners	No. of Prescribers	No. of Pharmacies	Start Date	End Date	No. of Weeks
Vendor 1 to retail	8	1	October 2, 2009	February 23, 2010	20.6
Vendor 2 to retail	3[a]	1	October 7, 2009	February 23, 2010	19.9
Vendor 1 to mail order	3	1	November 16, 2009	March 26, 2010	18.6
Vendor 2 to mail order	11	1	February 2, 2010	April 6, 2010	9.0
Total	25	3	n/a	n/a	n/a

[a] The three prescribers worked in two independent offices.

Table 3.12
Transaction Volumes for the RxNorm Live Pilot Test

Partners	No. of e-Prescriptions	No. of Refill Responses	No. of New Prescriptions	No. of New Prescriptions with NDCs	No. of New Prescriptions Without NDCs	No. of New Prescriptions Sent with an RxCUI (%)
Vendor 1 to retail	2,613	893[a]	1,720	1,688	32	1,603 (95.0%)
Vendor 2 to retail	614	0[b]	614	602	12	600 (99.7%)
Vendor 1 to mail order	179	0	179	179	0	179 (100%)
Vendor 2 to mail order	1,316	0	1,316	1,316	0	1,265 (96.1%)
Total	4,700	893	3,829	3,785	44	3,647 (96.3%)

[a] Only two matched to a prior NEWRX for the same patient.
[b] This pharmacy sent only 16 renewal requests to the participating prescribers during the ten months prior to the live pilot.

In the case of the "Vendor 1 to retail" pair, prescriptions had been generated using a drug knowledge base (MediSpan) that was not available to the pharmacy. This meant that some representative NDCs would likely prove unresolvable at the pharmacy (as explained in Chapter One). To judge the potential for the RxNorm information received to act as a supplement in cases when incoming NDCs do not match, we examined the interpretability of NDCs received at retail from Vendor 1, using the drug knowledge base used by the pharmacy. Of the 1,688 new pilot prescriptions containing an NDC that were transmitted between this dyad, 76 (4.5 percent) used an NDC that was not present in the target drug knowledge base. For 61 (80.3 percent) of these 76 prescriptions, an RxCUI had been included from the prescribing system. Manually comparing the RxCUIs and the string prescription drug name showed that the RxCUI accurately represented the string in 100 percent of cases.

At the mail order pharmacy, the pharmacists attempted to use the incoming RxCUI as an additional piece of information for clarifying incoming prescriptions that they considered ambiguous. Out of the 1,444 prescriptions that they received with RxCUIs, the pharmacists had flagged 28 (1.94 percent) as needing clarification that might be possible with RxNorm. Because this pharmacy used its own carefully curated NDC file, which merged information from more than one of the drug database vendors, only two of the 28 ambiguous prescriptions were due to an NDC being unresolvable with the pharmacy's file. In both cases, the pharmacy felt that the RxCUI it received clarified the prescription. However, the pharmacy rated the RxCUI as helpful for only one other case out of the 28: a prescription for potassium chloride in which the string drug name said "sustained release" whereas the NDC translated to "Klor con ER," which the pharmacy considered potentially nonequivalent. Because that prescription was also sent with an SBD for Klor-Con, the pharmacist rated this additional piece of information as sufficiently disambiguating. Two other flagged prescriptions involved an XR formulation: one for potassium chloride and one for bupropion. In both cases, the RxCUI sent was an SCD that did not include the specific duration (e.g., 12 hour or 24 hour), and the pharmacist rated the RxCUI as not helpful in disambiguating. Other flagged prescriptions that RxNorm did not help to disambiguate included prescriptions that could have been for either a device or the contents of a device (especially insulins), prescriptions that could have been for either generics or brands considered nonequivalent, and cases of errors in the concentration selected for an albuterol nebulizer solution. In this last instance, the RxCUI showed "albuterol 1 MG/ML" when in fact this solution is only available as albuterol 2.5 mg/3 ml, which should therefore be "albuterol 0.083 MG/ML." The pharmacists considered this to be a rounding error in the RxNorm concept.

Site Visit Results

Most of the physician practices and pharmacies enrolled in the study had been using e-prescribing for less than one year. Despite their recent adoption of the system, the participant pairs were exchanging a substantial volume of electronic prescription transactions. The primary focus of our study was on comparing issues that surfaced during RxNorm pilot testing with those evident immediately beforehand. Thus, most users had already become practiced at handling electronic prescriptions. However, many individuals interviewed at the sites commented on issues that arose during the process of adopting the e-prescribing process (e.g., entering patient demographic information at physician practices), and we have summarized that information in this report. We have also documented e-prescribing challenges that might be addressed through improvements in standards even though those standards could not have been improved in our current study (due to the lack of prescriber user interface changes).

Physician Offices

Prescribers, nurses, and other users of e-prescribing reported being generally pleased with e-prescribing. Several users indicated that they were pleased with the speed and efficiency, compared with other methods of prescribing, afforded by processing electronic prescriptions. For example, one physician office staff member said,

> I would say it's a lot faster this way. Before, we'd always have to wait on the phone and wait on hold to actually talk to a pharmacist because we prefer to actually talk to somebody and have them repeat the prescription back to us. And a lot of times it . . . [was] very time consuming.

One prescriber noted that e-prescribing "makes the clinic work much more efficiently." Prescribers and staff also indicated that e-prescribing reduced the number of errors attributable to misinterpreting prescriber handwriting. For example, one physician practice staff member said, "It seemed that we got a lot more calls before e-prescribe . . . [because the pharmacy could not] read the doctor's writing."

Despite their overall satisfaction, physicians and staff also described a few of e-prescribing's general disadvantages, including the potential for creating new kinds of errors by clicking on the wrong button, needing to log in frequently with a password, and the inability to issue cancellations once a prescription had been sent to the pharmacy. Even if they immediately noticed an error, they could not "undo" it through the system; rather they had to call the pharmacy.

Pharmacies

Pharmacy staff identified two main benefits from receiving and processing electronic prescriptions. First, interviewees noted a reduction in the likelihood of misinterpreting a prescription. For example, one interviewee said,

> You don't have to interpret anybody's handwriting so I think that's probably a big reason why we like to do it. And it does . . . [take] out one person's interpretation too, like when I talk on the phone to the nurses, I might hear something different than what they're actually saying or I might hear a different strength or a different quantity or even a different patient name, [whereas] when it's going through the computer there isn't somebody that has to interpret until it's already on paper the way they wanted it, and so I like that part of it.

One pharmacy technician also indicated that prescriptions received electronically were easier to interpret than notes jotted down by pharmacists during phone calls with prescribers: "The pharmacists, they kind of do the shorthand when they're writing it down and I'm sometimes like, what exactly is this? And usually it's all written out on the e-scribe, so I don't know, it helps in that way."

Pharmacy staff also indicated that receiving prescriptions electronically saved a substantial amount of time by reducing the need to speak with physician offices on the phone. One interviewee said,

> I think a big part for us is it keeps our pharmacists off the phone. . . . We were always on the phone taking new orders. And now that they're starting

to . . . [e-prescribe] more and more, I mean I don't find myself on the phone very much, and . . . [the prescription] goes right to the technician. They can process the new prescriptions and I like it. It works really well.

One pharmacy technician expressed the same sentiment:

The big difference I think is the phone time and transcribing prescriptions over the phone . . . . [E-prescribing is] going to save an awful lot of time, phone time for the pharmacist where they'll actually be able to talk with the patient more versus sitting there talking to the doctor or the nurse on the phone getting new prescriptions or refills.

Specific e-Prescribing Issues Related to RxNorm

A significant issue identified during site visits is that, compared with handwritten prescriptions, e-prescribing requires physicians to overspecify the prescriptions. This was evident across a variety of areas, including the drug itself, the container size or packaging, the drug form, and issues related to selecting brand-name or generic versions.

Issues Related to Drug Selection

Some interviewees in physician offices noted that they were presented with too many options when selecting a drug. For example, one nurse remarked, "I've heard other people complain that there [are] too many options." A physician office staff member said, "The thing sometimes that I don't like is if it's not a familiar prescription to me, being able to figure out which one to pick from, which, then again, you have to go back and check with your provider to make sure that you're picking correctly." Two prescribers provided more-detailed examples of difficulties related to the number of drugs available in the e-prescribing system. One said,

And just don't ever try to order anything with Tylenol in it because you have to go through dozens of screens before you find what you're looking [for] with Tylenol. . . . Because there's a little Tylenol in a lot of things. And it's always label[l]ed "Tylenol plus whatever" or "Tylenol Extra Strength" or "Tylenol this" or "Tylenol that." Well, that creates a screen where you have to drill down and you have to go through five or six screens sometimes to find what you're looking for.

Prescribers also described frustration with multiple listings for drugs they considered clinically equivalent. For example,

There's Verapamil, but then there's Verapamil HCL or with Toprol, it comes as a tartrate and a succinate and I don't know what the difference is there. And for a while there was a shortage of one and so I could never remember which one was short and we'd send . . . [a prescription] and then the pharmacies would be like, "Can we give them this instead?" . . . . I don't know how you could really clarify that, but you know, maybe put, like, "similar to."

Through this and similar comments, prescribers expressed a desire to be able to prescribe using drug concepts—or, in some cases, classes—represented on a more general level, leaving the final specification to be made by the pharmacist based on availability and cost.

Prescribers described difficulties in making drug selections caused by issues related to generic and brand-name identification of drugs. One said,

> I end up having to spend extra time trying to figure out what the medication might be listed as in the computer system . . . . [For example,] "Bactrim" . . . will normally come up, but if I'm putting a child on, like, a Bactrim suspension, it's not under "Bactrim suspension," it's under like the sulfamethoxazole, so you have to go . . . . And now I've figured it all out, but it's taken some time to have to research all that out, to find exactly what it's listed under in the computer, so that's a very frustrating part.

Similarly, another prescriber noted that,

> with Toradol, nothing comes up [in the search] for Toradol. But, if I put in "ketorolac," which is the generic for that, it comes up. So, now, sometimes when you put in, you know, the name brand, the generic will pop up with it. . . . But, like a lot of them, you know, and like this one, I put in Zestoretic which is a combination drug of hydrochlorothiazide and lisinopril, I just got Zestoretic. I didn't get the generics to pop up.

Problems also arose when not all dosages of a drug were listed under a brand-name or generic option: "Some of the strengths are in there under 'Phenergan,' but all of them are in there under 'Promethazine.'"

Pharmacies also had problems with overspecified prescriptions, especially when a generic medication was prescribed that might imply a salt or dose form that the pharmacist could not automatically interchange. One pharmacy technician said, "It comes down to specific types of drugs, like Diltiazems and Cardizems, [for] which there's a lot of AB equivalent stuff. . . . What does the doctor really want? Is this doctor just stating a generic extended release in this drug name?"[2] The same technician also said,

> I guess the best example would be, we have a lot of issues with potassium chloride 10s—ten milliequivalents. Sometimes the . . . [electronic prescription] would say like "pot chlor" and it would populate [based on the NDC] for like a Klor-Con brand name [which is extended release]. . . . Which product do they actually need? . . . So sometimes that has to be sent off for a doctor call or the pharmacist can make a judgment call on that. . . . There's I guess a gap in communication on what the doctor actually wants and what we're trying to give the . . . [patient].

---

[2] "AB" is one of the FDA's "Therapeutic Equivalence" codes. Used alone, it indicates that a given drug is considered equivalent to a reference drug, but, when a number is added (e.g., AB1, AB2), it indicates that there are nonequivalent drugs containing the same ingredients and strengths, each with its own family of equivalent generics. The interviewee is probably referring to the latter situation.

The retail pharmacies preferred that physicians prescribe using brand names because the pharmacy systems are set up to automatically suggest appropriate generic substitutions based on the brand name. One pharmacist said, "Personally I like it when they pick a brand name and then we just pick down from a list of generics that are associated with that brand name in our system." Similarly, a pharmacy technician noted,

> On the new prescriptions, to me it's more important to have the brand name there. That way I know I'm giving that patient exactly the drug that the doctor wants, versus the generic name that could be several different variations of the same drug. . . . If I put in a brand name and I tell the system whether I want it to be dispensed as a generic, our system automatically assigns the generic equivalent of that drug that we have in stock so there's no question as to whether we're dispensing the right or wrong generic drug.

Issues Related to the Formulary and Benefit Feature

Many prescribers and office staff members indicated that they were not familiar with the F&B feature or had never used it. One said, "If there is . . . [an F&B feature], I've not noticed it." Interviewees who had used the feature gave mixed feedback. Many indicated that a feature identifying specific coverage for each patient could be helpful in many ways, including in substituting a lower-cost alternative: "I'll tend to see what's on their formulary and go from there. I'll enter my first bid and see what the formulary pops up . . . and maybe I'll work within that." It would also be helpful in informing patients of the cost:

> If the patient has some financial constraints or they feel that they can't afford that higher co-pay, and even if there's only one medication in that group that they can get and it's going to be a higher co-pay, I can forewarn them . . . .

However, several interviewees indicated that the utility of the F&B feature was limited because the accuracy of information about individuals' coverage was questionable or was available only for a limited number of insurance plans. For example, one prescriber said, "I sometimes question the accuracy of it. . . . I'm sure it's hard to keep up with that because I'm sure the plans change their preferred [drugs] night and day." An office staff member remarked, "I wish they could have all the databases, so therefore everybody's formulary . . . [would] appear." Prescribers also expressed frustration that the differences in cost to the patient were not well represented in the feature: "The other thing is, with . . . [this specific symbol], that means that it's saving preferred costs or whatever, but it doesn't tell you what their [price] range . . . is."

Issues Related to Specifying Quantity and Container Size

Many e-prescribing systems do not allow the common practice of ordering a duration of therapy or a number of containers to dispense without specifying precise quantities. Prescribers may not know the exact container sizes available, and pharmacies may be unsure whether physicians intended to specify a certain container size or simply selected a container size because it was required in order to send the electronic prescription. One prescriber indicated that the problem was encountered especially frequently when e-prescribing liquid medications:

> When you're ordering . . . anything liquid form, . . . [the pharmacy has] had to call. . . . [Usually] I just put in my instructions and have them dispense whatever they need to dispense . . . [but] they've had to call before for clarifying the amount to dispense, whether I ordered too much on . . . [the e-prescribing system] or not enough.

Similarly, a nurse remarked,

> Say, for example, you're ordering a topical medication that comes in a 30 gram tube. Sometimes I end up having to call the pharmacy to ask them specifically . . . "How many uses does this have? How many times can they . . . how many days do they get out of it?" You know, so that I know that I'm sending the correct number of tubes.

Another prescriber indicated that quantity defaults sometimes caused erroneous prescriptions to be transmitted:

> If I put in Lovastatin, . . . it's got, under my choices for quantity or the type I want . . . it says "ea" for each, or it'll say "box of 12." . . . If it highlights "box of 12" [as the unit], and I don't actually go through and switch that to "each," I'll get [a large number of] pills that'll be sent to the pharmacist and the pharmacist will call me and say, "Did you mean to . . . send this many?" And, of course I don't mean to send that many pills.

Although the root causes of these problems are primarily related to the user interface and the drug knowledge base on the prescribing side, and although RxNorm probably could not be used to address these problems, they remain a substantial frustration for pharmacists and providers alike.

Drug Form

Sometimes the e-prescribing system required prescribers to identify the specific form of the drug (e.g., capsule, tablet). A nurse indicated that this was problematic because she was not sure whether the two forms were equivalent: "For instance, he picks a capsule in a 500 mg and I come up and it says 'tablet, 500 mgs.' You know, I'm not sure, is it the same, so that makes it kind of difficult there." This issue could also create difficulties for pharmacies, which may stock only one form of the drug.

Pharmacy Comments on RxNorm-Related Changes

During the follow-up site visits, we found that the expected RxNorm-based alerts were not functioning at one of the two retail pharmacy pilot sites. The staff there could not recall any alerts having occurred after the first few days of the pilot, and further investigation corroborated that the alerts had probably ceased functioning at that point, although the RxCUI was being received. The pharmacy software vendor subsequently diagnosed and fixed the problem, but the project's short timeline and limited travel budget prevented a repeat site visit.

At the other retail pharmacy pilot site, the RxNorm alerting module was effectively implemented. Two staff members provided feedback on the new features implemented in the module and offered very different perspectives: One staff member felt the change was very positive, and the other felt that the change was negative.

The first staff member said,

When we pick the medication from our list of medications in our system compared to the one that the doctor has sent over [electronically] from their office, for a while we had a check there where if—I don't know if they did it by the NDC or how it was screened—but if our medication that we picked in our system didn't match up with what the doctor sent over, it would flag it for us and it wouldn't let us go on further. It would pull up our list of medications again and let us make a correction if it was an error, or if it wasn't an error and it's just made by a different manufacturer—maybe the NDCs didn't match up but the medication is correct—we could bypass it at that screen. . . . I think it's a good feature. Myself personally, I can't remember processing a prescription that it did that to me or it flagged it, but there's always a chance. That's one field [the drug field] that isn't populated for us when the prescription comes through. When we're putting that new information in on the new prescription . . . we have to look at their list and go into our system and pick from our list. So there's a chance of error there; whether or not we read the correct strength or we pick from our list the correct strength. It's just a double check, I think that if it does flag something that's wrong, you can say hey, this doesn't exactly match up with the information we received from the doctor. Do you want to double check? Is this an error or if it's the same medication, same strength, same dose and everything, it might just be from a different manufacturer than what the doctor picked and then you can bypass it there. But it does give you a double check when you're picking the correct medication, which is good.

However, the second staff member said,

Also something else that's new is . . . on a new prescription if the nurse selects a drug that doesn't match our NDC number, it will come up with a screen—when you're creating the new prescription—a screen pops up that says that it doesn't correlate and it tries to get you to select a different one from a list and if you don't, it won't let you save the prescription on the page. You just have [to] go ahead and fill it without saving it, I guess. . . . A lot of times it seems like it happens when we have Z-Paks, azithromycin. I'll get a prescription for it and we have two different NDC numbers of that. We have the packs that have six tablets in it or a bottle that has 30. If it's a Z-Pak we will usually pick the one with the six tablets and it seems like the nurse will pick a different one and so it will . . . [alert us that] the NDC numbers don't correlate. So I just go ahead and I use the one that we use because we have to do that so we [know] our inventory level, but basically that's one of the ones I noticed the most that it was doing it on, was the Z-Paks."

This staff member viewed this feature as

mainly an intrusion because there's no way that the nurses would know what we have on inventory, and so basing it off of the NDC number on that just to make sure that they correlate probably isn't the best way to do it because we're always changing brands or—not brands, but companies—

just so that we get the best price for the customers, and the SKU [stock-keeping unit] number will always change.

In reality, these interviewees were mistaken in thinking that the alerts were based on NDC mismatches. They were in fact based on RxCUI mismatches, and azithromycin was a particularly frequent trigger because the vendor of the drug knowledge base used by the e-prescribing partner transmitting to this site had made a decision not to implement the RxNorm "pack" concepts (such as the Z-pack) and instead used the concept representing the contents of the pack (such as the SBD for Zithromax). The pharmacy system, on the other hand, did use RxNorm "pack" concepts in representing the medication selected, so prescriptions for what were in fact pack concepts always generated alerts on the pharmacy side.

Discussion

The Readiness of RxNorm for Ambulatory e-Prescription Transactions

The Completeness and Accuracy of Prescribable Concepts in RxNorm

Our laboratory evaluation suggests that RxNorm includes nearly all prescribable drug concepts needed to represent in-scope electronic prescriptions from ambulatory primary care settings. Furthermore, we found very few concepts that suggested the persistence of errors or unresolved synonyms in RxNorm at the level of generic prescribable drugs. Overall, these results suggest that the processes put in place by the NLM for maintaining RxNorm are effectively identifying the available prescribable entities and are mostly effective in resolving synonyms to a single concept identifier.

In live pilot testing, both the e-prescribing system vendors and the retail pharmacy were able to include RxCUIs with the vast majority of prescription transmissions. Furthermore, among prescriptions transmitted between partners that were using different drug knowledge bases, the representative NDC was not interpretable in the case of approximately one in 20 prescriptions. In 80 percent of these instances, the RxCUI had been transmitted, and in 100 percent of these cases, the RxCUI accurately represented the prescription. Thus, RxNorm offers value by automatically disambiguating representative NDCs that the recipient cannot map. The frequency of such exceptions was great enough that our retail pharmacy partner had designed its work process to disregard the representative NDC. However, using RxNorm as a secondary supplement to an unreliable primary identifier is unnecessarily complex, and this use fails to capture the potential value of RxNorm for representing the prescriber's intent (as discussed later in this chapter). Future work should focus on using RxNorm as the primary identifier in prescriptions.

The scope of RxNorm was also broad enough to cover more than 98 percent of prescriptions transmitted from the outpatient settings involved. For out-of-scope prescriptions, automated interpretation would need to continue based on representative NDCs alone. However, our findings suggest that diabetes supplies should be the top priority for expanding the scope of RxNorm, as these constitute approximately 90 percent of ambulatory prescriptions that are currently out of scope. Although diabetes supplies do not fit the basic pattern that is currently the foundation of prescribable concepts in RxNorm (i.e., [drug, strength, dose form]), other normalizing principles could be sought to fill the apparent need. The numbers suggest that adding supplies would outweigh other areas of current activity, such as adding multi-ingredient vitamins.

Several important limitations need to be considered in the interpretation of these results. First, with the exception of a few general surgeons, the study sample included only primary care physicians. Although primary care physicians write a large majority of outpatient prescriptions in the United States, it is possible that the prescriber needs of some specialists may be less well represented in RxNorm. Future evaluation could therefore focus on the use of RxNorm for prescriptions from

specialists who would prescribe substantively different kinds of drugs compared with those used in primary care. Second, controlled substances were largely unrepresented in the samples because, at the time of the study, Drug Enforcement Agency regulations prohibited the electronic transmission of such prescriptions. However, there is no reason to believe that RxNorm's handling of these concepts would differ. Furthermore, the data distributed with RxNorm includes the controlled-substance status of prescribable concepts (in the "DCSA" attribute [the Controlled Substance Act designation code] within the "RXNSAT" distribution file); thus, NDCs should not be necessary to detect and filter controlled-substance prescriptions. Finally, our evaluation of completeness and accuracy focused on largely generic concepts. All branded concepts in RxNorm have a generic representation, and the cases in which physicians specify that brands be dispensed as written are relatively rare; therefore, the generic concept is typically the central expression. However, further evaluation of brand concept accuracy in RxNorm, using a larger sample that could be enriched for "dispense as written" events, may be warranted.

Fixing some of the persistent errors in RxNorm may require better mechanisms for identifying the details of the actual underlying drugs that are being represented by the source terms that RxNorm is operating on to normalize. Probably the most common issue is with drug strengths that have been rounded to one or two significant figures prior to inclusion in RxNorm. (The RxNorm standard is to include three significant figures.) To determine whether "azithromycin 20mg/ml oral suspension" is in fact the same as "azithromycin 16.7mg/ml oral suspension" may require substantial investigation that could include tracing the "20mg/ml" concept to its source, to the manufacturer, or both. Drug manufacturers could contribute to this process by ensuring that the FDA has complete and accurate information (including NDCs) for each drug manufacturers make available. This information could then be automatically fed into the RxNorm maintenance process. Manufacturers could also participate directly in maintaining or checking the accuracy of NDC-to-RxNorm mappings.

The Stability of RxNorm Identifiers

The rate of change in currently valid RxNorm identifiers—8 percent of RxCUIs changed over a six-month period—was relatively substantial, given that RxCUIs are intended to be permanent identifiers for distinct drug concepts. Some of these changes are likely due to one-time corrections in unresolved synonyms, and others to changes in editorial policy. We expect this rate of change to decline after editorial policies are refined to reflect real-world experience with RxNorm.

During the live pilot test, the archiving and replacement of RxCUIs did result in some false alarm alerts for possible dispensing errors in the pharmacy, although these constituted only a minority of alerts. Taken together, our findings suggest that users must frequently update their RxNorm distributions. Furthermore, to make historical RxCUI data interpretable, it will also be very important for RxNorm users to maintain forward translations from retired and archived RxCUIs to the current RxCUIs that have replaced them.

Challenges Due to Nonspecific RxNorm Terms

The remaining challenges to the usability of RxNorm relate to the existence of prescribable concepts that could specify more than one clinically different prescribable entity. An example is "Verapamil 240 MG Extended Release Tablet," a nonspecific term that could indicate either the 12-hour or the 24-hour form of the medication (both of which are also represented in RxNorm). For the majority of extended-release cases in our sample that resulted in a mismatch, there was in fact only one extended-release duration available, making the nonspecific version of the concept functionally a

synonym. However, in the case of verapamil and similar examples, a prescription using the nonspecific extended-release term would be inadequately specified and would require a pharmacy callback. Drugs that are expressed both as a base and as one or more possibly equivalent salts are the other major source of such ambiguities (e.g., buspirone vs. buspirone HCl, metoprolol vs. metoprolol tartrate vs. metoprolol succinate).

The problem with nonspecific extended-release forms could potentially be addressed by using an algorithm to flag for nonuse in e-prescribing the SCD and SBD concepts that represent extended-release forms that have no specified duration of action. The "multiple ingredient" concept type (abbreviated "MIN") recently added to RxNorm, in combination with the RXN_QUANTITY attribute and the related dose form, might enable such concepts to be flagged algorithmically. In brief, a query could identify all SCD or SBD concepts with the dose form "Extended Release Capsule" or "Extended Release Tablet" and for which there is more than one such concept linked to the same multi-ingredient combination or Semantic Clinical Drug Component (SCDC). Of these identified concepts, those with no value for RXN_QUANTITY (which contains durations of action, such as "24 HR") would be the nonspecific extended-release terms that should be suppressed for purposes of prescribing. To enable entering complete duration-of-action information on extended-release forms, manufacturers should consistently specify the expected duration of action for extended-release forms in their product information, and the FDA should carry this information through to the NLM. Removing these nonspecific extended-release forms would preclude prescribers from *intentionally* leaving the duration of action unspecified for an extended-release form, but we are not aware of situations in which leaving the duration unspecified would be desirable, at least in the context of electronic prescriptions to be filled in pharmacies.

A limitation of our analysis is that our strategy for discovering ambiguities in RxNorm was based on only two NDC-to-CUI mappings. It is conceivable that additional mismatches and mismatch types would have been discovered if additional vendor mappings had been compared. However, the fact that different drug knowledge base vendors disagree on NDC mappings despite the independent efforts of each to canvass packagers for updated NDCs illustrates the intractability of this decentralized approach. The knowledge base vendors are now collaborating to ensure that RxNorm can serve as the authoritative reference source for NDCs, but, to truly ensure the accuracy of this source, the FDA should also enforce the universal reporting of updated NDCs by packagers.

RxNorm's Potential to Serve as the Primary Medication Identifier in Prescriptions
Our site visit interviews, both with physicians and pharmacists, revealed that the e-prescribing systems often caused prescriptions to be issued with a level of specificity that did not exactly capture the clinician's intent. In most cases, the systems tended to force the selection of a medication name that matched an individual NDC, leading to overspecification compared with the clinical intent (e.g., specifying a capsule when a tablet would be equally appropriate). However, in some cases, prescriptions with NDC (usually for a generic drug) were considered underspecified by the pharmacist due to the existence of nonequivalent branded drugs that the generic concept could match. In conclusion, we found in live pilot testing that RxNorm could potentially reduce the need for pharmacy callbacks, improving efficiency both for prescribers and pharmacies. However, prescription overspecification will not be addressed as long as NDC remains the primary system for drug identification within e-prescribing systems.

RxNorm's Potential in Checking for Pharmacy Dispensing Errors

In our pilot test of RxNorm's ability to automatically check the accuracy of prescription fill selections, we found a high rate of arguably false alerts. Some of these alerts were due to differences in the RxNorm versions used by each partner, which illustrates the importance of frequently updating the RxNorm version in use. However, the majority of false alerts were due to the pharmacy technician essentially creating an interchange at the time of data entry by selecting a brand name or a dose form that was actually different from the prescribed concept (e.g., selecting Keflex for a cephalexin prescription or a tablet when the prescription was for a capsule). Because the intent in the pharmacy system interface was for the pharmacy technician to precisely capture the medication prescribed and then to make any interchanges in a later step, these are arguably not false alerts but rather alerts indicating that the user has essentially taken a shortcut. This may explain why, during interviews with users at the one pharmacy where the RxNorm-based alerting had worked prior to our site visit, we learned that pharmacy technicians found the feature annoying but the pharmacist found the feature potentially useful—despite an apparently high false-positive rate—for preventing drug-selection errors.

An alternative use case for dispensing error checking is to compare the final medication selection (after any interchange) with the medication in the prescription. For this use case, RxNorm provides aggregate concepts that may be useful: namely, the SCDC, which represents drug-dose pairings without the dose form (e.g., "cephalexin 500 mg"), and a new concept type, the MIN, which essentially represents specific combinations of SCDCs (e.g., Trimethoprim 160 mg/ Sulfamethozazole 800 mg). However, a false alert would still be generated in the case of an interchange to a different strength with a concomitant change in the patient instructions to achieve the same total dose (e.g., changing a prescription for 40 mg, one tablet daily to 20 mg, two tablets daily). A standard for codifying the patient instructions portion of the prescription would be needed for accurate checking of the total dose. In a related project, we recently evaluated the NCPDP's current standard format for codifying the patient instructions (Liu, 2011).

RxNorm Readiness for Use in the Formulary and Benefit Standard

This study demonstrated that 98 percent of the relevant entries in a large PBM's FSL could be represented using RxNorm with no loss of FS information. The remaining 2 percent of entries represented manufacturer-level differences in coverage within the same clinical drug. The need to represent these distinctions in the F&B file and to present them to the prescriber is questionable because the drugs should be clinically interchangeable at the pharmacy.

We found that using only "prescribable" RxCUIs (i.e., SCD, SBD, GPCK, or BPCK) in the FSL would enable the same formulary information to be represented with one-third the number of entries used in systems based only on NDCs. If RxNorm were used to its fullest extent, allowing higher-level drug–dose form concepts (i.e., SBDF or SCDF) in addition to "prescribable" concepts, the same information could be represented with roughly one-quarter the number of entries. Although the complexity of allowing two different classes of RxNorm terms to be used in formulary data files might appear challenging, the "condensed" files could easily be expanded by vendors to contain only prescribable concepts if the same relations that we used in analyzing the F&B files were used (e.g., linking an SBDF to each of its SBD children). The prescribable concepts generated by expanding drug–dose form concepts would simply need to be the superseded by any prescribable concepts that were already represented in the files.

Either use of RxNorm could enable streamlined maintenance of F&B files, as coverage decisions could be standardized at meaningful levels of abstraction (e.g., deciding to cover all generic amlodipine oral tablets rather than making intentionally different coverage decisions for different brands or dose forms). In the Klor-Con example discussed in Chapter Three, the PBM would cover three out of the four available strengths (8, 10, and 20 MEQ, but not 15 MEQ). Despite this, the use of RxNorm would still allow 23 independent products to be represented by four RxCUIs instead of 23 NDCs, with no loss of FS information.

Therefore, for the NCPDP F&B standard, we recommend that the RxCUI serve as the primary index and that use of the NDC field cease except to represent products that are out of RxNorm's scope. If the scope of RxNorm were extended to include diabetes supplies, a substantial amount of additional F&B content might be similarly condensed. Additionally, the usefulness of RxNorm in the F&B standard could be further increased if the NLM were able to provide a list of NDCs that are explicitly excluded from RxNorm. The NLM already provides NDC-to-CUI mappings; this proposed out-of-scope list would essentially be the inverse.

One limitation of our study is that we analyzed only the FSL from PBM 1. It is possible that our findings would have been different if we had analyzed PBM 2's FSL. However, because PBM 1 had a much lower match rate than PBM 2 (51.9 percent vs. 70.8 percent), our estimates of the benefit of RxNorm are likely to be conservative. In addition, the F&B standard includes "Formulary Alternatives" and "Benefit Coverage" Lists, which we did not evaluate. However, the FSL is the largest and most diverse list in the standard, and any efficiency benefits seen in the FSL are likely to be seen in the Alternatives and Coverage Lists as well. Finally, we did not conduct live pilot testing to evaluate RxNorm-based F&B files. The retooling required to use RxNorm for managing and presenting drug coverage information will likely require considerable effort from industry. However, this approach appears to be the best path for resolving the inaccuracy of F&B information that is currently shown to prescribers.

References

Bell DS, Cretin S, Marken RS, Landman AB. A conceptual framework for evaluating outpatient electronic prescribing systems based on their functional capabilities. *Journal of the American Medical Informatics Association*. 2004;11(1):60–70.

Bell DS, Schueth AJ, Guinan JP, Wu S, Crosson JC. Evaluating the technical adequacy of electronic prescribing standards: Results of an expert panel process. *Proceedings of the AMIA Annual Symposium*. 2008:46–50.

Brailer DJ. Translating ideals for health information technology into practice. *Health Aff* (Millwood). 2004;Suppl Web Exclusives:W4-318–320.

Brailer DJ. Interoperability: The key to the future health care system. *Health Aff* (Millwood). 2005;Suppl Web Exclusives:W5-19–21.

Cimino JJ. Desiderata for controlled medical vocabularies in the twenty-first century. *Methods Inf Med*. 1998;37:394–403.

Donyai P, O'Grady K, Jacklin A, Barber N, Franklin BD. The effects of electronic prescribing on the quality of prescribing. *Br J Clin Pharmacol*. 2008;65:230–237.

Eslami S, Abu-Hanna A, de Keizer NF. Evaluation of outpatient computerized physician medication order entry systems: A systematic review. *J Am Med Inform Assoc*. 2007;14:400–406.

Grossman JM, Gerland A, Reed MC, Fahlman C. Physicians' experiences using commercial e-prescribing systems. *Health Aff* (Millwood). 2007;26:w393–404.

Hammond WE. The role of standards in electronic prescribing. *Health Affairs* (Millwood). 2004;Suppl Web Exclusives:W4-325–327.

Jani YH, Ghaleb MA, Marks SD, et al. Electronic prescribing reduced prescribing errors in a pediatric renal outpatient clinic. *J Pediatr*. 2008;152:214–218.

Lau LM, Lam SH. Applying the desiderata for controlled medical vocabularies to drug information databases. *Proceedings of the AMIA Annual Symposium*. 1999:97–101.

Levinson DR. *The Food and Drug Administration's National Drug Code Directory*. Department of Health and Human Services, Office of Inspector General. 2006.

Liu H, Burkhart Q, Bell DS. Evaluation of the NCPDP Structured and Codified Sig Format for e-prescriptions. *Journal of the American Medical Informatics Association*. 2011 (*in press*).

National Association of Boards of Pharmacy. Model Act. As of April 28, 2010: http://www.nabp.net/publications/model-act/

National Library of Medicine. An Overview to RxNorm. Web page, July 2009. As of June 30, 2010: http://www.nlm.nih.gov/research/umls/rxnorm/overview.html

National Library of Medicine. RxNorm Project History. Web page, June 2006. As of June 30, 2010: http://www.nlm.nih.gov/research/umls/rxnorm/history.html

NLM—*See* National Library of Medicine.

Wang CJ, Patel MH, Schueth AJ, et al. Perceptions of standards-based electronic prescribing systems as implemented in outpatient primary care: A physician survey. *J Am Med Inform Assoc*. 2009;16:493–502.

Wolfstadt JI, Gurwitz JH, Field TS, et al. The effect of computerized physician order entry with clinical decision support on the rates of adverse drug events: A systematic review. *J Gen Intern Med*. 2008;23:451–458.