A Perioperative Medicine Clinical Decision Support System:

Foundation, Design, Development, Evaluation, and the Standards

A Dissertation

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Dedication

To Bayee; I am forever grateful to you!

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Chapter 1

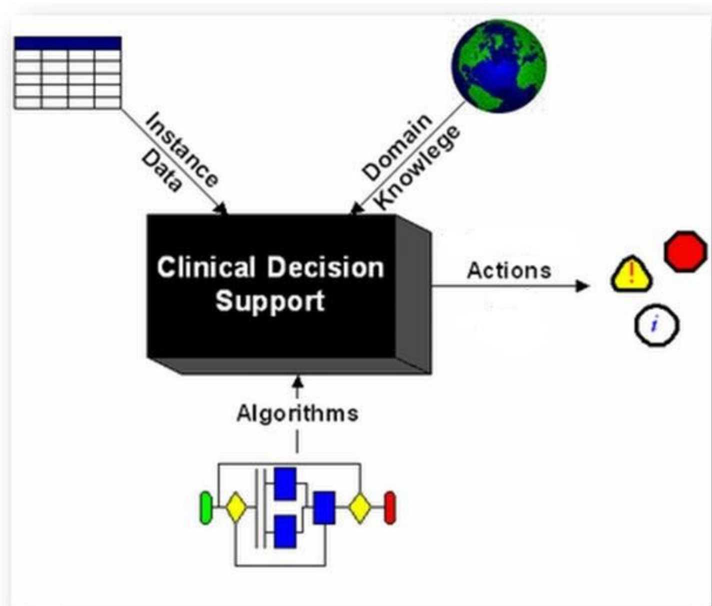
Introduction

The US population is aging[1] and living longer. These twin phenomena are bringing with them increases in surgeries, surgery-related complications, and costs.[2-5] Roughly, half of patients undergoing surgery take medications unrelated to surgery, with a significant increased risk of post-operative complications compared to patients taking no medications.[6] Consequently, there is considerable potential for adverse drug reactions in the perioperative period. Current perioperative morbidity and mortality is frequently associated with patient medical co-morbidities and patient safety problems in the context of surgery or anesthesia.

As a result, perioperative medicine- the consultation, care, and co-management of patients undergoing surgery- is becoming an ever-increasing area of clinical focus in primary care. A key step in the perioperative medicine process is providing medication management recommendations to patients and providers. These recommendations are decisions on stopping or continuing the patient's medications prior, during and after a planned surgery. Due to the paucity of clinical research perioperative medication management recommendations are largely a provider-specific practice. Hence, practice variations exist in making the most appropriate recommendations in the perioperative setting.

Clinical decision support systems (CDSS) are "active knowledge systems, which use two or more items of patient data to generate case-specific advice." [7] This implies that a CDSS is simply a decision support system that is focused on using knowledge management in such a way to achieve clinical advice for patient care based on some number of items of patient data. CDS tools can help enhance doctor-patient communication[8] and potentially improve workflow, efficiency, and patient outcomes. Clinical decision support systems are typically designed to integrate a medical knowledge base, patient data and an inference engine to generate case specific advice (Figure 1-1).

Figure 1-1. Clinical Decision Support Components and outputs



A 2005 systematic review by Garg et al [9] concluded that CDSSs improved practitioner performance in 64 of 100 studies. Sustainable CDSS features associated with improved practitioner performance include the following:

- HIT systems can improve access to pieces of information, organize them, and identify links between them

- Clinicians often ‘know’ the information (e.g. drug–drug interaction) but forget to consider it
- HIT systems are effective in bridging this ‘knowing–doing’ gap by presenting the relevant information to the clinician at the time of decision making[10]

Medication management recommendations can effectively be thought of as guidelines. They are generally broad-based statements that apply to a general class of patients; however, patient specific criteria must be considered for the optimal application of a recommendation. The promise of guidelines, especially automated ones, to reduce practice variability and improve outcomes is great[11], and previous work has shown that computer-generated, patient-specific reminders can positively influence practice.[12 13] As computers become standard tools of clinical practice, computer-based guidelines can increasingly be integrated into routine workflow, so that “clinicians can have more immediate access to the most current and relevant information at the time they most need it--when making clinical care decisions.” [14]

Furthermore, these recommendations are documented in EHR systems in free-text, unstructured format, making statistical analysis, indexing, storing, and timely retrieval of data practically intractable. Standardized structured terminology development will be useful to better understand the clinical work and associated clinical decisions in perioperative medication management. The meaningful use of EHRs aims to establish the effective use and exchange of health care information in order to support better decision making and more effective processes. In fact, Stage 2 of Meaningful Use of EHR systems recommends SNOMED CT [15] (Systemized Nomenclature of Medicine Clinical Terms) for structured coding of clinical data in EHRs[16]. SNOMED CT is a comprehensive clinical terminology which provides a consistent way to index, store, retrieve, and aggregate clinical data across disparate specialties and health care facilities. Expressing perioperative medication management recommendations in SNOMED CT can potentially help reduce practice variability in data capture and encoding.

Two great opportunities exist to help improve patient outcomes in the perioperative setting: 1) utilizing Health Information Technology (HIT) to put medical information from trusted sources in the hands of providers by creating a CDSS to aid physicians with making drug management recommendations at the point of care; and 2) evaluating the use of structured clinical concepts in SNOMED CT for expressing perioperative medication management recommendations in order to make this clinical information computable, and thus usable, for efficient and more accurate population studies, outcomes research, and cost-benefit analyses.

Study Objectives

The overall research project described here consists of three studies. In the first two studies we utilized fundamental principles in clinical informatics combined with qualitative and quantitative methodologies to design, develop, and evaluate a medication management recommendation CDSS. This system would be deployed during a pre-op physical exam evaluation when the patient’s medications are reviewed and decisions on stopping or continuing them prior to surgery are made. In the first study we developed the necessary heuristics (rule-based system) to provide the foundation for an eventual CDSS in perioperative medication management. The heuristics were developed using methodical searches of trusted medical sources. To vet the knowledge within, and results of relevant studies, we enrolled domain experts in perioperative medicine to provide context as well as interpretation of study findings. The “rules” file containing the heuristics was developed with the portable XML markup language, using established literature search techniques on trusted medical sources. In the second study we designed, developed and evaluated a medication management recommendation system from the rules engine in the previous study and other web-based software components. In the final step of this study, we evaluated the accuracy and performance of the tool with a test set of actual, annonymized patient cases.

In the third and final study we incorporated inter-rater reliability and questionnaires to evaluate the use of a standard terminology for expressing medication management recommendations in a structured, portable, and computable format. Because those components of the EHR demonstrated to improve quality (e.g. Computerized Provider Order Entry (CPOE) and CDSSs) depend on the ability of EHRs to code clinical data in a structured and standardized format[17-19], the ability to improve quality of medication management recommendations is contingent upon the use of standardized terminologies as a prerequisite to improving health outcomes.

In what follows this introduction details of these studies will systematically discuss and achieve the following objectives:

1. Collecting, analyzing, and vetting medication management recommendations from trusted medical sources

2. Building and evaluating a decision support system based on Objective 1
3. Evaluating the use of existing structured terminology standards to express medication management recommendation concepts

Using pharmacy data, evidence-based literature, and expert panel opinions, these three studies serve to fill fundamental gaps in two critical areas: 1) making the best known medication management recommendations in the preoperative setting; and 2) the feasibility of using structured clinical terms to express medication management recommendation concepts currently documented in free-text style. Our studies can serve as a blueprint for constructing and evaluating future systems in similar environments. The ultimate goal of this project is helping to improve patient outcomes by creating a decision support system and utilizing structured data to assist in making clinical decisions and creating more accurate patient data.

Chapter 2

Perioperative Medication Management Decision Heuristics: Foundational Development of a Clinical Decision Support Tool

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Introduction and Background: *Decisions regarding medication management during the perioperative period are often made based on clinical anecdotes and vary by provider. Clinical decision support (CDS) tools aid physicians with decision making tasks at the point of care. We have developed a set of perioperative medication management recommendation decision heuristics based on evidence-base literature, clinical notes, and expert opinions. These heuristics will serve as the foundation for a subsequent CDS tool in perioperative medicine.*

Methods: *In this descriptive study, we manually extracted key demographic and medication-related data from the records of 100 randomly-selected patients at the Minneapolis VA's preoperative medicine clinic. We then searched PubMed for studies in perioperative medication management as well as other web sources for expert opinions in the field. Relevant studies, clinical notes, and expert opinions were distilled into an XML-based set of heuristics "rules" file.*

Results: *We have developed medication management recommendation heuristics for the entire VA's formulary of drugs based on evidence-base literature, actual clinical notes, and expert opinions.*

Discussion and Conclusion*: This work shows a proof of concept for the full-scale system development of similar decision support systems.*

Background

Decision making in medicine is complex because a substantial amount of knowledge is required even to solve seemingly simple clinical problems.[20] A physician is required to remember and apply the knowledge of a large array of entities such as disease presentations, diagnostic parameters, drug combinations and guidelines.[21] However, the physician's cognitive abilities are challenged by factors such as multi-tasking, limited reasoning, and memory capacity.[22 23] These challenges are particularly difficult in perioperative medicine, where providers must recall large amounts of information and process clinical data spanning multiple clinical specialties.[24] With an aging population [1] there has been a substantial increase in the number of surgeries, surgery-related costs, and complications from surgery.[2-5] At least 50 percent of patients undergoing surgery take medications on a regular basis [6], and as many as 44% take one or more medications prior to surgery.[25] Furthermore, half of the general surgical patients take medications unrelated to surgery, with a significantly increased risk of post-operative complications compared to patients taking no medications.[6] With the induction of anesthesia – sometimes with the introduction of ten or more drugs- the probability of an adverse drug interaction increases substantially with the number of drugs a patient receives.[26] Consequently, there is considerable potential for adverse drug reactions in the perioperative period. Current perioperative morbidity and mortality is frequently associated with patient medical co-morbidities and patient safety problems in the context of surgery or anesthesia.

Although the surgical burden in the U.S. is increasing, some perioperative medicine providers feel that they are inadequately trained to perform preoperative evaluations.[27] Unfortunately, there is limited outcome data related to the majority of medications taken in the perioperative period, and few controlled trials regarding perioperative medication discontinuation and resumption, so decisions regarding medication management are often made based on pharmaceutical manufacturer recommendations, expert consensus, in vitro studies, or clinical anecdotes.[28] This lack of medical evidence is reflected by the large variation in perioperative medication management recommendations among providers.[29-31]

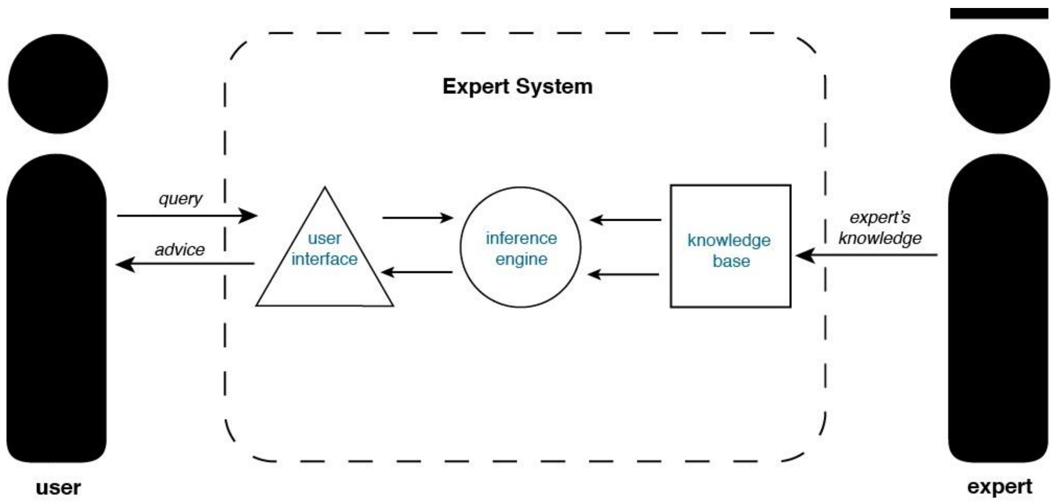
On the other hand, clinical decision support systems (CDSS) aid health care professionals with decision making tasks at the point of care.[32] These systems provide evidence-based knowledge in the context of individual patient parameters.[7] CDSSs have been shown to be effective tools in aiding with providing alerts and reminders[33], computerized provider order entry (CPOE) support[34], and making recommendations.[35 36] The popularity and usage of CDSSs have been growing due to the evidence that they improve clinical practice and physician performance.[9 37]

Rule-based expert systems are a special class of CDSS in which computers emulate the decision-making ability of a human expert.[38] The building, maintenance and development of expert systems is known as knowledge engineering,[39] a "discipline that involves integrating knowledge into computer systems in order to solve complex problems normally requiring a high level of human expertise".[40] Expert systems (Figure 2-1) have three basic components[32]:

1. Knowledge Base: a set of expertise supplied by domain experts

2. Inference Engine: the component which processes the knowledge (heuristics) furnished by domain experts. Domain expert inputs are translated to a representation system of concepts by a knowledge engineer (i.e. the informatician) who then supplies them to a programmer who writes the software based on the concepts in a specific programming language
3. User Interface: The "visible" part of the system with which users interact to solve a particular problem.

Figure 2-1. An Expert system and components



We have a unique opportunity to build the foundations of informatics in Perioperative Medication Management (PMM) by collating the knowledge (decisions on managing medications prior to surgery) from evidence-based literature, expert opinions, and actual patient notes and distilling this knowledge into a set of clinically actionable decision heuristics. Based on the heuristics, we can then build the necessary CDS tools for PMM to help improve the practice of perioperative medicine [41] and potentially improve patient outcomes.

Methods and Materials

Institutional approval was sought and deemed not necessary for this descriptive study, with the activities in the project being deemed quality improvement in their nature.

Philosophy

PMM is a complex clinical task and the provision of decision support in this complex web has a number of inherent challenges. We chose to be guided by the philosophy of *primum non nocere* ("first, do no harm") in providing recommendations when to stop or continue a medication. Medications associated with known morbidity when stopped abruptly should be continued. [42] Medications believed to increase the risk of surgical complications that are not essential for short-term improvement in quality of life [43], or medications thought to interact negatively with anesthetic agents should be stopped perioperatively. Clinical judgment should be exercised in other cases where the clinical evidence and drug mechanisms of action do not give clear guidance for definitive decision making. In this work, medication is defined to include: prescribed medications, over-the-counter medications, supplements, and herbal products.

Study Goal

Our over-arching goal in this project was to improve PMM by promoting safe and effective use of medications. To achieve this goal we sought to identify clinical knowledge sources to supply our heuristics engine with the necessary know-how that later will become a working CDSS for PMM.

Study Scope

It is beyond the scope of this study to investigate all aspects of perioperative medicine use or to develop a clinical data set for all perioperative medications; hence, the authors decided to focus on developing a set based on the Veterans Affairs National Drug File (NDF), a centrally maintained electronic drug list used by the Veterans Health Administration (VHA) hospitals and clinics.[44] Since the NDF is updated frequently by the VHA, we froze the version with which we worked to the revision released in June 2011. This represents a substantial medication formulary of about 12,000 unique drugs used in the treatment of 8 million veterans in the VHA clinical system.

Setting

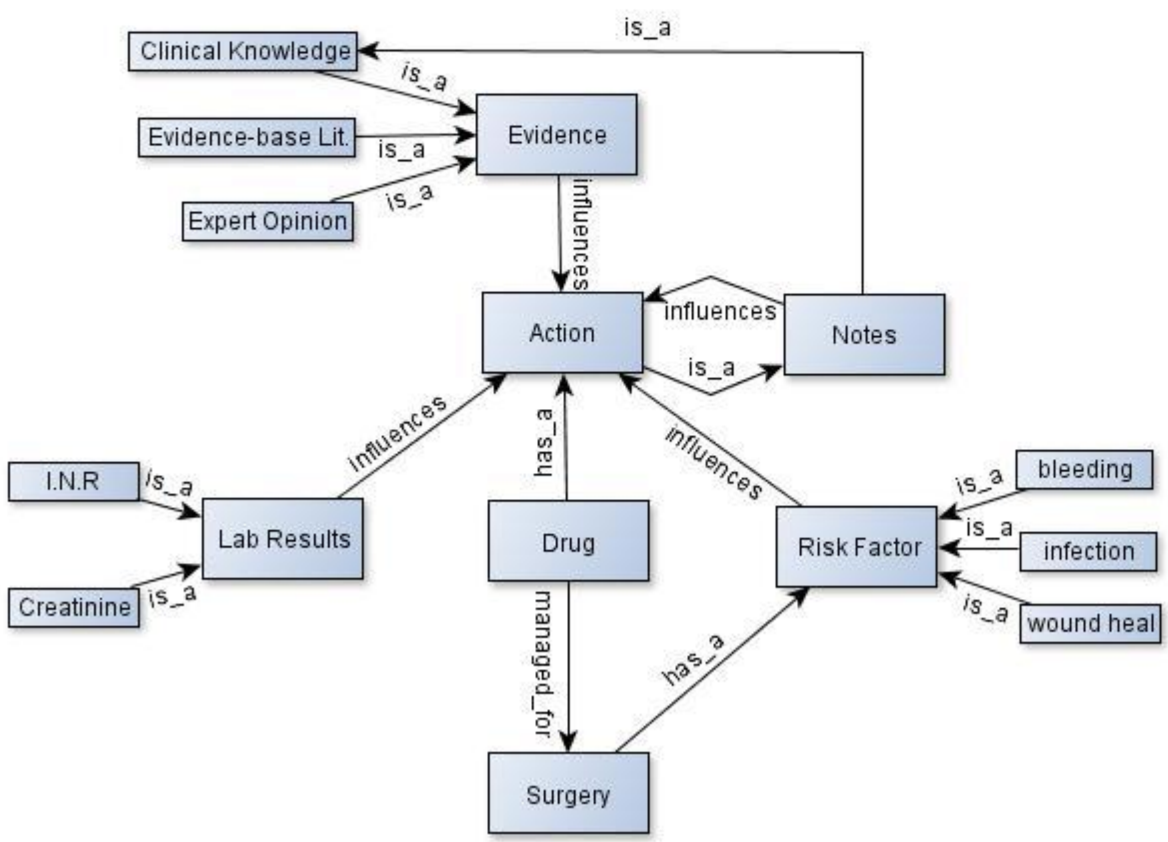
The study was conducted at the Preoperative Medicine Clinic of the Veterans Affairs Medical Center (VAMC) in Minneapolis, Minnesota. The Clinic is composed of 10 clinical providers with a 90% adult male, and 10% adult female patient population. Providers and other clinicians use the enterprise-wide VistA Electronic Health Record (EHR) system for clinical care.

Design and Implementation

Knowledge Management

Before developing the medication management heuristics, we took the initial step of developing a model to formally represent the knowledge within the domain of PMM by constructing the PMM Ontology of Concepts and Relationships (Figure 2-2). With the help of an ontology, the knowledge is not only human readable, but also computer-interpretable.[45] The development of the ontology followed standard techniques[46] and with consultation with two expert team members (TA, SS). The ontology provided a structural framework for the organization and use of clinical information and helped capture the flow of information and data. For instance, with the help of the ontology's architecture, the team quickly discovered that drug actions are often contextually influenced by medication type, surgery risks, laboratory and imaging results, and co-morbidities noted in the patient's record.

Figure 2-2: Perioperative medication management Ontology of Concepts and Relationships



Data Collection and Sources

This was a retrospective descriptive study using records of 100 randomly-selected patients seen at the preoperative medicine clinic between 8/1/2010 and 7/31/2012 representing 1,272 medication assessment and management decisions. Each patient had been given a comprehensive history and physical exam prior to surgery. Due to the relative paucity of females compared to males in the study population, female patients were oversampled to better represent a typical clinical population. The distribution of patients per gender per provider is given in Table 2-1. The minimum age (Female/Male) and maximum age were (27/27) and (75/87), respectively.

Table 2-1: Per-provider patient gender distribution

Provider	No. of Female Patients	No. of Male Patients	Total
P_1	15	14	29
P_2	3	12	15
P_3	16	10	26
P_4	16	14	30
Total	**50**	**50**	**100**

From each patient record, the following data fields were manually extracted and entered into a clinical database for heuristics development: Surgery, Active Medications, Medication Management Recommendations (actions), as well as INR (International Normalized Ratio- a measure to test how fast blood clots) and Creatinine lab values. INR and Creatinine values were chosen by the clinical reviewers as important data points for their significance in reflecting the overall liver and kidney health and ability to metabolize and excrete drugs.[47] Surgical procedure types were collected and stratified to nominal risk categories of bleeding risk, poor wound healing risk, and risk of infection. See Table 2-2 for sample data points collected from one patient record.

Table 2-2: Sample data points taken from one patient record

Patient	Medication Action
ID: 000 Male Age: 68 Surgery: Left Total Knee Arthroplasty Creatinine: 0.7 INR: 1.05	
Medication: DOXYCYCLINE HYCLATE 100MG	Take A.M. of surgery
Medication: FISH OIL 1000MG	Hold 7 days prior to surgery
Medication: ALBUTEROL 90MCG (CFC-F)	Take 30-60 minutes before surgery
Medication: GABAPENTIN 300MG	No recommendation provided

Supporting Evidence

Medication management recommendation knowledge was extracted from evidence-based literature, expert opinions, and public web sources. With advice from two reference librarians, the following search terms were entered as keywords and MeSH terms into PubMed®:

Drug Name (N); Drug Category (C); perioperative care (p); perioperative period (p'); anesthetic (a); anesthetics (a'). We combined the above search terms in the following combinations and looked within each set S_i for relevant articles:

$S_1 = (N \cup C) \cap (p \cup p')$

$S_2 = N \cap (a \cup a')$

$S_3 = C \cap (a \cup a')$

Google, Google Scholar, UpToDate®, and DynaMed were also searched with the search term “perioperative medication management”. Additional information required to complete or enhance the results was obtained through specific searches and perusal of reference lists of retrieved articles and “cited by” links (see Table 2-3).

Table 2-3: Supporting sources and types of evidence

Knowledge Source	Physical Source	Comments
Evidence-Based	PubMed	Select, peer-reviewed journal articles
Literature	Authoritative textbooks in perioperative medicine and anesthesiology[24 48 49]	Select chapters or sections
Expert Opinions	Medical domain experts, UpToDate®, DynaMed, Google, Google Scholar	Editorials, case presentations, comments, etc.

Drug Decisions

We enrolled three physicians trained in general internal medicine to review the sample data and make medication management recommendations for each patient. We recorded each reviewer's recommendations and compared it to the actual recommendation in the EHR notes. If the recommendation matched, we marked it as agreeable; otherwise we noted the decision as disagreeable. Lastly, we computed agreement percentages between the reviewers' recommendations and the EHR notes. To identify correlations between drug categories and actions, medications were further grouped by category as defined in VA's Class Index file.[50] We did this as to enable us to make medication recommendations at the category level as much as possible, instead of the untenable task of making decisions at the individual drug level. We also noted any exceptions (different actions) within individual categories. For instance, while ASPIRIN and ACETAMINOPHEN were both in the NON-OPIOID ANALGESICS category, the action recommended for each would be different. Exceptions were discovered during the literature search or in consultation with domain experts during the review process.

We defined "evidence-backed" drugs as those with:

- the same decision in the EHR notes and by all the reviewers, at least 80% of the time, averaged across all patients taking the drug

OR

- less than 80% inter-rater agreement for decision, but adjudicated by a 4th domain expert

OR

- supporting evidence from evidence-base literature

For example, in Table 2-4, the drug INSULIN,ASPART,HUMAN has the action "Hold A.M. of surgery" with an overall inter-rater agreement of 93.75%. Drugs with less than 80% agreement were classified as "Indeterminate" and were further adjudicated by additional domain expert reviewers. We created a list of drug categories that were not in our sample records and solicited the assistance of one of the authors (SS) to review and choose two prototypical drugs from each category. We then provided this list to two domain experts and asked them to record their recommendations for each drug in the list. All discrepancies in recommendations at this step were adjudicated by three additional domain experts. Actions that could not be agreed upon even after further review were marked as "no consensus/standard of care" recommendations.

Table 2-4: Sample drug and its management recommendations

ID	Drug	Category	Notes	Expert 1	Expert 2	Expert 3	% Agreed
44	INSULIN,ASPART, HUMAN	INSULIN	Hold A.M. of surgery	Hold A.M. of surgery	Hold A.M. of surgery	Hold A.M. of surgery	100
2023	INSULIN,ASPART, HUMAN	INSULIN	---	Hold A.M. of surgery	Hold A.M. of surgery	Hold A.M. of surgery	75
3050	INSULIN,ASPART, HUMAN	INSULIN	Hold A.M. of surgery	Hold A.M. of surgery	Hold A.M. of surgery	Hold A.M. of surgery	100
4037	INSULIN,ASPART, HUMAN	INSULIN	Hold A.M. of surgery	Hold A.M. of surgery	Hold A.M. of surgery	Hold A.M. of surgery	100
							93.75(mean)

The following is a list of actions extracted from sample records:

- Take A.M. of surgery
- Take P.M. prior to surgery
- Take *m* minutes before surgery
- Take perioperatively
- Take a reduced dose *n* [hours/days/weeks] before surgery
- Take a varied dose *n* [hours/days/weeks] before [and/or after] surgery
- Hold A.M. of surgery
- Hold P.M. prior to surgery
- Hold perioperatively
- Hold for *n* [hours/days/weeks] days before surgery
- Hold for *n* [hours/days/weeks] before and after surgery

Heuristics Implementation

We structured the heuristics in XML schemas "rules" file in order to optimize access to information and resources that incorporates relevant clinical concepts. XML provided a hierarchical structure to store information (e.g. categories, drugs, exceptions, recommendations) in a web-based, platform-independent manner. Furthermore, instead of being in vendor-specific non-human readable binary format, the rules file is machine as well as human readable [51] making it very easy for debugging, software maintenance, and data exchange. This file contains drug action heuristics for the entire VA drug formulary and provides decisions (recommendations) for each drug based on a tiered supporting evidence structure (see Figure 2-3).

Figure 2-3: Evidence types and levels

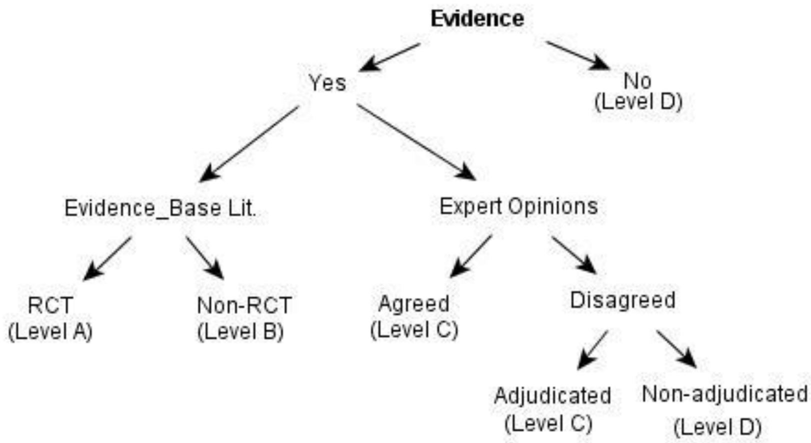
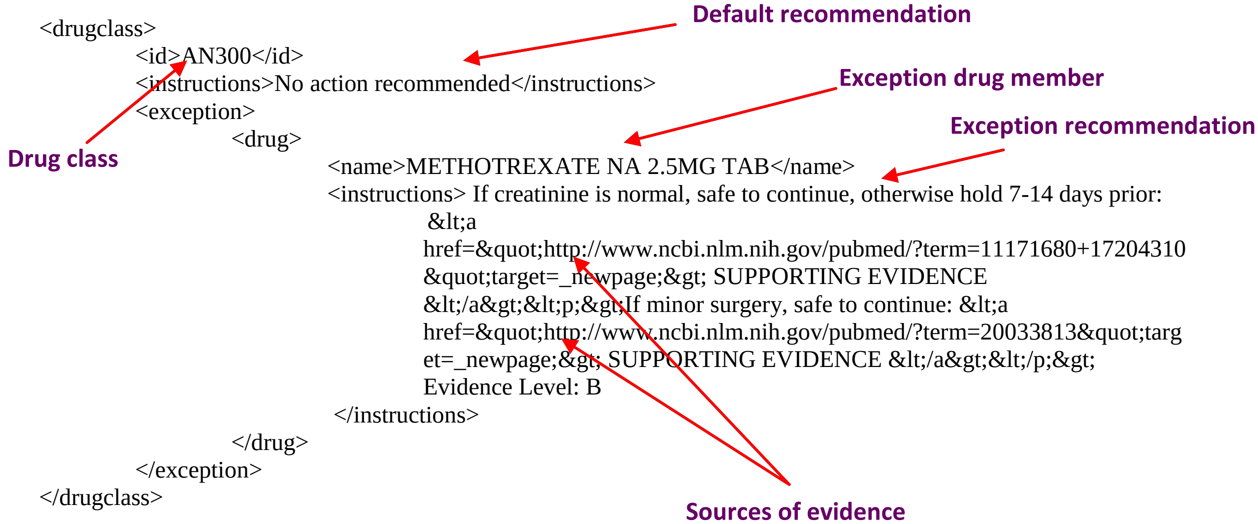


Figure 2-4 shows how categories, drugs, and actions are coded in this portable form. Each action, when supported by evidence, has a link to the evidence as well as the level of the evidence.

Figure 2-4. A category-level medication management recommendation in XML with exception handling and supporting evidence level and evidence hyperlinks



Results

Table 2-5 depicts the drug burden statistics in the sample population.

Table 2-5: Drug burden frequencies in the sample population

Gender	Count	Mean Age	No. of drugs	Mean No. of drugs (SE)	Median No. of drugs	Mode of No. of drugs
Female	50	50	430	8.60 (0.88)	7	12
Male	50	64	584	11.68 (0.89)	11	15
Total	100	57	1014	10.14 (0.64)	9	8

Overall, our sample population used 252 unique drugs from 122 categories. The distribution of patient chart-reviewed actionable drug categories, associated recommendations, and the mean agreement percentage among the reviewers and the EHR notes is given in Table 2-6.

Table 2-6: Patient chart-reviewed actionable drugs and recommended actions. †Consensus < 80% threshold, action determined by evidence-base literature or external adjudicator. ‡Exceptions exist within the category, see the rules file for details. *Consensus >= 80% threshold, but different from evidence-base literature; action from literature chosen

Drug Category (n)	Class [50]	Action	Mean Percent Agreement	Evidence Level	References
ACE INHIBITORS (16)	CV800	Hold A.M. of surgery	86	A	[52-58]
ANGIOTENSINII INHIBITOR (10)	CV805	Hold A.M. of surgery	70†	B	[52 54-56 59 60]
ANTIANGINALS (2)	CV250	Take A.M. of surgery	100	B	[61]
ANTIARRHYTHMICS (1)	CV300	Take A.M. of surgery‡	100	A	[62]
ANTICOAGULANTS (1)	BL110	Hold 5-7 days before surgery‡	100	A	[63-78]
ANTICONVULSANTS (31)	CN400	Take A.M. of surgery	90	C	[79]
ANTIDEPRESSANTS,OTHER (SSRI's) (46)	CN609	Hold 1-5 days before surgery‡	84	B	[80-86]
ANTIDOTES/DETERRENTS,OTHER (7)	AD900	Hold peri-operatively‡	96	A	[87]
ANTIGOUT AGENTS (1)	OP109	Take A.M. of surgery	100*	C	
ANTIHYPERTENSIVE COMBINATIONS (5)	CV400	Hold A.M. of surgery‡	90	A	[62 88]
ANTIHYPERTENSIVES, OTHER (1)	CV490	Take A.M. of surgery‡	100	C	
ANTI-INFLAMMATORIES,RECTAL (2)	RS100	Hold 1 day before IBD surgery	100*	B	[89]
ANTILIPEMIC AGENTS (non-statins) (9)	CV350	Hold A.M. of surgery‡	83*	B	[90 91]
ANTILIPEMIC AGENTS (Statins) (41)	CV350	Take A.M. of surgery	96	A	[92]

ANTIMALARIALS (2)	AP101	Take in outpatient surgeries with expected quick recovery	75†*	B	[93]
ANTINEOPLASTICS,ANTIMETABOLITES (2)	AN300	Hold 14 days before major surgery if Creatinine level abnormal‡	63†	A	[94 95]
ANTIPARKINSON AGENTS(4)	CN500	Take perioperativ e -ly	88*	B	[96-98]
ANTIRHEUMATICS, OTHER (1)	MS190	Hold 7 days before surgery and 7 days after surgery‡	100	B	[24]
BETA BLOCKERS/RELATED (28)	CV100	Take A.M. of surgery	94	B	[99-101]
BRONCHODILATORS, ANTICHOLINERGIC (5)	RE105	Take A.M. of surgery	76†	B	[48]
BRONCHODILATORS, SYMPATHOMIMETIC, INHALATION (27)	RE102	Take A.M. of surgery	75†	C	[91]
CALCIUM CHANNEL BLOCKERS (11)	CV200	Take A.M. of surgery‡	86	B	[102-104]
CARDIOVASCULAR AGENTS,OTHER (2)	CV900	Take A.M. of surgery‡	75†	B	[105]
CONTRACEPTIVES,SYSTEMIC (5)	HS200	Hold 4-6 weeks before surgery‡	65†	B	[91 106]
ESTROGENS (5)	HS300	Hold 4-6 before surgery	65†	B	[107-109]
GASTRIC MEDICATIONS,OTHER (42)	GA900	Take before surgery‡	82	B	[110-113]
GENITO-URINARY AGENTS,OTHER (11)	GU900	Hold 7 days prior to surgery	91*	B	[49 114]

GLUCOCORTICOIDS (6)	HS051	Vary dose‡	67†	B	[91 115]
HERBS/ALTERNATIVE THERAPIES (52)	HA000	Hold 7 days before surgery	93	B	[116-119]
HISTAMINE ANTAGONISTS (12)	GA301	Take A.M. of surgery	81	B	[120 121]
HORMONES/SYNTHETICS/MODIFIERS, OTHER (5)	HS900	Hold 1-6 weeks before surgery‡	80	B	[122]
INSULIN (quick-acting) (4)	HS501	Hold A.M. of surgery	94	B	[123 124]
INSULIN (intermediate-acting) (3)	HS501	Take 50% of usual dose	92	B	[123 124]
INSULIN (long-acting) (6)	HS501	Take 50% of usual dose	83	B	[123 124]
LOOP DIURETICS (8)	CV702	Hold A.M. of surgery‡	88	B	[24 88]
NICOTONIC ACID (4)	VT103	Hold 1 day before surgery	81	B	[24]
NONSALICYLATE NSAIs, ANTIRHEUMATIC (48)	MS102	Hold 5-7 days before surgery	92	B	[76 125-129]
OPIOID ANALGESICS (31)	CN101	Hold prior to surgery	94*	B	[130]
ORAL HYPOGLYCEMIC AGENTS, ORAL (Sulfonylurea) (11)	HS502	Hold P.M. prior to surgery	84	B	[124]
ORAL HYPOGLYCEMIC AGENTS, ORAL (Biguanide) (13)	HS502	Hold 36 hours before and after surgery	98	B	[124]
PLATELET AGGREGATION INHIBITORS (3)	BL117	Hold 5-7 days before surgery‡	100	A	[65 66 68 70-73 75-77 126 131-140]
POTASSIUM SPARING/COMBINATIONS DIURETICS (3)	CV704	Hold A.M. of surgery	83	C	
SALICYLATES, ANTIRHEUMATIC (52)	MS101	Hold 7 days before surgery‡	93	A	[68 70-73 75-77 126 131-140]
THIAZIDES/RELATED DIURETICS (11)	CV701	Hold A.M. of surgery	75†	B	[88]

THYROID SUPPLEMENTS (10)	HS851	Take A.M. of surgery	90	C	
TRICYCLIC ANTIDEPRESSANTS (8)	CN601	Hold 7 days before surgery for low-dose patients‡	97	B	[141]
VITAMIN E (5)	VT600	Hold 7 days before surgery	100	B	[142 143]

Table 2-7 contains the distribution of non-chart-reviewed actionable categories and the corresponding recommendations.

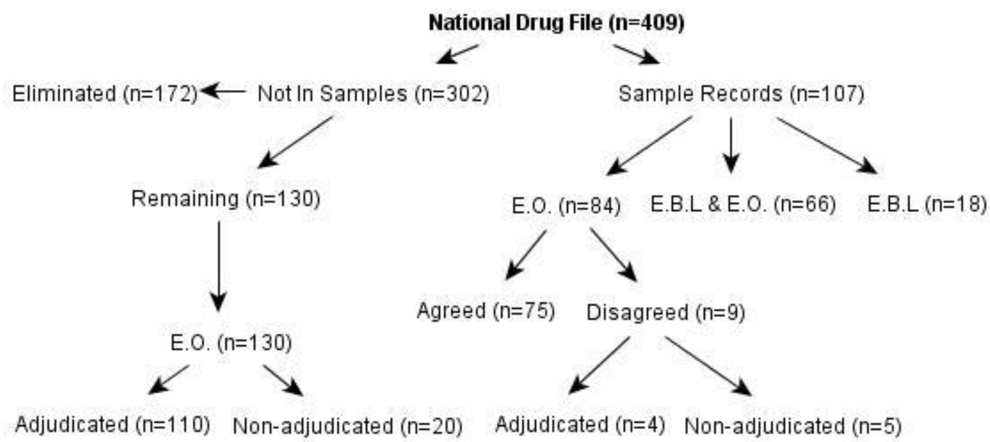
Table 2-7: Non- chart-reviewed actionable drugs and recommended actions. ‡Exceptions exist within the category, see the rules file for details.

Drug Category Name	Drug Class[50]	Action	Evidence Level	References
ANTINEOPLASTICS, ALKYLATING AGENTS	AN100	Hold 1 week before surgery	C	
OPIOID ANTAGONIST ANALGESICS	CN102	Wean off if opioid will be given for pain control post-op	C	
NON-STEROIDAL ANTI-INFLAMMATORY ANALGESICS	CN104	Hold 5 days before surgery, or 10 days if Creatinine level abnormal	A	[76 125-129]
MONAMINE OXIDASE INHIBITOR ANTIDEPRESSANTS	CN602	Hold per anesthesia preference‡	B	[144]
DIGITALIS GLYCOSIDES	CV050	Take A.M. of surgery	C	
DIRECT RENIN INHIBITOR	CV806	Hold the evening prior and A.M. of surgery	C	
HYPOGLYCEMIC AGENTS, OTHER	HS509	Hold A.M. of surgery if surgery in the afternoon; Hold PM prior if surgery in the morning	B	[124]
BRONCHODILATORS, SYMPATHOMIMETIC,ORAL	RE103	Take A.M. of surgery	C	
BRONCHODILATORS, XANTHINE-DERIVATIVE	RE104	Take A.M. of surgery	C	
OPIOID-CONTAINING ANTITUSSIVES/EXPECTORANTS	RE301	Hold 1 day before surgery	C	

In consultation with two team members (TA and SS), we excluded 172 categories from the study. The eliminated categories included but are not limited to: 1) non-patient-administered drugs; 2) durable medical equipment (DME); 3) corrective vision products; 4) eyewashes; 5) sun protectants; 6) emollients; 7) personal and dental hygiene products; 8) dental products; 9) enteral nutrition products; 10) some topical products (Figure 2-5).

For a complete list of the eliminated categories see Appendix 1. The resulting data file contains over 9,000 drugs in 409 categories.

Figure 2-5: Sources of supporting evidence for medication management recommendations. E.B.L: Evidence-Base Literature; E.O: Expert Opinion; n=number of drug categories



Discussion

In this work we have shown the methodology and framework for building a CDSS knowledge engine. To the best of our knowledge this work is a first attempt at developing a heuristics-based rules engine for drug-based decision support. Because it is written in XML format, the rules file can be transported to any perioperative medicine healthcare facility and operationalized as part of a CDS tool with minimal effort. The knowledge engine contains heuristics for medication management recommendations covering approximately 10,000 drugs in 237 categories in the VA's formulary. While not complete in developing decisions for all drugs, the work presented shows a proof of concept for the full-scale system development of similar decision support systems by replicating the methodology described here. This work will be used as the knowledge engine in a future perioperative medicine CDS tool.

Physicians and informatics specialists were involved in the design and accuracy of clinical information system. The team chose from a catalog of expert rules that were supported by expert panels, guidelines, or clinical evidence. The design process ensured that each expert rule followed evidence-based guidelines and was programmed to automate steps in planning and delivering patient care.

As with all evidence-based decision making, clinical judgment and experience factors into the process. This heuristics system is no exception. Given the scanty nature of strong scientific evidence supporting perioperative medication management decision-making, the development of this system also relied upon clinical experience and judgment in order to stratify the multiple risk factors as well as provide guidance along the medication decision pathway.

It should be kept in mind that in addition to the medication's inherent pharmacological characteristics the patient's clinical status, as well as the surgical procedure also influences the decision to stop or continue a medication. Risks pertaining to each drug should be carefully evaluated. For example, several drugs can affect coagulation and discontinuation of others can lead to withdrawal symptoms with both cases leading to potential pre- and post-surgical clinical complications.

Our work provides an evaluation of the potential problems and proposed approach to perioperative medication decision making using a national medication formulary.

However, our findings are limited in that many of our experiences to date come from a single, large, tertiary care institution; the practice patterns and clinical co-morbidities and patient populations at other types of institutions may vary from our findings. Other clinical formularies may also contain a broader set of medications to manage which would need to be evaluated prior to system implementation outside a VHA setting.

Chapter 3

PeriMed: Development and Evaluation of a Perioperative Medicine Decision Support Tool

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Target Publication: Perioperative Medicine

Background*: A clinical decision support tool to manage medications can help perioperative medicine clinicians avoid spending valuable time looking for drug management information during a pre-op physical exam evaluation. Our objective was to develop and validate a clinical decision support (CDS) tool for managing medications perioperatively.*

Methods*: We developed a CDS tool based on a set of heuristics classifiers developed in a previous study, and tested the tool using medication data extracted from the electronic records of 100 randomly selected perioperative medicine patients including medications in use. For each medication, the tool-generated recommendation was compared with actual recommendations in the EHR by experienced preoperative medicine providers.*

Results*: A total of 879 medications were used by the sample population. We extracted 378 "actionable" drugs from the EHR Notes section, compared to 479 identified by the tool, while 334 were identified in both. The total number of "non-actionable" drugs in the EHR notes was 132 compared to 18 flagged by the tool, while 369 were identified by both. In the initial testing phase the tool generated provider-matched recommendations 76% of the time. After correcting for errors and adjudicating the differences by a perioperative medicine domain expert, the tool's matching performance increased to 95%. These results are encouraging.*

Conclusion*: The CDS tool compared favorably with other similar tools and thus can be used as a support tool at the point of care.*

Background

There has been an increased emphasis on the use of clinical decision support systems (CDSS) to improve the quality of health care.[145] The main objective in using CDSSs is to provide patient-specific recommendations generated through a comparison of patient information with clinical knowledge sources.[9 146] In general, CDSSs can enhance clinical effectiveness by improving the quality of care[147] and patient outcomes by aiding health care providers in the decision making process.[148 149] As a technology tool, CDSSs can be utilized to align clinical decision making with best practices and the latest guidelines at the point of care and provide a potential means to change clinical practice. When these systems are used effectively they can reduce workload and help improve health care quality, efficiency, and outcomes.[150]

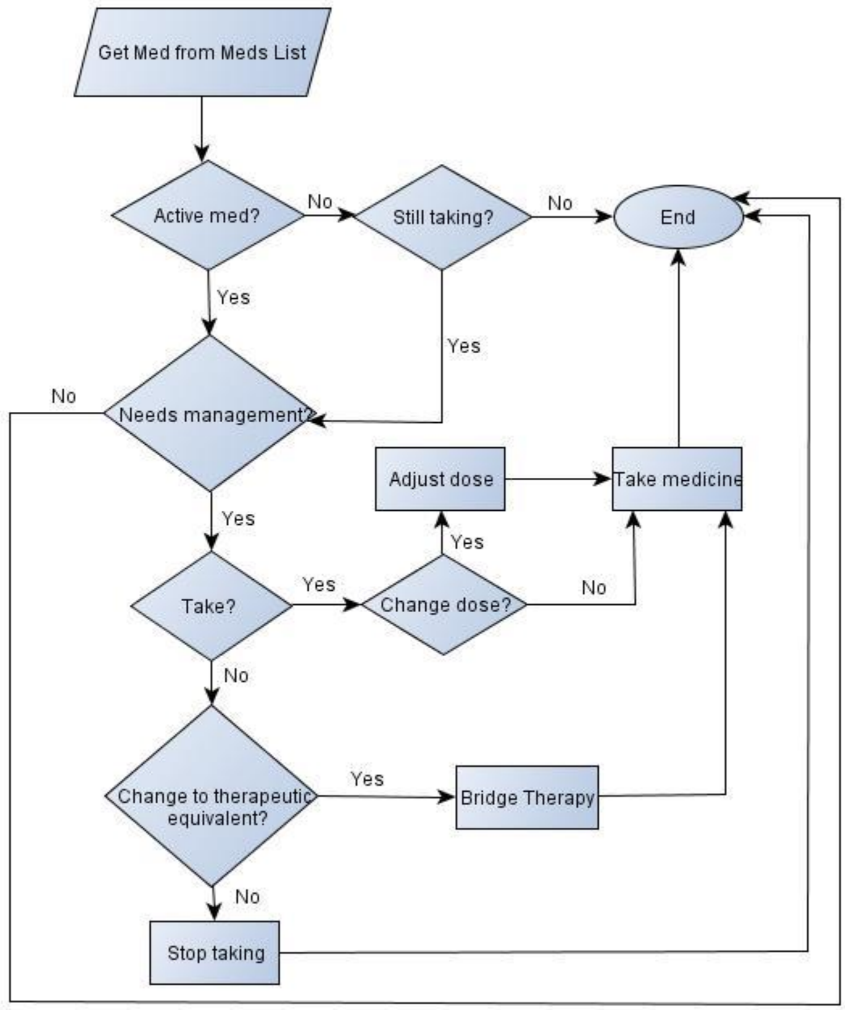
During the course of a preoperative physical examination the provider needs to review, document, manage the usage and dosage, and potentially administer the patient's various medications. This includes the clinical indication and therapeutic need for each medication; the effect on the primary disease of stopping a drug; drug pharmacokinetics and changes in the perioperative setting; potential adverse effect of the medication on perioperative risk (e.g. bleeding, hypoglycemia); potential benefits of starting a drug prophylactically (e.g. prevention of ischemia, thrombosis, infection, aspiration); and potential drug interactions with anesthetic agents. Considering these variables and a risk-benefit analysis, the consulting provider must decide whether to continue, discontinue, or modify the regimen for each medication based on the patient's characteristics. Although the surgical burden in the U.S. is increasing, some perioperative medicine providers feel that they are inadequately trained to perform preoperative evaluations.[27] Unfortunately, there is limited high quality outcome data related to the majority of medications taken in the perioperative period. Furthermore, very few controlled trials regarding perioperative medication discontinuation and resumption have been conducted. Consequently, decisions regarding medication management are often made based on pharmaceutical manufacturer recommendations, expert consensus, in vitro studies, or clinical anecdotes.[28] This lack of evidence is reflected by the large variation in perioperative medication management recommendations among providers.[29-31] A critical foundation for improving the way technology and information resources support perioperative clinicians would be an enhanced knowledge set which is developed to support perioperative care.[41] Developing health service interventions that address medication management decision making challenges are essential for reducing practice variability and potentially improving patient outcomes. A decision support system may provide such an intervention.[151 152] Ideally, capture of coded clinical information can be linked to the knowledge of evidence-based medicine to provide tailored recommendations at the point of care and close the gap between best evidence and actual practice.[153 154] Many studies have shown beneficial effects of CDSS on clinical decision making.[9 12 35 155-157] The key tools for closing this gap will be information systems that provide decision support to medical consultants at the time the point of care to optimize clinical quality of care. Furthermore, in the current health care system, scientific knowledge about best care is not applied systematically or expeditiously to clinical practice. An average of nearly 17 years is required for new knowledge generated by randomized controlled trials to be incorporated into practice.[154] Having clinically meaningful decision support may help reduce the timing of adoption. In this article we will lay the foundations for such a decision support system.

An immediate and effective way to help collate and extract new knowledge in perioperative medication management (PMM) is to improve the structure and effectiveness of PMM data for research and development. The disparity between clinical evidence and practice demonstrates a critical need for clinical decision support in preoperative medicine. Platform-independent, web-based preoperative decision support systems are needed to help meet clinical care guidelines and to improve care delivery.[158] Use of health information technology helps improve clinical process quality and quick updating of medical knowledge by accessing the evidence-based literature quickly.[159 160] The goal of this study is to develop such a system for perioperative medication management based on an earlier study [161] that addresses the critical information needs of clinical providers. In this study we demonstrate how to potentially close the 'knowing–doing' gap by presenting the relevant information to the clinician at the time of decision making.[10]

Workflow Analysis

In order to gain a thorough understanding of the necessary decision making steps in perioperative medication management, we distilled this macro task into several finer micro tasks as depicted in Figure 3-1. From the flowchart we discerned that this step alone requires a high level of cognitive ability and memory capacity; the provider needs to remember what action to take for each medication in the patient's medication profile.

Figure 3-1: Medication management recommendation workflow flowchart



Materials and Methods

A thorough description of the rules engine of the CDSS has been discussed elsewhere.[161] Institutional Review Board approval was sought for this study. It was deemed by the authorizing institution that the nature of this work is quality improvement and therefore exempt from approval.

Setting

The study was conducted at the Preoperative Medicine Clinic of the Veterans Affairs Medical Center (VAMC) in Minneapolis, Minnesota. The Clinic is composed of 10 clinical providers with a 90% adult male, and 10% adult female patient population. Providers and other clinicians use the enterprise-wide VistA Electronic Health Record (EHR) system for clinical care.

Data Sources and Subjects

In this retrospective descriptive study we sampled electronic medical records of 100 randomly-selected patients seen at the clinic between 8/1/2010 and 7/31/2012. Each patient had been given a comprehensive history and physical exam prior to surgery. Due to the relative paucity of females compared to males in the study population, female patients were oversampled to better represent a typical clinical population. From each patient record, the following data fields were manually extracted and entered into a clinical database for heuristics development: type surgery, active medications, medication management recommendations (actions), as well as INR (International Normalized Ratio- a measure to test blood clotting rate), and creatinine lab values. INR and creatinine values were chosen by the clinical reviewers as important data points for their significance in reflecting overall liver and kidney health and the ability to metabolize and excrete drugs[47], and were typically completed as part of the preoperative evaluation.

Development

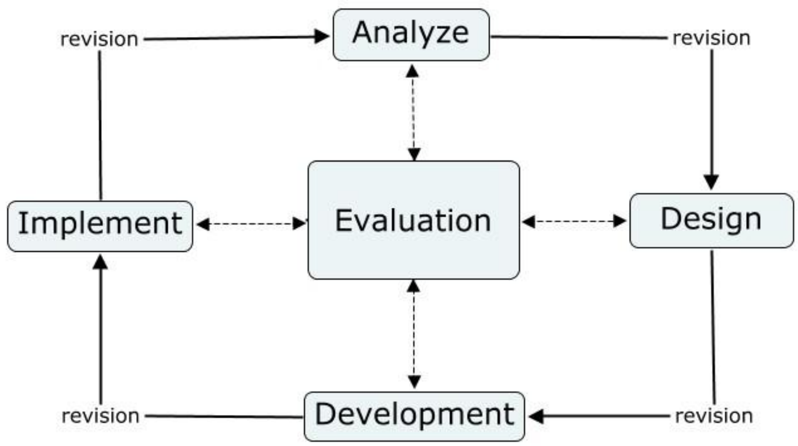
System Description and Goals

We describe our system as a "knowledge-based" expert system focusing "on the accumulation, representation, and use of knowledge specific to the particular task" [162] of perioperative medication management recommendations. We used an iterative process of design, testing, and revision of the system by a diverse team including informaticians and clinical content experts. Here, we describe the process of the method which we used to operationalize medication management recommendations into a computer-interpretable knowledge base to provide patient-specific recommendations for care. A valuable part of our process was collaboration of the developer (MR) directly with the clinical content experts to help contextualize recommendations from evidence-base literature and expert opinions into recommendations encoded into the CDSS.

The goals included using evidence-based research to improve practice and promote uniformity of care. For our purposes, the CDSS was designed to assist, rather than to replace, the clinician in medication management decisions.[163 164] Our design strategy was threefold: 1) define and code medication management recommendation concepts using a "rules" knowledge base, 2) acknowledge that there are limits to how much a CDSS can "know" about a patient compared with the provider, and 3) not alienate clinicians by making recommendations that unnecessarily limit therapeutic choices.

We based our system on the iterative process of interim evaluation and testing as in the ADDIE (Analysis, Design, Development, Implementation and Evaluation) model [165] (Figure 3-2).

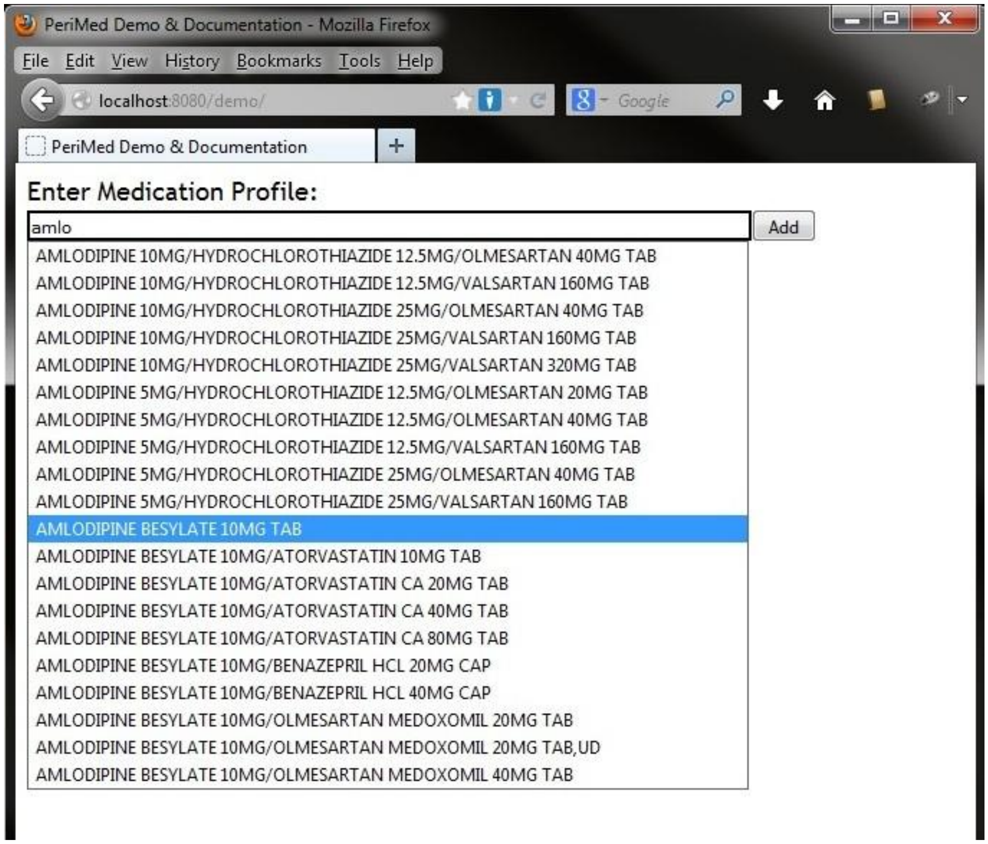
Figure 3-2: The ADDIE (Analysis, Design, Development, Implementation, Evaluation) Model



User Interface

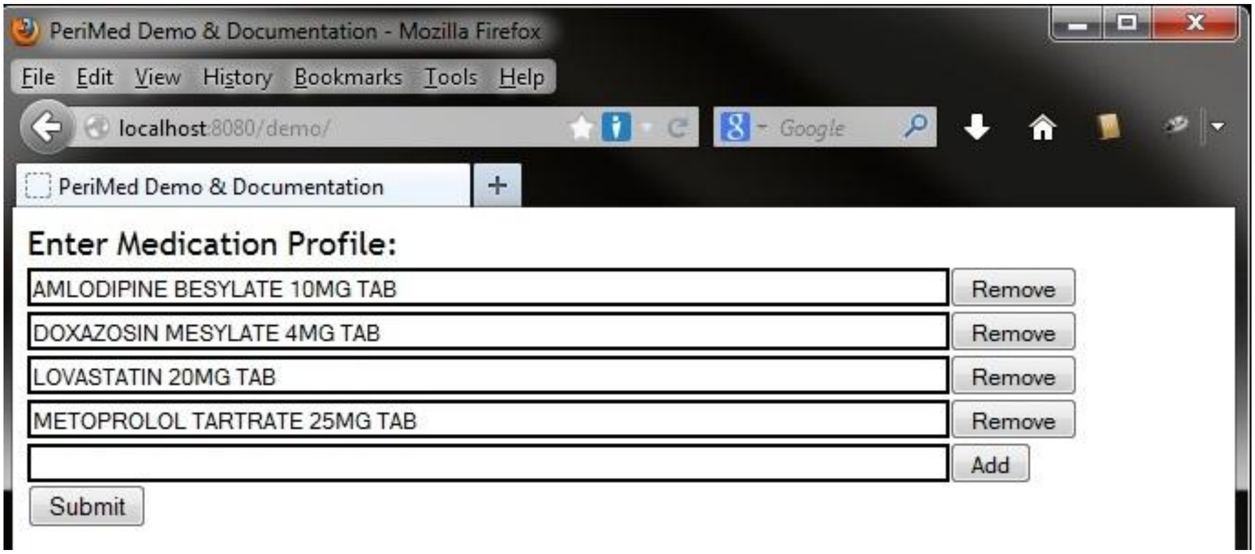
Our system is a web-based system implemented with Python, JavaScript, and HTML components. The CDSS user interface (PeriMed) queries the clinician for the patient's medication profile. Once the clinician starts typing the name of a medication, a focused list of 20 possible matches, designed to not overrun the screen is displayed in a drop-down list from which the clinician can choose. This un-fragmented display promotes a coherent view of medications as studied by Koppel, et al.[166] The "pick list" feature of PeriMed saves the clinician a substantial amount of data entry time as drug names can get lengthy and time-consuming to type (Figure 3-3).

Figure 3-3: User can choose drugs from an auto-suggesting dropdown list



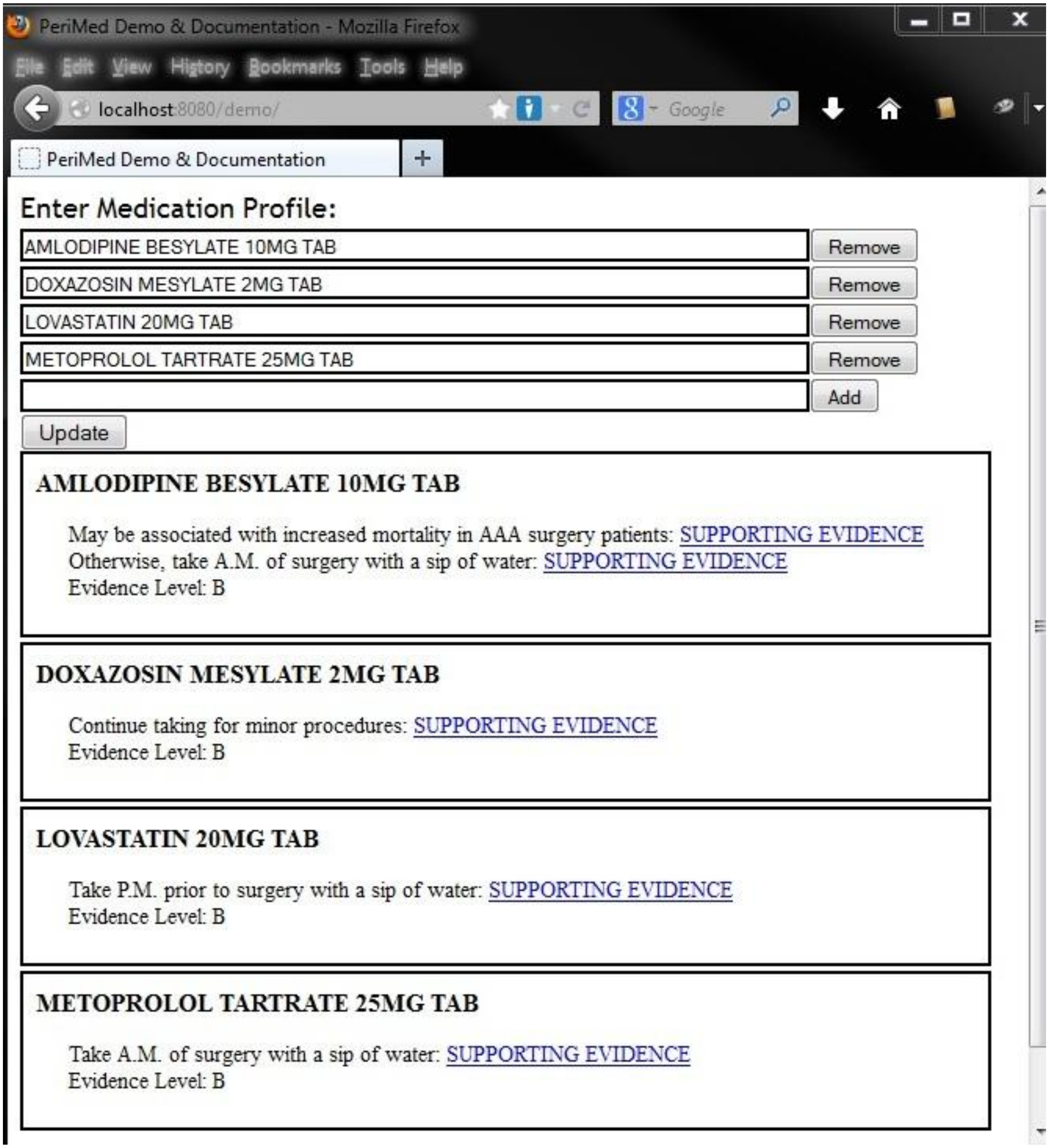
The provider can continue entering medications by pressing the Add button until all the medications have been entered (Figure 3-4).

Figure 3-4. Drug entry screen



The Remove button can be used to remove medications entered in the tool erroneously. Once all the medications in the profile have been entered, pressing the Submit button sends the list to the rules engine. The rules engine in turn processes the list, looks up the category and class, finds the appropriate rule for medication management, and returns a recommendation for each drug entered. If available, link(s) to supporting evidence in the literature are also presented (Figure 3-5). Throughout the interaction described, the clinician can follow links to relevant citations.

Figure 3-5: Medication management recommendation screen. Each recommendation has an evidence level: A=RCT study; B=non-RCT study; C=Expert panel opinion; D=non-adjudicated expert opinion (standard of care)



Evaluation and Classification

The medication profiles of 100 patients, as described above, were entered into PeriMed, and tool-generated outputs were compared manually with corresponding recommendations in the EHR notes. The authors believe that this was a representative sample size as it contained 92% (33/36) of clinically-significant categories of drugs as presented in Cohn, et al.[24], an authoritative source in perioperative medicine. Medications without an explicit management instruction or "NPO (nothing by mouth) after midnight" were classified as non-actionable; those with an explicit recommendation (e.g. "take A.M. of surgery with a sip of water") were classified as actionable. Frequency of agreement with classification and the specific recommendation between the tool and the EHR notes were manually compared. All discrepancies were manually reviewed and adjudicated by a domain expert in perioperative medicine and informatics.

Results

The distribution of patients per gender per provider is given in Table 3-1. The minimum and maximum ages (F/M) were (25/27) and (87/86), respectively.

Table 3-1: Per-provider patient gender distribution

Provider	#Male Patients	#Female Patients	Total
1	18	10	28
2	10	--	10
3	15	17	32
4	16	14	30
Total	**59**	**41**	**100**

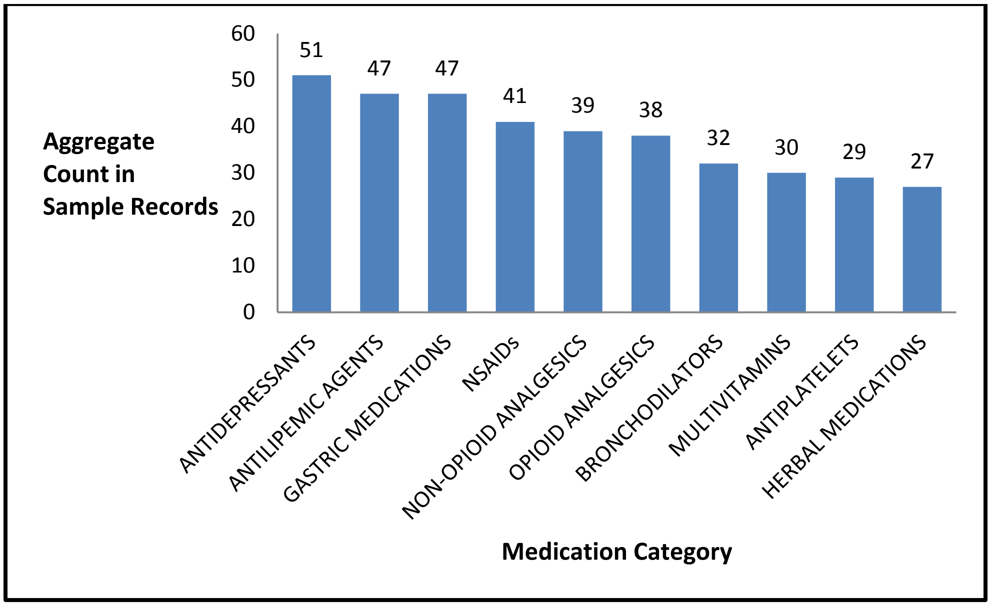
Overall, the sample population used 241 unique drugs from 102 categories representing 43% (102/237) of drug categories studied in the VA's formulary. Table 3-2 depicts the drug burden statistics in the sample population.

Table 3-2. Drug burden frequencies in the sample population

Gender	Count	Mean Age	Total No. of drugs	Mean No. of Drugs (SE)	Median No. of Drugs	Mode of No. of Drugs
Female	41	52	340	8.2 (0.7)	8	6
Male	59	63	539	9.2 (0.7)	8	10
Total	100	57	879	8.8 (0.5)	8	5

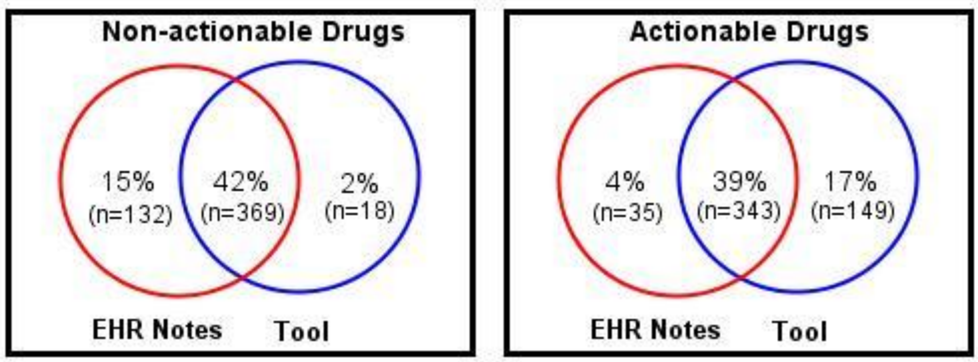
The top ten drug categories accounted for 381 (43%) of all medications in the sample population (Figure 3-6).

Figure 3-6: Top 10 medication categories used by the sample population



The EHR notes contained actions for 43% (n=378) of all medications compared to 56% (n=492) in PeriMed, while 39% (n=334) were flagged as actionable in both (Figure 3-7). In the non-actionable categories, we found 15% (n=132) flagged in the EHR notes, 2% (n=18) by the tool, and 42% (n=369) by both. In 80% (n=82) of categories PeriMed and the EHR notes were in 100% agreement.

Figure 3-7. Frequency of classification agreements between PeriMed and EHR notes



In the initial pass-through, the tool-generated recommendations agreed with the EHR notes 76% (n=665) of the time, averaged over all medications.

Of particular significance was the accuracy of PeriMed on clinically significant medications with corresponding recommendations in Cohn, et al [24] (Table 3-3).

Table 3-3. Tool's performance for clinically significant medications

Drug Category (VA Class[50])	Cohn, et al.[24] †	Tool's† Recommendation	N	No. of matches (Tool-EHR)	% Match
Anticoagulants (BL110)	Hold	Hold	2	2	100
Antiplatelets (BL117)	Hold	Hold	29	28	97
NSAID's (MS102)	Hold	Hold	41	41	100
COX-2 Inhibitors (MS102)	Hold	Hold	1	1	100
β-Blockers (CV100)	Continue	Continue	25	25	100
α_2-Agonists (CV490)	Continue	Continue	0	N/A	N/A
α Blockers (CV150)	Continue	Continue	15	14	93
Calcium Channel Blockers (CV200)	Continue	Continue	15	15	100
Nitrates (CV250)	Continue	Continue	9	9	100
ACE Inhibitors (CV800)	Hold	Hold	17	17	100

ARB’s (CV805)	Hold	Hold	9	9	100
Diuretics (CV701)	Hold	Hold	15	14	93
Antiarrhythmics (CV050, CV300)	Continue	Continue	3	3	100
H_2 Blockers (GA301)	Continue	Continue	7	7	100
Proton-pump Inhibitors (GA900)	Continue	Continue	47	45	96
Inhaled Bronchodilators (RE102)	Continue	Continue	32	32	100
Corticosteroids (HS051)	Continue	Continue	6	6	100
Insulin (HS501)	Various	Various	10	9	90
Oral Hypoglycemics (HS502)	Hold	Hold	16	14	88
Thyroid Agents (HS851)	Continue	Continue	9	9	100
Oral Contraceptives (HS200)	Hold	Hold	0	N/A	N/A
Estrogens (HS300)	Hold	Hold	2	0	0
Antilipemics/Statins (CV350)	Continue	Continue	44	9	20
Antilipemics/Non-Statins (CV350)	Hold	Hold	3	1	33
Opioid Analgesics (CN101)	Continue	--	38	36	95
Psychotropics (SSRI’s/SNRI’s) (CN609)	Hold	Hold	41	30	73
Psychotropics (Non-SSRI’s/SNRI’s) (CN609)	Continue	Continue	10	10	100
Tricyclic Antidepressants (CN601)	Continue	Continue	4	4	100
Benzodiazepines (CN302)	Continue	Continue	8	1	13
Antipsychotic Agents (CN709)	Continue	Various	4	4	100
MAOI’s (CN602)	Hold	Hold	0	N/A	N/A
DMARD’s (AN300)	Various	Various	2	2	100
Antigout Agents (MS400)	Continue	Continue	4	4	100
Antiseizure Medications (CN400)	Continue	Continue	23	23	100
Antiparkinson Agents (CN500)	Continue	Continue	2	2	100
Herbal Medications (HA000)	Hold	Hold	26	24	92

†Broad recommendation; see source for specific exceptions

The remaining 24% (n=214) of recommendation discrepancies were manually reviewed and adjudicated by one of the authors who is a domain expert in perioperative medicine and informatics (TA). The expert identified two areas of discrepancies:

- Misinterpretation of recommendations in the EHR notes (e.g. a "do nothing" recommendation was interpreted as "continue taking") (n=34)
- Outright recommendation differences between the tool and the EHR notes (e.g. "continue taking" in the EHR notes as opposed to "stop taking" by the tool) (n=127)

In sum, the adjudicator agreed with the tool's recommendations 69% of the time (n=124). Data entry errors were corrected and wording of the disparate recommendations was edited as recommended by the external expert. Table 3-4 shows examples of disagreement between PeriMed and the EHR notes, and the revisions made to the tool post-adjudication. After the rules engine was modified based on the comments from the initial pass-through, we retested the tool a second time with the evaluation dataset. In the second round PeriMed generated the appropriate recommendation 96% of the time (n=840).

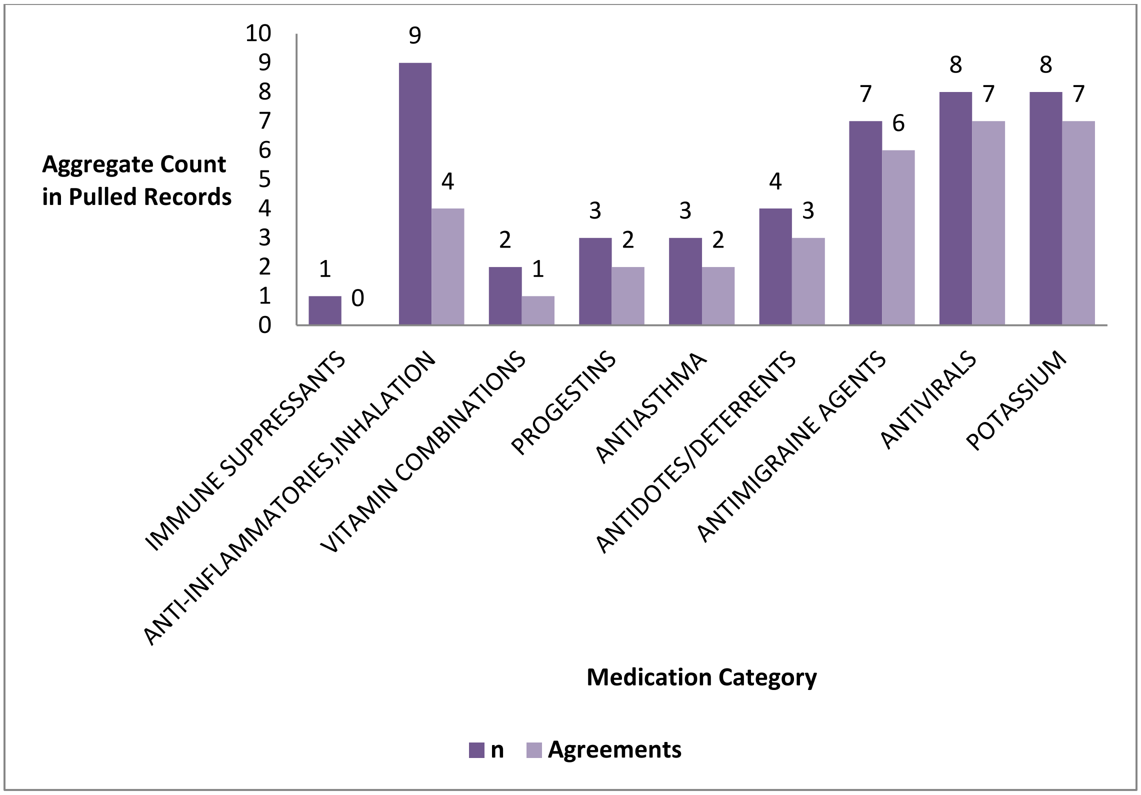
Table 3-4. Examples of categories of disagreement between PeriMed and EHR notes

Category	Examples of disagreement	Resolution by expert
Statins	EHR notes: No action Tool: Take A.M. of surgery	Take P.M. before surgery unless an A.M. dose, in which case take A.M. of surgery
SSRI's/SNRI's	EHR notes: Hold A.M. of surgery Tool: Hold 1-5 days pre-op	Consider holding 1-5 days pre-op if risk of bleeding

Estrogens	EHR notes: No action Tool: Hold 4-6 weeks pre-op	Hold 4-6 weeks pre-op if risk of DVT
Oral Hypoglycemic Agents	EHR notes: Hold A.M. of surgery Tool: Hold P.M. before surgery	Hold A.M. of surgery

The weighted average of agreement in clinically significant cases was 94%. We computed the weighted average because of the significant variability (SD=14) in the number of medications in these categories. In the non-clinically significant medications, we identified 9 categories with discrepant recommendations. The aggregate match in these categories was 71% (32/45). The categories and the corresponding number of matches are depicted in Figure 3-8.

Figure 3-8: Non-clinically significant Medication Category Agreements



Discussion

Summary

We have developed a CDS tool to help perioperative medicine physicians with making medication management recommendations during a preoperative physical examination evaluation. The tool is an expert system based on a rules engine developed in an earlier study by the authors. In processing 879 medications from our sample population, the tool (PeriMed) generated the correct (matching the EHR note and/or the external adjudicator) recommendation 96% of the time. In clinically significant categories, the accuracy of the tool was 94%. This, according to Landis et al [167], translates to an "almost perfect" match between the clinical experts' recommendations and the tool's output. In a substantial majority of disparate cases (69%, n=124) between the clinical notes and the tool's recommendations, an external subject matter expert agreed with the tool's recommendations. Furthermore, our tool performed favorably compared to other similar CDSS systems.[168 169]

It became clear that even simple and relatively straightforward recommendations can be interpreted in different ways, depending on one's perspective or specialty. Much effort was spent trying to achieve agreement among our experts about details of the recommendations. Although initial efforts tried to put too much specificity into the algorithm's recommendations, we ultimately focused on a more pragmatic goal. This goal was simply to ensure that the basic and most important recommendations of medication management recommendation practice were being followed, not to pre-specify every medical decision related to the management of medications, replace the clinician, or substitute for the clinician's education. For example, rather than recommend one particular drug (or drug class) over another (which entails factoring in highly nuanced patient-specific data that is not stored in or easily accessible from the EHR), we decided to implement the more general reminder that the patient simply qualified for pharmacologic treatment. Then, by linking to background reference information about the mechanism, effectiveness, costs, and side effects of various medications, the autonomy of the clinician to make the best decision for the patient was preserved.

Our system possesses three key features associated with CDSS success as found by Kawamoto et al [37]:

- The CDSS is electronic rather than paper-based templates

- The tool provides decision support at the time and location of care rather than prior to or after the patient encounter.
- The CDSS provides recommendations for care, not just assessments

As with all evidence-based decision making, clinical judgment and experience factors into the process. This system is no exception. Given the scanty nature of strong scientific evidence supporting perioperative medication management decision-making, the development of this system also relied upon clinical experience and judgment in order to stratify the multiple risk factors as well as to provide guidance along the decision pathway.

Elements of perioperative medicine practice have been previously noted to have deviation from clinical guidelines for some clinical assessments.[170-172] Moving toward a more evidence-based practice has the potential to improve quality and safety while simultaneously reducing costs. We believe that the implementation of computerized decision support utilizing EHRs will be a key means with which to improve care practice and knowledge. While CDSSs should not replace a provider's knowledge, experience, intuition or judgment, they can complement the clinician's skills and enhance the quality of care provided. Perioperative medication management is an ideal setting for development tools that help reduce the incidence of preventable medical errors and adverse events given the potential risks of surgical care delivery. These adverse events range from potentially stopping a medication that is critical to the patient's care, or perhaps continuing a drug that might interact negatively with anesthesia during the intra-operative period.

Study Limitations

Our findings are limited in that many of our experiences to date come from a single, large, tertiary care institution, and issues in other types of institutions may vary. The gender distribution of cases is a limiting factor that was theoretically addressed by the oversampling. The lack of full EHR integration is a limiting factor; however, the medications are mapped to the drug formulary which makes EHR integration feasible for potential future implementation.

Maintenance and Portability

One of the core challenges facing PeriMed is difficulty in incorporating the extensive quantity of ongoing research on mediation which is being published. In a given year, thousands of clinical trials are published many of which have implications for perioperative management.[173] Currently, these studies must be carefully searched, retrieved, manually read, evaluated for scientific merit, and incorporated into the CDSS in an accurate way. In addition to being laborious, integration of new data can sometimes be difficult to quantify or incorporate into the current version of PeriMed, particularly in instances where different clinical papers may appear conflicting. To properly resolve these sorts of discrepancies often requires carrying out meta-analyses, which often take a long time to complete.

On the other hand, the methodologies with which were developed PeriMed make the tool very portable to other care facilities. Software elements used to develop PeriMed are platform-independent and web-based; with minimal coding effort PeriMed can become operationalized at a care facility within a short period of time.

Future Directions

Caution should be exercised when employing CDS tools such as PeriMed. It should be kept in mind that, apart from the drug itself, the patient status, as well as the surgical procedure also influences the decision to stop or continue a medication, as well as individual patient's response to medication and the possibility of creating adverse drug events.[174-176] Risks pertaining to each drug should be carefully evaluated. For example, several drugs can affect coagulation and discontinuation of others can lead to withdrawal symptoms. We speculate that in the future we will incorporate more patient-specific data points such as surgery type to the tool in order to enhance the specificity of its recommendations.

Chapter 4

SNOMED CT for the Structured Expression of Perioperative Medication Management Recommendations: A Validation Study

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Background*: Perioperative medicine data is mostly in non-standard, unstructured free-text, making the measurement and assessment of clinical outcomes challenging using electronic medical record data. Perioperative medication management, managing the patient's medications during the perioperative period, is a complex clinical problem. SNOMED CT (Systematized Nomenclature of Medicine Clinical Terms) is a comprehensive clinical terminology which provides a consistent way to index, store, retrieve, and aggregate clinical data. Our objective was to validate the use of Medication Therapy Management (MTM) concepts within SNOMED to express perioperative medication management recommendations.*

Methods*: Perioperative medication management recommendations of 100 randomly-selected patients were extracted from their electronic medical records. Keyword searches of MTM concepts were performed on the March 2013 of SNOMED CT and candidate concepts were manually extracted and verified for relevance by domain experts. Two domain experts rated the cross-mappings as a "match" or "non-match".*

Results*: A total of 11 unique recommendations were aggregated from the sample population. A search of SNOMED CT yielded 47 concepts. The inter-rater agreement statistic between the two experts was 0.77 (substantial).*

Conclusion*: MTM concepts in SNOMED CT can be used reliably to code perioperative medication management recommendations with sufficient clarity.*

Background

With an aging U.S. population[1] there has been a progressive growth in the number of surgeries, surgery-related costs, and complications from surgery.[2-5] At least 50 percent of patients undergoing surgery take medications on a regular basis [6], and as many as 44%

take medications prior to surgery.[25] Furthermore, half of the general surgical patients take medications unrelated to surgery, with a significant increased risk of post-operative complications compared to patients taking no medications.[6]

Perioperative Medication Management (PMM)

Perioperative medication management (PMM), managing the patient's active medications during the perioperative period, is a complex clinical problem. The state of the underlying disease, the risk(s) of withdrawing medication(s), the patient's response to stresses of surgery, the patient's co-morbidities, and drug-anesthesia interactions are factors that the perioperative medicine provider needs to consider for each medication recommendation.[24 177] While the surgical procedural burden in the U.S. is increasing, some perioperative medicine providers feel that they are inadequately trained to perform preoperative evaluations because until recently, most of the perioperative literature was published in a variety of specialty journals. Only in the last few years has more information appeared in the general medical literature.[27] Good medication management can improve postoperative outcomes[178] and plays a key part in successful and safe transitions of care[179-181] as well as the prevention of adverse drug events (ADEs).[182]

PMM recommendations lack detailed clinical guidelines, resulting in clinical practice variations with a variety of provider-specific evaluations. These, in turn, create management problems due to practice variation. Besides the paucity of randomized clinical trials (RCT) in PMM, perioperative medicine data is mostly in non-standard, unstructured free-text, making the measurement and assessment of clinical outcomes challenging using electronic health record (EHR) data. Unstructured free-text is not amenable to effective indexing, aggregation, searching, and analysis in EHR systems. The meaningful use of EHRs aims to establish the effective use and exchange of health care information in order to support better decision making and more effective processes. In fact, Stage 2 of Meaningful Use of EHR systems recommends SNOMED CT [15] (Systemized Nomenclature of Medicine Clinical Terms) for structured coding of clinical data in EHRs.[16]

History of SNOMED CT

Reference terminology development and use is becoming an important aspect of health informatics.[183 184] SNOMED CT is a comprehensive clinical terminology which provides a consistent way to index, store, retrieve, and aggregate clinical data across disparate specialties and health care facilities, hence reducing variability in data capture and encoding.[185] The structure of SNOMED CT is a hierarchy of concepts and relationships which link concepts together.[186] Support for multiple levels of granularity allows SNOMED CT to be used to represent clinical data at a level of detail that is appropriate to a range of different uses.[186] The January 2013 release of SNOMED CT includes more than 297,000 active concepts and more than 890,000 logically-defining relationships to enable consistency of data documentation, retrieval, and analysis. These numbers suggest roughly 39 trillion ($2^{297,000}$ * 890,000) possible combinations of concepts and relationships as the upper bound, making a strong case for healthcare data analytics by using structured data.

History of Medication Therapy Management (MTM)

Medication therapy management (MTM)[187] is a distinct group of services performed by the pharmacist that “optimize therapeutic outcomes for individual patients.” [181] MTM services are distinct from medication dispensing and focus on a patient-centered care.[188] Proper documentation of MTM services includes facilitating communication between the pharmacist and the patient's other healthcare professionals regarding recommendations intended to resolve or monitor actual or potential medication-related problems.[187] Similar to PMM recommendations, MTM clinical efforts contains a set of medication management recommendations, albeit substantially broader. In 2006, two pharmacy organizations, the Pharmacist Services Technical Advisory Coalition (PSTAC)[189] and the Pharmacy e-Health Information Technology (HIT) Collaborative[190], submitted the MTM-related definitions for proposed codes to SNOMED CT.[191] Of the submitted set of proposed codes, 228 were approved for inclusion, and are now part of the March 2013 release of SNOMED CT, U.S. edition.

Significance

Standardized structured terminology development will be useful to better understand the clinical work and associated clinical decisions in PMM. Such a system can enhance clinical documentation, data aggregation and integration, inter-practice communication, comparative effectiveness research, data exchange, and quality measures.[192 193] Furthermore, The Joint Commission requires the use of terminologies in EHR systems.[194] Standardized healthcare terminologies are essential in the development of electronic health record information and to facilitate quality, safety, and outcomes research.[195] In this article we describe a validation study of using MTM concepts for expressing medication management recommendations in the context of surgical planning.

Methodology

Study Objectives

The main objectives of our study were to: 1) validate the use of SNOMED CT concepts to express Perioperative Medication Management Recommendations (PMMRs); 2) identify any gaps in SNOMED CT in the context of PMMRs; 3) determine the need for, and propose any new PMMR concepts to be added to SNOMED CT.

Study Design

A retrospective study using secondary EHR data was conducted to validate the use of SNOMED-CT concepts to express PMMRs. We manually extracted PMMRs from the electronic records of 100 randomly-selected patients where each patient had been given a pre-operative medical examination between 8/1/2010 and 7/31/2012. Perioperative medication management had been performed for all the patients and recommendations were documented in each patient's record. We defined "medication" to refer to prescription and over-the-counter drugs, supplements, and herbal products. Unlike other terminology validation studies[196-198] where the terminology to be validated had existed prior to validation, our study was attempting to validate use of concepts from one domain of health care (pharmacy) in another domain (perioperative medicine).

Setting

The study was conducted at the General Internal Medicine Pre-Operative Clinic, Veterans Affairs Medical Center (VAMC) in Minneapolis, Minnesota. The Clinic is comprised of 10 primary care physicians with an approximately 90% adult male, and 10% adult female patient population. Providers and other clinicians use the enterprise-wide VistA EHR system for clinical care.

Standardized Terminology Utilization

In order to introduce terminology tools in perioperative medicine, the authors found it necessary to establish a foundation by defining data elements (medications) and use of data (medication management recommendations) upon which to conduct our validation study. We determined that the necessary steps in building this foundation are defined in the following tasks:

1. Operational tasks
    a. Collecting medication recommendations
    b. Vetting the set of recommendations through domain experts
    c. Aggregating concepts that are "match candidates" in SNOMED-CT
    d. Cross-mapping recommendations to candidates in SNOMED-CT
2. Validation tasks
    a. Verifying the validity of the mappings with domain experts
    b. Identifying any gaps that might exist post-mapping

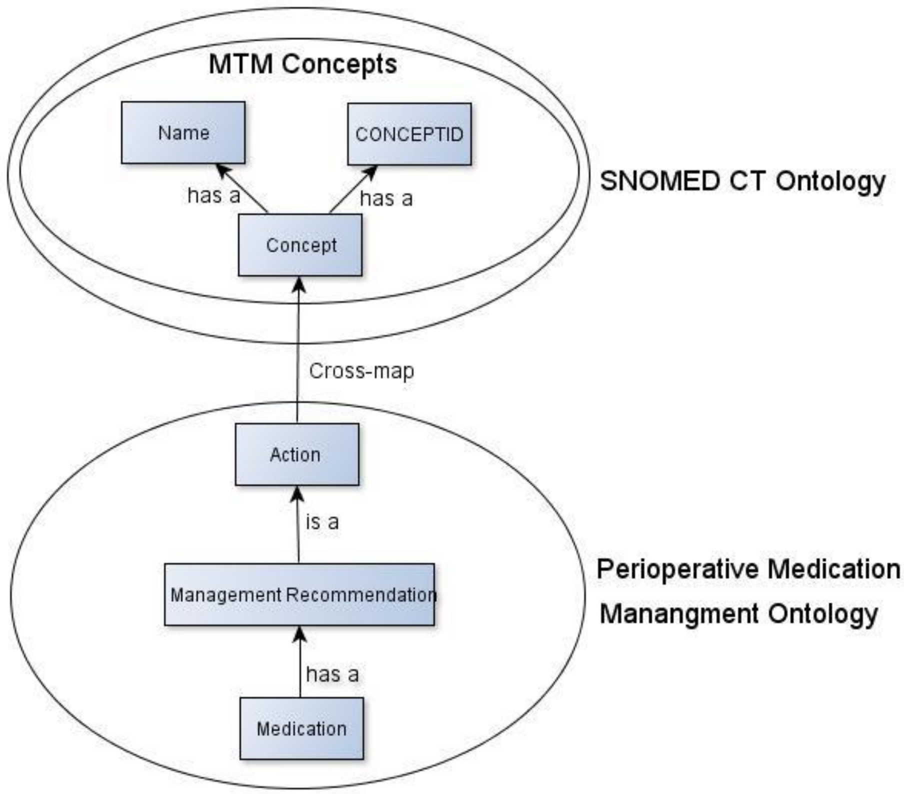
Operational Tasks

After removing duplicates, reconciling synonyms, and disambiguating terms by a perioperative medicine domain expert, a distilled list of PMMRs was produced. Our sample records revealed five top-level medication management recommendations: 1) stop medication; 2) take medication; 3) dose-adjust medication; 4) start new medication; and 5) change to a different medication. Recommendations were further refined to more specific subclasses. For example "stop taking 5 days before surgery" contains the "stop" recommendation and the "5 days" temporal specificity.

To cross-map the recommendations, we downloaded the latest release of SNOMED-CT, U.S. edition (March 31, 2013) from the National Library of Medicine (NLM)[199] to conduct a manual search of MTM concepts (Figure 4-1). The team was informed by an NLM staff member that concepts in this version could not be searched with the latest

SNOMED CT browser[200], the usual medium for searching. Hence, we conducted a manual search of the release files using the following keyword terms and phrases: medication, drug, prescription, supplement, herb, over-the-counter, dose, stop, discontinue, start, initiate, continue, recommend, “Stop/Discontinue Medication/Drug”, “Start/Continue Medication/Drug”.

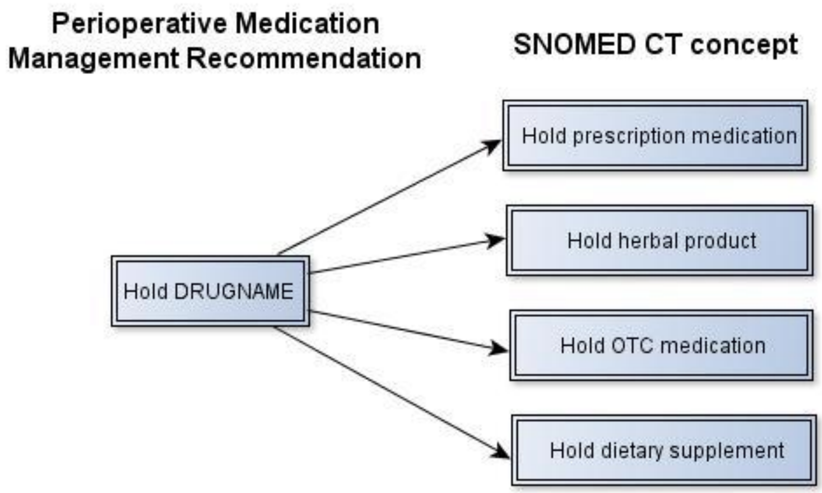
Figure 4-1: Cross-mapping of medication management recommendations to concepts in MTM-SNOMED CT



Validation tasks

We organized all SNOMED CT synonym candidates into separate but semantically equivalent subcategories of prescription medications, herbal products, over-the-counter medications, and dietary supplements. The rationale behind subdividing was due to the fact that perioperative medication management recommendations are category-agnostic. For example, the recommendation "Hold fish oil for 7 days before surgery" does not contain any explicit information about the category of medicine (herbal product) to which the medication (fish oil) belongs. This meant that for every PMM concept we collected several synonym candidates in SNOMED CT. Figure 4-2 depicts one such example of a one-to-many mapping.

Figure 4-2: One-to-many mappings between perioperative medication management recommendations and SNOMED CT concepts



We compiled a list of all the PMM concepts with their synonym candidates in a two-column text file format. In the first column we entered the PMM concept; the second column contained synonym candidates. To verify the validity of the mappings, we enrolled two domain experts in internal medicine to review the mappings and score each mapping as a "match" or "non-match". The inter-rater reliability statistic (Cohen's kappa) was then calculated for the two raters. The kappa statistic tests inter-rater independence between chance alone (kappa=0) and complete agreement (kappa=1). Landis et al[167] offer the following interpretation of inter-rater agreement:

$$\kappa = \begin{cases} 0.00 - 0.2 \text{ (slight)} \\ 0.21 - 0.40 \text{ (fair)} \\ 0.41 - 0.60 \text{ (moderate)} \\ 0.61 - 0.80 \text{ (substantial)} \\ 0.81 - 1.00 \text{ (almost perfect)} \end{cases}$$

Gap Identification

Perioperative medication management makes extensive use of temporal concepts such as "one day prior". Although SNOMED CT contains atomic temporal concepts pertinent in perioperative medication management (e.g. one, two… ten, day, week, before, after), simply combining these concepts with recommendation concepts in MTM will not produce the desired results given the SNOMED CT concept model and expression syntax for post coordination.[201] This implies that any recommendation containing a temporal concept cannot in fact be fully expressed in SNOMED.

Results

After manually searching through the notes, collecting all medication management recommendations, and removing duplicates and resolving ambiguities, a total of 11 unique recommendations were aggregated from the records of the sample population. Table 4-1 shows all the recommendations and the frequency with which each recommendation appeared in the sample.

Table 4-1: Perioperative medication management recommendations and frequencies in sample patient records

Medication Management Recommendation (n)
1. Hold A.M. of surgery (45)
2. Hold P.M. prior to surgery (9)
3. Hold perioperatively (17)
4. Hold for *n* [hours/days/weeks] prior to surgery (159)
5. Hold for *m* [hours/days/weeks] pre-, and *n* [hours/days/weeks] post-op (16)
6. Take A.M. of surgery (164)
7. Take P.M. prior to surgery (3)
8. Take perioperatively (13)
9. Take 30-60 minutes pre-op (7)
10. Take a reduced dose *n* [hours/days/weeks] before surgery (8)
11. Take a varied dose *n* [hours/days/weeks] before [and/or after] surgery (1)

A search of SNOMED CT yielded 47 concepts that were deemed by a domain expert as possible synonym candidates for the 11 PMM recommendations. For each PMM recommendation the number of synonym candidates ranged from a minimum of 1 to a maximum of 5. Table 4-2 shows the mappings between PMM recommendations and the synonym candidate concept in SNOMED CT for prescription medications. Equivalent mappings exist for herbal products, over-the-counter medications and supplements (see Appendix 2).

Table 4-2: Cross-mappings between PMM and MTM-SNOMED CT for prescription medication

Medication Management Recommendation	SNOMED-CT Concept (CONCEPTID)
1. Hold A.M. of surgery 2. Hold P.M. prior to surgery 3. Hold perioperatively 4. Hold for *n* [hours/days/weeks] prior to surgery 5. Hold for *m* [hours/days/weeks] pre-, and *n* [hours/days/weeks] post-op	1-5. Recommendation to discontinue prescription medication (4781000124108)
6. Take A.M. of surgery 7. Take P.M. prior to surgery 8. Take perioperatively 9. Take 30-60 minutes pre-op	6-9. Recommendation to continue a medication (4761000124103)
10. Take a reduced dose *n* [hours/days/weeks] before surgery	10. Recommendation to decrease medication dose (428801000124104)
11. Take a varied dose *n* [hours/days/weeks] before [and/or after] surgery	11. Recommendation to change medication dose (428791000124100)

After collecting their answers we calculated the inter-rater agreement statistic between the two experts. Extent of inter-rater reliability on our test was kappa = 0.77 (substantial). Since there was no natural ordering of the data, we believe the kappa value accurately reflects the reliability of the mappings.

Discussion

We conducted a study to validate the use of structured terminology concepts in pharmacy to express clinical procedures. By manually extracting, examining, and vetting MTM concepts in SNOMED CT we were able to show that they can be used to code perioperative medication management recommendations with sufficient clarity. Re-use of existing machine-interpretable concepts from one domain (pharmacy) in another domain (perioperative medicine) was shown to be sufficiently reliable.

We propose the possible use of SNOMED CT concepts in the Notes section of the VistA EHR system for perioperative physical examinations. The purpose is to enhance patient safety, decision support capability for clinicians, and error free data transmitted across healthcare facilities.

One caveat which remains, however, is that temporal concepts (e.g. “one day”) which are normally part of PMM recommendations are not present in pre-coordinated form in SNOMED CT. The post-coordination feature of SNOMED – the feature that allows combining of atomic concepts for building more complex concepts- was investigated in this study as a possible solution for fully expressing PMM recommendations. Following the rules of post-coordination[201] and in compliance with the SNOMED CT concept model and expression syntax would only allow the temporal concept in a recommendation (e.g. “one day” in “recommendation to stop taking medication one day prior to surgery”) to be applied to the action (i.e. stop taking medication), not the recommendation. It is unlikely that Representational forms for expressions will be altered in SNOMED to accommodate expressing temporal concepts in PMM. Perhaps these concepts will remain as free-text in EHR notes for the foreseeable future.

Study Limitations

This was a single-site study with a specific patient population, and medication recommendations were limited to the clinical context in the perioperative period. Also, our sample size may not have captured all possible medication management recommendations. However, we feel confident that the recommendations captured are representative. In the absence of a working SNOMED browser we were unable to validate the placement of the MTM concepts in the SNOMED CT hierarchy.

Future Directions

Our cross-mappings did not consider the possibility of "partial match" scorings. This is due to the fact that SNOMED-CT concepts lacked the temporal axis present in PMM concepts (e.g., while "Recommendation to Discontinue Prescription Medication" was a match, the timeline on how long to stop a medication was not). For instance, discontinue in the context of "Recommendation to discontinue prescription medication" (CONCEPTID=4781000124108) is arguably problematic since there is not a clear mechanism to restart the medication. There is likely a need to tether the "stop" recommendation in SNOMED with a "start/restart" term. This is one of the core problems in clinical care transitions where the system should provide some sort of HIT-driven memory to help manage appropriate continuity.

Conclusion

We showed that as computerized health care systems are becoming more knowledge-intensive and the representation of medical knowledge in a format that is computable as well as human readable is becoming more necessary, we need to find ways to start expressing clinical thoughts in standardized medical terminologies. SNOMED CT has been proven to be an excellent mechanism via which we can accomplish this task.

The findings in this study are comparable to other similar studies which assessed the use of SNOMED CT for expressing clinical terms and encounters reliably.[198 202] However, SNOMED CT is less-suitable for representing the full extent of information collected in perioperative medication management recommendation notes.

Chapter 5

Conclusion

Developing high quality information systems capable of supporting research and clinical care in perioperative medicine requires the existence of robust Clinical Decision Support (CDS) tools and the use of standardized terminologies which have proven to be effective for Health Information Exchange (HIE). These informatics tools must be robust enough to have the capability of delivering the right information for the right patient at the right time. The studies we conducted in the preceding chapters identified gaps in two areas of perioperative medicine: 1) making the best-known medication management recommendation during a pre-op physical evaluation; 2) lack of standardized terminology concepts to express these recommendations. We therefore offered specific solutions- through established research methodologies- on how to address narrowing these gaps.

Our findings revealed that noticeable differences exist in choosing from several medication management recommendations among perioperative medicine providers. This is largely due to the fact that practice is provider-specific, lacking any large body of research or a determined pool of trusted sources for support. We also discovered that these recommendations- when entered in the patient's record- are in free-text format, making them virtually unusable for statistical and outcomes research.

To address the first gap, the first study developed a methodology and framework for building a CDSS knowledge engine based on trusted medical sources (evidence-base research, expert opinions, and actual EHR notes). This engine holds medication management recommendations for all of the Veterans Affairs drug formulary containing approximately 9,000 drugs in 409 categories. This engine served as the main component for development of the full CDSS in the second study.

In the second study we developed the necessary web-based software components independent of any particular hardware platform, in order to operationalize the knowledge engine developed in the previous study into a fully functioning decision support system. We then utilized established qualitative and quantitative methodologies to assess the accuracy of the CDSS in the context of making suitable medication management recommendations during a pre-op physical examination evaluation. Our findings showed the CDSS performed at a very high accuracy averaged across all patient medications sampled, which compares favorably with similar decision support tools. We thus concluded that our CDSS can be used effectively in a clinical setting.

Having developed and evaluated a decision support system in the previous two studies, we turned our attention to health information exchange in the third and final study. This study evaluated the use of SNOMED CT [15] for expressing medication management recommendations. Currently, these recommendations are stored in free-text, incomputable format. Hypothesizing that existing medication-related recommendations in SNOMED CT can be used, we converted all recommendations from our sample records into terminology concepts. Using quantitative statistical methods and qualitative adjudication processes, this study yielded a high inter-rater agreement as the measure of effective use of SNOMED CT in lieu of free-text.

Taken as a whole, these studies have shown significant gaps in uniformity of practice and use of computable constructs to express medication management recommendations. Narrowing these gaps will provide the ability to provide decision support in perioperative medication management. Furthermore, utilizing structured terminologies to express concepts, and activities related to medication management is essential to the provision of high quality care in perioperative medicine.

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Appendix 1: Eliminated Drug Categories

Eliminated Classes	Eliminated Categories
AD200	CYANIDE ANTIDOTES
AD400	ANTIDOTES,DETERRENTS,AND POISON CONTROL EXCHANGE RESINS
AM550	METHENAMINE SALTS ANTIMICROBIALS
AN200	ANTINEOPLASTIC ANTIBIOTICS
AN600	ANTINEOPLASTIC RADIOPHARMACEUTICALS
AN700	PROTECTIVE AGENTS
AS000	ANTISEPTICS/DISINFECTANTS
BL115	THROMBOLYTICS
BL116	ANTIHEMORRHAGICS
BL500	BLOOD DERIVATIVES
BL800	VOLUME EXPANDERS
BL900	BLOOD PRODUCTS,OTHER
CN200	ANESTHETICS
CN201	ANESTHETICS,INHALATION
CN202	BARBITURIC ACID DERIVATIVE ANESTHETICS
CN203	GENERAL ANESTHETICS,OTHER
CN204	LOCAL ANESTHETICS,INJECTION
CN205	ANESTHETIC ADJUNCTS
CN301	BARBITURIC ACID DERIVATIVE SEDATIVES/HYPNOTICS
CV600	SCLEROSING AGENTS
CV709	DIURETICS,OTHER
DE101	ANTIBACTERIAL,TOPICAL
DE102	ANTIFUNGAL,TOPICAL
DE103	ANTIVIRAL,TOPICAL
DE109	ANTI-INFECTIVE,TOPICAL,OTHER
DE200	ANTI-INFLAMMATORY,TOPICAL
DE250	ANTI-INFECTIVE/ANTI-INFLAMMATORY COMBINATIONS,TOPICAL
DE300	SUN PROTECTANTS/SCREENS,TOPICAL
DE350	EMOLLIENTS
DE400	SOAPS/SHAMPOOS/SOAP-FREE CLEANSERS
DE450	DEODORANTS/ANTIPERSPIRANTS,TOPICAL
DE500	KERATOLYTICS/CAUSTICS,TOPICAL
DE600	ANTINEOPLASTIC,TOPICAL
DE650	ANALGESICS,TOPICAL
DE700	LOCAL ANESTHETICS,TOPICAL
DE752	ANTIACNE AGENTS,TOPICAL
DE820	ANTIPSORIATICS,TOPICAL

DE900	DERMATOLOGICALS,TOPICAL OTHER
DX101	NON-IONIC CONTRAST MEDIA
DX102	IONIC CONTRAST MEDIA
DX109	CONTRAST MEDIA, OTHER
DX200	RADIOPHARMACEUTICALS,DIAGNOSTIC
DX201	IMAGING AGENTS (IN VIVO) RADIOPHARMACEUTICALS
DX202	NON-IMAGING AGENTS RADIOPHARMACEUTICALS
DX300	DIAGNOSTIC ANTIGENS
DX900	DIAGNOSTICS,OTHER
GA400	TUMOR NECROSIS FACTOR BLOCKER
GU300	ANTI-INFECTIVES,VAGINAL
GU500	ESTROGENS,VAGINAL
HS701	ANTERIOR PITUITARY
HS702	POSTERIOR PITUITARY
IM100	VACCINES
IM105	TOXOIDS
IM109	VACCINES/TOXOIDS, OTHER
IM300	ANTIVENINS/ANTITOXINS
IM400	IMMUNE SERUMS
IM500	IMMUNOGLOBULINS
IP100	INTRAPLEURAL SCLEROSING AGENTS
IR100	IRRIGATION SOLUTIONS
IR200	PERITONEAL DIALYSIS SOLUTIONS
IR300	HEMODIALYSIS SOLUTIONS
MS140	PENICILLAMINE
MS160	GOLD COMPOUNDS,ANTIRHEUMATIC
MS205	VESICULAR MONOAMINE TRANSPORT TYPE 2 BLOCKER
MS300	NEUROMUSCULAR BLOCKING AGENTS
NT900	NASAL AND THROAT,TOPICAL,OTHER
OP103	ADRENERGICS,TOPICAL OPHTHALMIC
OP300	ANTI-INFLAMMATORIES,TOPICAL OPHTHALMIC
OP400	CONTACT LENS SOLUTIONS
OP500	EYE WASHES/LUBRICANTS
OP700	ANESTHETICS,TOPICAL OPHTHALMIC
OR100	CARIOSTATICS,TOPICAL
OR200	DENTAL PROTECTANTS
OR300	DENTIFRICES
OR400	DENTURE ADHESIVES
OR500	MOUTHWASHES
OR900	DENTAL AND ORAL AGENTS,TOPICAL,OTHER
OT101	ANTIBACTERIALS,TOPICAL OTIC

OT109	ANTI-INFECTIVES,TOPICAL OTIC OTHER
OT200	ANTI-INFLAMMATORIES,TOPICAL OTIC
OT250	ANTI-INFECTIVE/ANTI-INFLAMMATORY COMBINATIONS,TOPICAL OTIC
OT400	ANALGESICS,TOPICAL OTIC
OT900	OTIC AGENTS,OTHER
PH000	PHARMACEUTICAL AIDS/REAGENTS
RE600	NON-ANESTHETIC GASES
TN101	IV SOLUTIONS WITHOUT ELECTROLYTES
TN102	IV SOLUTIONS WITH ELECTROLYTES
TN200	ENTERAL NUTRITION
TN470	FLUORIDE
TN476	BICARBONATES
TN501	AMINO ACIDS/PROTEINS,PARENTERAL,WITHOUT ADDED ELECTROLYTES
TN502	AMINO ACIDS/PROTEINS,PARENTERAL,WITH ADDED ELECTROLYTES
VT107	PANTOTHENIC ACID
VT503	DIHYDROTACHYSTEROL
VT701	MENADIOL
XA000	PROSTHETICS/SUPPLIES/DEVICES
XA100	BANDAGES/DRESSINGS
XA101	PADS,GAUZE,STERILE
XA102	PADS,GAUZE,NON-STERILE
XA103	PADS,NON-ADHERING
XA104	PADS,GAUZE WITH ADHESIVE
XA105	PADS,GAUZE WITH MEDICATION ADDED
XA106	GAUZE,FINE MESH
XA107	BANDAGE,FILM
XA108	BANDAGE,ELASTIC
XA109	BANDAGE,STRETCH
XA110	FOAM WITH ADHESIVE
XA111	PACKING,GAUZE,PLAIN
XA112	PACKING,GAUZE,MEDICATED
XA199	BANDAGES/DRESSINGS,OTHER
XA201	TAPE,PAPER
XA202	TAPE,CLOTH
XA203	TAPE,PLASTIC
XA204	TAPE,FOAM
XA205	STRAPS,MONTGOMERY
XA206	TAPE,TRACH
XA299	TAPE,OTHER
XA301	PADS,BED
XA304	LINER,RUBBER PANTS

XA305	DIAPERS
XA399	PADS/DIAPERS,OTHER
XA400	COLOSTOMY/ILEOSTOMY COLLECTION DEVICES
XA401	BAG,DRAINABLE WITH ADHESIVE,COLOSTOMY/ILEOSTOMY
XA402	BAG,DRAINABLE WITHOUT ADHESIVE,COLOSTOMY/ILEOSTOMY
XA403	BAG,CLOSED WITH ADHESIVE COLOSTOMY/ILEOSTOMY
XA404	BAG,CLOSED WITHOUT ADHESIVE COLOSTOMY/ILEOSTOMY
XA405	BAG,DISPOSABLE WITH ADHESIVE,COLOSTOMY/ILEOSTOMY
XA407	SETS,APPLIANCE,COLOSTOMY/ILEOSTOMY
XA499	COLOSTOMY/ILEOSTOMY COLLECTION DEVICES,OTHER
XA500	UROSTOMY/URINARY COLLECTION DEVICES
XA501	BAG,BEDSIDE URINARY COLLECTION DEVICE
XA502	BOTTLES/OTHER BEDSIDE URINARY COLLECTION DEVICES
XA503	SETS,APPLIANCE,UROSTOMY
XA504	BAG,DRAINABLE WITH ADHESIVE,UROSTOMY
XA505	BAG,DRAINABLE WITHOUT ADHESIVE,UROSTOMY
XA507	BAG,CLOSED WITHOUT ADHESIVE,UROSTOMY
XA508	BAG,LEG URINARY COLLECTION DEVICE
XA509	CATHETER,FOLEY
XA510	CATHETER,COUDE-TIP
XA511	CATHETER,BALLOON
XA512	CATHETER,RED RUBBER
XA513	CATHETER,EXTERNAL URINARY
XA515	KIT,CATHETER CARE
XA516	SET,IRRIGATION
XA599	UROSTOMY/URINARY COLLECTION DEVICES,OTHER
XA600	OSTOMY SUPPLIES,OTHER
XA601	RINGS,OSTOMY
XA602	DISCS,OSTOMY
XA603	ADHESIVES,OSTOMY
XA604	PROTECTANTS,SKIN,OSTOMY
XA605	BELTS,OSTOMY
XA606	ODOR CONTROL PRODUCTS,OSTOMY
XA607	IRRIGATORS/SETS,OSTOMY
XA608	CAPS,OSTOMY
XA699	OSTOMY SUPPLIES,OTHER
XA701	BAGS,FEEDING
XA703	TUBES,FEEDING
XA799	BAGS/TUBES/SUPPLIES FOR ORAL NUTRITION,OTHER
XA801	SETS,VOLUMETRIC,INTRAVENOUS
XA802	SETS,MAXI-DRIP,INTRAVENOUS

XA805	SETS,BUTTERFLY,INTRAVENOUS
XA809	INTRAVENOUS SETS,OTHER
XA850	SYRINGES/NEEDLES
XA851	SYRINGES,SLIP TIP,INJECTION
XA852	SYRINGES,LUER LOCK,INJECTION
XA853	SYRINGES WITH NEEDLE,INJECTION
XA854	SYRINGES,INSULIN,INJECTION
XA855	CAPS,SYRINGE
XA856	NEEDLES,INJECTION
XA859	SYRINGES/NEEDLES,OTHER
XA900	SUPPLIES,OTHER
XX000	MISCELLANEOUS AGENTS

Appendix 2: SNOMED CT Medication Management Concept Candidates

CONCEPTID	FULLYSPECIFIEDNAME
182838006	Change medication (procedure)
432811000124101	Change medication course (procedure)
432841000124102	Change medication dosage form (procedure)
432751000124106	Change medication dose (procedure)
432781000124103	Change medication dosing interval (procedure)
407611006	Change medication to generic equivalent (procedure)
432901000124105	Change medication to therapeutic equivalent (procedure)
432911000124108	Change medication to therapeutic equivalent on formulary (procedure)
432771000124101	Decrease medication dose (procedure)
432791000124100	Decrease medication dosing interval (procedure)
432761000124108	Increase medication dose (procedure)
432801000124104	Increase medication dosing interval (procedure)
432821000124109	Lengthen medication course (procedure)
428711000124105	Recommendation to change medication (procedure)
428721000124102	Recommendation to change medication course (procedure)
428791000124100	Recommendation to change medication dose (procedure)
428751000124106	Recommendation to change medication dose form (procedure)
428761000124108	Recommendation to change medication dosing interval (procedure)

428831000124107	Recommendation to change medication to generic equivalent (procedure)
428841000124102	Recommendation to change medication to therapeutic equivalent (procedure)
428851000124100	Recommendation to change medication to therapeutic equivalent on formulary (procedure)
4761000124103	Recommendation to continue a medication (procedure)
306806004	Recommendation to continue medication (procedure)
428801000124104	Recommendation to decrease medication dose (procedure)
428781000124103	Recommendation to decrease medication dosing interval (procedure)
4711000124101	Recommendation to discontinue dietary supplement (procedure)
4791000124106	Recommendation to discontinue herbal supplement (procedure)
4701000124104	Recommendation to discontinue medication (procedure)
304540007	Recommendation to discontinue medication (procedure)
4801000124107	Recommendation to discontinue over-the-counter medication (procedure)
4781000124108	Recommendation to discontinue prescription medication (procedure)
428811000124101	Recommendation to increase medication dose (procedure)
428771000124101	Recommendation to increase medication dosing interval (procedure)
428881000124108	Recommendation to initiate laboratory results monitoring (procedure)
428871000124105	Recommendation to initiate medication monitoring (procedure)
428741000124109	Recommendation to lengthen medication course (procedure)
428731000124104	Recommendation to shorten medication course (procedure)

4831000124104	Recommendation to start dietary supplement (procedure)
4821000124102	Recommendation to start herbal supplement (procedure)
428861000124103	Recommendation to start medication therapy (procedure)
4811000124105	Recommendation to start over-the-counter medication (procedure)
428821000124109	Recommendation to start prescription medication (procedure)
432831000124107	Shorten medication course (procedure)
432871000124105	Start dietary supplement (procedure)
432881000124108	Start herbal supplement (procedure)
432851000124100	Start over-the-counter medication (procedure)
432861000124103	Start prescription medication (procedure)