### Definitions Color-Coding Key

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| --- | --- |
|  | Clinical Consequence |
|  | Evidence |
|  | Recommended Actions |
|  | Mechanism of Interaction |
|  | Contextual Evidence/Modifying Factors |
|  | Seriousness Rating |
|  | Frequency of Harm/Exposure |

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### User Stories

#### Treatment Planning, Physician

Simvastatin + Amiodarone

* Kathleen is a physician who is treating a patient who has a ventricular arrhythmia. Kathleen would normally prescribe amiodarone for this particular patient, but he is being treated with simvastatin for dyslipidemia, and she knows that a potentially serious interaction may occur leading to rhabdomyolysis. Kathleen wants to know what the patient’s risk factors are for rhabdomyolysis, what the benefits and risks would be to switching him to an alternative statin, and if amiodarone is not the best option for this patient, what alternatives to amiodarone exist for this patient, and what the available evidence shows in terms of ventricular arrhythmia patient outcomes.

(Pediatrics) Fluoxetine + Ondansetron

* Evelyn is a pediatric emergency medicine physician caring for an adolescent with a history of major depressive disorder treated with fluoxetine, who presents with acute onset of vomiting and diarrhea. Evelyn’s usual first-line antiemetic for acute gastroenteritis is ondansetron, but Evelyn knows that both fluoxetine and ondansetron are listed as QTc-prolonging medications. Evelyn would like to know the likelihood of clinically significant QTc prolongation due to a brief course of co-administration of fluoxetine and ondansetron, and if there is a recommendation for dose adjustment or an alternate antiemetic.

(Pediatrics) Azole antifungals + Tacrolimus

* William is a pediatric hospitalist caring for a child with a history of liver transplant due to congenital liver disease, treated with tacrolimus to prevent organ rejection. The patient is admitted with a fever and starts broad anti-infective therapy, including vancomycin, piperacillin-tazobactam and fluconazole. William knows that azole antifungals can increase tacrolimus levels and wants to know if there is evidence to guide a decrease the patient’s tacrolimus dose to prevent tacrolimus toxicity. He additionally wants to know the mechanism of interaction to avoid further interacting medications.

#### Evaluation of Management Options for Drug-Drug Interactions, Physician

Warfarin + Naproxen

* Melissa is a family physician whose patient called because he is experiencing noticeable bruising. Melissa knows that the patient is taking warfarin, but he has not experienced bruising before. She asks if the patient has taken any new medications recently, and he mentions that he visited a pain clinic for his chronic back pain and they prescribed the NSAID naproxen. Melissa knows that NSAIDs can increase the risk of bleeding when taken with warfarin, and she wants to know the best way to manage this interaction.

#### Evaluation of Management Options for Drug-Drug Interactions, Pharmacist

Atorvastatin + Clarithromycin

* James is a community pharmacist reviewing an electronic prescription that just came in for clarithromycin; an alert in his pharmacy’s information system indicates that there is a potential interaction between the clarithromycin and the atorvastatin that the patient was prescribed a year ago by different physician. James calls the patient in order to discuss her medications; she tells him that she is taking the atorvastatin as prescribed, and cannot remember if she has ever taken clarithromycin in the past. In preparation for following up with the patient’s physician, James would like to know the likelihood of an adverse drug event such as rhabdomyolysis occurring due to a potential interaction and how serious the interaction could be. He would also like to know if monitoring would be appropriate for this patient, or if a dose adjustment or temporary discontinuation of one of the drugs would be best.

#### **Screening for Drug-Drug Interactions, Nurse**

Glipizide + Lisinopril (Sulfonylureas + ACE Inhibitors)

* Nancy is a licensed practice nurse who works in a skilled nursing facility. She has noticed that her patient is experiencing symptoms of hypoglycemia. She sees that the patient was recently prescribed lisinopril, and is wondering if it interacts with one of the five medications that she is taking. Nancy remembers reading about a potential interaction with the glipizide that the patient is currently taking. She would like to know if the patient’s symptoms are a possible consequence of an interaction between the glipizide and the lisinopril, or the lisinopril and one of the other medications that the patient is taking, and if so, what information she should pass along to the registered nurse in charge in order to help treat the patient.

#### **Synthesis for Dissemination, Drug Compendium Editor** Tyrosine Kinase Inhibitors + Proton Pump Inhibitors

* Olivia is a drug compendium editor who is reviewing the available literature for the potential interaction between tyrosine kinase inhibitors and proton pump inhibitors. She would like to review the most recent literature available surrounding the interaction, and would like to compare it against the existing entry in her drug compendium. She would like to understand more about the mechanism of the interaction, whether it applies to all drugs within the classes, whether certain populations are at greater risk, and the types and strength of the evidence available. She would also like to learn more about recommended management options.

#### **Synthesis for Dissemination, Librarian**

* Michael is a librarian who works for the medication safety unit in a regulatory agency. He has graduate training in library and information science, and has a good understanding of medical reference sources. When he is asked to locate information about a potential drug drug interaction, he wants to understand more about the terms used to describe the drugs so that he can develop search strategies to run daily, weekly, and monthly searches. He would like to find terms used to describe the specific drugs involved in the interaction, drug class concepts, clinical consequences of the interaction, and existing types of evidence of the interaction.

#### Synthesis for Dissemination, Clinical Decision Support Team - Systems Analyst & Content Specialist

* Richard is a systems analyst who is working with Joe, a content specialist, in order to design a new clinical information system which can provide personalized clinical knowledge and patient information for clinicians to improve healthcare quality. Richard is professionally trained in algorithms, databases, and programming. He also has some knowledge about electronic medical records. In order to help Richard design and implement the system, Joe would like to know about the evidence, clinical consequences, and mechanisms of interactions of potential drug-drug interactions so that he can develop rules for the most clinically relevant interactions. With that information, he can help Richard create linkages and designs algorithms based on electronic medical records. Joe can also help Richard prioritize what to display and how to display information or alerts for clinicians.

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| **Tasks/Goals** | **Users** | **Info Needs** | **Aspects of Info Users Value to Make a Decision** | **Barriers** |
| Evaluation of Management Options for Drug-Drug Interactions | General Practitioner (Physician) | * EHR/patient data   + Patient History   + Lab Results, Tests   + Patient Medications   + Potentially Interacting Drugs * Patient Assessment   + Signs/ Symptoms * Prescriber’s Knowledge and Experience * Knowledgebase   + DDI Symptoms   + Mechanism of Interaction   + Potential Substitutes   + Indications   + Evidence | * Conciseness and Clarity * Timeliness * Accuracy * Grading of Evidence   + Type of Evidence   + Study Methods * Patient Context/ Relevance   + Disease States   + Risk Factors * Frequency   + Populations   + Demographics   + Risk Factors   + Comorbidities * Seriousness * Clinical Guidelines * How Colleagues Addressed Similar Scenarios | * Incomplete Medication List, Allergies * Irrelevant Alerts/ Lack of Evidence/ Not Graded * No Recommendations * Formulary Restrictions * Incomplete Information (e.g., Patient Report) |
| Community Pharmacist | * EHR/patient data   + Patient History   + Lab Results, Tests   + Patient Medications   + Duration of Therapy   + Potentially Interacting Drugs * Pharmacist’s Knowledge and Experience * Knowledgebase   + DDI Symptoms   + Mechanism of Interaction   + Potential Substitutes   + Indications   + Evidence | * Conciseness   + Grading of Evidence   + Type of Evidence   + Study Methods * Accuracy * Frequency   + Populations   + Demographics   + Risk Factors   + Comorbidities * Seriousness * Patient Context/ Relevance   + Compliance   + Disease States   + Risk Factors * Clinical Guidelines | * Incomplete Medication List, Allergies * Delayed Information * Irrelevant Alerts/ Lack of Evidence/ Not Graded * No Recommendations * Incomplete Information (e.g., Patient Compliance) |
| Screening for a Drug-Drug Interactions | Licensed Practical Nurse | * EHR/patient data   + Patient History   + Lab Results, Tests   + Patient Medications   + Potentially Interacting Drugs * Nurse’s Knowledge and Experience * Patient Assessment   + Signs/ Symptoms * Knowledgebase   + Symptoms   + Potential Substitutes   + Evidence | * Conciseness * Evidence (to support discussion with physician) * Patient Context/ Relevance * Recommendations * Institutional Protocols | * Not Empowered to Confront Physician * Detecting Symptoms (e.g., nonverbal patients) * Irrelevant Alerts/ Lack of Evidence/ Not Graded * Incomplete Medication List, Allergies * No Recommendations |
| Treatment Planning  (Source: Russ et al., *Health Informatics Journal*. 2010;16(4):287–305) | Physician | * EHR/patient data   + Patient’s Medical History and Allergies   + Patient’s Medications   + Potentially Interacting Drugs * Patient Assessment   + Signs/ Symptoms * Prescriber’s Knowledge and Experience   + Conditions   + Medication/ Class * Knowledgebase   + Mechanisms   + Potential Substitutes | * Conciseness * Grading of Evidence * Patient Context/ Relevance * Timeliness * Accuracy * Recommendations * Clinical Guidelines | * Lack of Guidelines/ Evidence * Incomplete Medication List, Allergies * Evidence Not Graded * Lack of Recommendations * Incomplete Information (e.g., patient report) |
| Synthesis for Dissemination  (source: unpublished manuscript) | Drug Compendium Editorial Board | * Literature   + Patient Demographics   + Patient-Specific Clinical Characteristics   + Temporal Overlap in Drug Administration * Member Knowledge * Knowledgebase   + Evidence   + Information Quality   + Mechanism of Interaction   + Biological Plausibility of Interaction   + Treatment Comparisons | * Grading of Evidence   + Type of Evidence   + Source of Evidence   + Study Methods * Relevance to DI Question * Study Results in Statistical Form * Result Magnitude * Statistical vs. Clinical Significance * Patient Populations   + Disease States   + Risk Factors * Frequency   + Populations   + Demographics   + Risk Factors   + Comorbidities * Seriousness | * Difficulty of Showing Lack of Association * Lack of Evidence (e.g., RCTs) or Weak Evidence * Access to Newly Published Research * Comprehensiveness vs. Clinically Relevance |
| Librarian | * Literature   + Drugs   + Patient Demographics   + Patient-Specific Clinical Characteristics * Librarian Knowledge * Knowledgebase   + Mechanism of Interaction   + Information Quality | * Evidence Grading * Patient Populations * Summary of Study Results * Result Magnitude * Clinical Relevance | * Lack of Evidence (e.g., RCTs) * Weak Evidence * Information Overload |
| Clinical Decision Support Team  (Systems Analyst & Content Expert) | * EHR/patient data   + Patient Baseline (lab results, tests, etc.)   + Patient Medical History   + Patient Medications   + Patient Symptoms   + Family History   + Genetics   + Historical and Geographical trends of disease occurrence   + Published Clinical Data * EHR Standards/Schema * Knowledgebase   + Schema   + Adverse Drug Events * Algorithm | * Patient Context/ Relevance * Clinical Guidelines * Recommendations * Medicinal Effectiveness * Accuracy * Consistency * Severity * Type of DDI * Specification of Data * Simplicity * Minimizing cognitive load * Efficient interactions | * No Personalized Recommendation * No Patient Improvement * No Personalized Alerts(Alerts should be personalized and identified with EHR) * Data is not been filtered before it was given to physicians |