GUIDANCE FOR LEAPFROG HOSPITAL SURVEY PARTICIPATING HOSPITALS
CLINICAL DECISION SUPPORT RELATED TO THE CPOE EVALUATION TOOL
INTRODUCTION

To fully meet Leapfrog’s Computerized Physician Order Entry (CPOE) Standard, each adult and general hospital must (1) ensure that licensed prescribers enter at least 85% of inpatient medication orders via a computer system that includes decision support software to reduce prescribing errors, and (2) demonstrate, via a test, that its inpatient CPOE system can alert physicians to at least 60% of common serious prescribing errors. Hospitals are asked to use Leapfrog’s CPOE Evaluation Tool to complete an Adult Inpatient Test to fulfill the second requirement of our standard.

Upon successful completion of an Adult Inpatient Test, a hospital’s responses are immediately scored and available to be viewed and printed. Results from the test are also archived and can be accessed anytime by logging back into the CPOE Evaluation Tool from the Survey Dashboard.

DESCRIPTION OF THE CPOE EVALUATION TOOL

The CPOE Evaluation Tool was designed by medication safety experts and researchers at Brigham and Women’s Hospital and the University of Utah to test the ability of inpatient CPOE systems to alert prescribers to common, serious medication errors. In addition, the Tool was designed to help hospitals improve their use of clinical decision support to reduce adverse drug events (ADEs) and improve medication safety. The Tool was first included in the Leapfrog Hospital Survey in 2008. This is the third release of the Tool (Version 3.5) and includes updates to test patients and orders, as well as the Orders and Observation Sheet and Online Answer Form.

The timed test provides users with a set of Test Patients, along with a corresponding set of Test Medication Orders, that users enter into their hospital’s CPOE and related clinical systems. The physician conducting the test records the advice or information they received, if any, from their hospital’s CPOE system onto the Orders and Observation Sheet, and then completes the Online Answer Form. Users receive immediate scoring and feedback summarizing the results of the test. The Tool includes several order checking categories including drug-drug interaction, drug-allergy interactions, therapeutic duplications, single and daily dose limits, and others.

ORDER CHECKING CATEGORIES

The CPOE Evaluation Tool calculates the results from the Adult Inpatient Test and displays a report that includes 10 individual category scores and an overall score using the criteria described below. Each category included in the CPOE Evaluation Tool represents an area where a serious ADE could occur if the CPOE system’s clinical decision support fails to alert the prescriber. The intent of the test is to measure and improve on hospitals’ use of clinical decision support to reduce ADEs and improve medication safety.

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<tr>
<th>Order Checking Category</th>
<th>Description</th>
<th>Example</th>
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<tr>
<td>Therapeutic Duplication</td>
<td>Medication combinations overlap therapeutically (same agent or same class)</td>
<td>Using clonazepam and lorazepam together</td>
</tr>
<tr>
<td>Order Checking Category</td>
<td>Description</td>
<td>Example</td>
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<td>-------------------------</td>
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<tr>
<td><strong>Drug-Dose (Single)</strong></td>
<td>Specified dose of medication exceeds safe range for single dose</td>
<td>Tenfold overdose of digoxin</td>
</tr>
<tr>
<td><strong>Drug-Dose (Daily)</strong></td>
<td>Specified frequency of administration results in daily dose that exceeds safe range for daily dose</td>
<td>Ordering ibuprofen regular dose every three hours</td>
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<tr>
<td><strong>Drug-Allergy</strong></td>
<td>Medication (or medication class) is one for which patient allergy has been documented</td>
<td>Penicillin prescribed for patient with documented penicillin allergy</td>
</tr>
<tr>
<td><strong>Drug-Route</strong></td>
<td>Specified route of administration is inappropriate and potentially harmful</td>
<td>Use of vitamin K intramuscular injection</td>
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<tr>
<td><strong>Drug-Drug</strong></td>
<td>Medications in pairs of orders result in known harmful interaction when used in combination</td>
<td>Concurrent linezolid and sumatriptan</td>
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<tr>
<td><strong>Drug-Diagnosis</strong></td>
<td>Medication contraindicated based on documented problem/diagnosis</td>
<td>Nonspecific beta-blocker in patient with asthma</td>
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<tr>
<td><strong>Drug-Age</strong></td>
<td>Medication contraindicated based on patient age</td>
<td>Prescribing diazepam for a patient over 65 years old</td>
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<tr>
<td><strong>Drug-Lab</strong></td>
<td>Medication contraindicated based on documented laboratory test results (includes renal status)</td>
<td>Use of enalapril in patient with severe renal failure</td>
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<tr>
<td><strong>Drug Monitoring</strong></td>
<td>Medication for which the standard of care includes subsequent monitoring to avoid harm</td>
<td>Prompt to monitor drug levels when ordering aminoglycoside.</td>
</tr>
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</table>

The Tool also includes an “Alert Fatigue” test category, which checks if prescribers are receiving alerts or information for inconsequential medication interactions that clinicians typically ignore. An example would be alerting on the concurrent use of hydrochlorothiazide and captopril. This test category is not included in scoring.

The Tool also includes a “Deception Analysis” test category, which checks for “false positives” (e.g., orders that should not have generated any warning in the hospital’s CPOE system). Hospitals that “fail” the Deception Analysis are scored as “Incomplete Evaluation” and will not be able to retake an Adult Inpatient Test for 120 days.
GENERAL GUIDANCE

HARD STOPS VS. DISRUPTIVE ALERTS

The CPOE Evaluation Tool gives hospitals credit for the use of hard stops and disruptive alerts. For example, if a hospital reports not being able to electronically enter a medication order via an unsafe or inappropriate route, they receive the same credit as a hospital that reports receiving a disruptive alert about the selected route being unsafe or inappropriate.

The CPOE Evaluation Tool developers recommend a “hard stop” when a medication order is absolutely contraindicated because a “hard stop” prevents the licensed prescriber from entering the unsafe order and prevents manual overrides. However, “hard stops” should be used judiciously and infrequently as there are very few contraindications that warrant a hard stop. Some examples include:

- Drug-Drug Interactions (DDIs) where there is no benefit of the drug combination that outweighs the risk (i.e., Monoamine Oxidase Inhibitors and Sumatriptan).
- Vincristine given intrathecally should be a hard stop since there have been multiple cases of this resulting in death or serious harm.

Other contraindicated DDIs do not warrant a hard stop. For example, Sildenafil and Nitroglycerin should trigger an alert, but would not warrant a hard stop.

GUIDANCE FOR SPECIFIC ORDER CHECKING CATEGORIES

DRUG-DRUG INTERACTION 1–7

Drug-Drug Interaction (DDI) Severity level 1 are drug combinations that are contraindicated for concurrent use. These DDIs have a high potential for patient harm where the risk definitely outweighs the benefit.

Some examples of Level 1 DDI include:

- Concurrent use of Simvastatin and Verapamil may result in increased exposure to Simvastatin and an increased risk of myopathy or rhabdomyolysis.
- Concurrent use of Tizanidine and Ciprofloxacin may result in increased Tizanidine plasma concentrations resulting in increased hypotensive and sedative effects.
- Concurrent use of Monoamine Oxidase Inhibitors and Sumatriptan may result in increased risk of serotonin syndrome (hypertension, hyperthermia, myoclonus, mental status changes).

DDI Severity level 2 are severe adverse interactions where action by a licensed prescriber is required to reduce the risk to the patient. These actions may include monitoring drug levels and/or making dose adjustments as needed. The examples listed are level 2 DDIs that Bates, et al. found to cause patient harm or had the potential to cause harm because appropriate prescriber action was not taken. 7
Some examples of Level 2 DDI include:

- Concurrent use of Levofloxacin and Warfarin may result in an increased risk of bleeding. Concomitant use has been associated with increases in INR or prothrombin time and clinical episodes of bleeding. If concomitant use is required, early and more frequent monitoring of the patient’s INR is recommended.

- Bactrim DS (sulfamethoxazole 800 mg and trimethoprim 160 mg) and Warfarin sodium
  - Concurrent use of Sulfamethoxazole and Warfarin may result in increased warfarin exposure. If coadministration is required, monitor prothrombin time and INR early and closely, especially during initiation. Discontinuation of SMX is recommended. Preemptive warfarin dose reductions may be considered to prevent INR prolongation during coadministration.

- Drugs that both cause QT prolongation (see [http://www.torsades.org](http://www.torsades.org) for list of known risk drugs)
  - Haloperidol and Citalopram or Haloperidol and Ondansetron
    - Concurrent use of Haloperidol and Citalopram or Haloperidol and Ondansetron may result in prolonged QTc interval or torsades de pointes. Recommend avoiding concurrent use, but if co-therapy is warranted, recommend monitoring QTc closely.
  - Levofloxacin and Amiodarone
    - Concurrent use of Levofloxacin and Amiodarone may result in an increased risk of cardiotoxicity (QT prolongation, torsades de pointes, cardiac arrest).
  - Citalopram and Omeprazole
    - Concurrent use of Citalopran and Omeprazole may result in increased citalopram exposure and risk of QT interval prolongation. If coadministration of citalopram with omeprazole is required, do not exceed citalopram doses of 20 mg/day and discontinue citalopram in patients who have persistent QTc measurements greater than 500 milliseconds.

**DRUG-DIAGNOSIS**

Drug Diagnosis alerts should occur when drug combinations are contraindicated based on a patient’s documented problem or diagnosis.

- Focus on drugs to avoid in patients with:
  - GI bleeds – avoid Ketorolac
    - Black Box warning: Contraindicated in active or history of peptic ulcer disease, recent gastrointestinal bleeding or perforation, or history of gastrointestinal bleeding
  - Stroke – avoid Prasugrel
    - Black Box warning: Prasugrel can cause significant and sometimes fatal bleeding. Do not use Prasugrel in patients with active pathological bleeding or a history of transient ischemic attack or stroke
  - Asthma – avoid Propranolol, Carvedilol
    - Non-cardioselective beta-blockers were associated with a significantly increased risk of moderate asthma exacerbations when initiated at low to moderate doses and both moderate and severe exacerbations when prescribed chronically at high dose ([https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5270217/](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5270217/)).
  - Liver disease and use of hepatotoxic drugs
Drug-Age alerts should occur when drug combinations are contraindicated based on a patient’s age. The CPOE Evaluation Tool focuses on drug combinations that are contraindicated for geriatric patients in particular. There are two important resources that hospitals should consult to ensure their clinical decision support alerts their prescribers to these unsafe combinations, including:

- Screening Tool of Older Persons’ Prescriptions (STOPP) version 2
  - Potentially inappropriate medications listed in STOPP criteria, unlike some of those listed in Beers criteria, are significantly associated with avoidable ADEs in older people that cause or contribute to urgent hospitalization
- 2015 American Geriatrics Society Beers Criteria for Potentially Inappropriate Medication Use in Older Adults. Hospitals should focus on those recommendations where quality of evidence and strength of recommendation is high, which includes the following:
  - Dronedarone – Avoid in individuals with permanent atrial fibrillation or severe or recently decompensated heart failure
  - Nifedipine, immediate release – Avoid
  - Amiodarone – Avoid amiodarone as first-line therapy for atrial fibrillation unless patient has heart failure or substantial left ventricular hypertrophy
  - Antidepressants, alone or in combination (Amitriptyline, Amoxapine, Clomipramine, Desipramine, Doxepin >6 mg/d, Imipramine, Nortriptyline, Paroxetine, Protriptyline, Trimipramine) – Avoid
  - Barbiturates (Amobarbital, Butabarbital, Butalbital, Mephobarbital, Pentobarbital, Phenobarbital, Secobarbital) – Avoid
  - Ergoloid mesylates (dehydrogenated ergot alkaloids, Isoxsuprine) – Avoid
  - Growth hormone – Avoid, except as hormone replacement after pituitary gland removal
  - Sulfonylureas, long-duration (Chlorpropamide) – Avoid
  - Proton-pump inhibitors – Avoid scheduled use for >8 weeks unless for high-risk patients (e.g., oral corticosteroids or chronic NSAID use), erosive esophagitis, Barrett’s esophagitis, pathological hypersecretory condition, or demonstrated need for maintenance treatment (e.g., due to failure of drug discontinuation trial or H2 blockers

In addition, hospitals should focus on drugs that are known to induce a patient’s risk of falling such as: Antihypertensive agents, Diuretics, Sedatives and hypnotics, Neuroleptics and antipsychotics, Benzodiazepines, Narcotics.

Drug-Laboratory and Drug Monitoring

Drug-Laboratory alerts should occur when drug combinations are contraindicated based on documented laboratory test results, which includes renal status. Some examples of contraindicated combinations include:

- Ordering Potassium Chloride (KCL) or a potassium sparing diuretic (Spironolactone) in a patient with a high Potassium level
- Ordering Digoxin in a patient with a high Digoxin level
- Ordering nephrotoxic and/or renally cleared medications in a patient with a high Creatinine level
Drug Monitoring alerts should occur for drug combinations where the standard of care includes subsequent monitoring to avoid harm. Hospitals should focus on drugs with a narrow therapeutic range, such as aminoglycosides, carbamazepine, digoxin, lithium, phenytoin, phenobarbital, theophylline, and warfarin. Hospitals should ensure that when ordering these medications, their systems are alerting them or providing a laboratory order to monitor the patient’s potassium levels, creatinine level, INR, and therapeutic drug levels.

**THERAPEUTIC DUPLICATION**

Therapeutic Duplication alerts should occur when drug combinations overlap therapeutically (same agent or same class).

- Therapeutic Duplication alerts should fire on drugs within the same drug class, such as:
  - 2 Ace Inhibitors – Captopril and Lisinopril
  - 2 Statins – Atorvastatin and Simvastatin
  - 2 NSAID – Ibuprofen and Naprosyn
  - 2 Benzodiazepine – Diazepam and Alprazolam
  - Some drug classes are much more important than others; avoid those with evidence supporting e.g. ACE and ARB
- Therapeutic Duplication alerts should fire on brand and generic name of the same drug
  - Ibuprofen and Motrin

**DRUG-DOSE**

Drug-Dose alerts should occur when the specified dose or frequency of a medication or administration exceeds the safe range for a single dose or daily dose.

Hospitals should focus on drugs with a narrow therapeutic range, such as digoxin, as well as drugs that can cause serious or immediate toxicity if given in excessive amounts, such as narcotics and benzos. Hospitals should consult the [Institute for Safe Medication Practices High-Alert Medications](https://www.ismp.org) to ensure their clinical decision support alerts their prescribers to drugs that are known to cause harm if given in excessive doses, including:

- Hypoglycemic agents
- Anticoagulants
- Neuromuscular blockers
- Narcotics / Opioids

**DRUG-ALLERGY**

Drug-Allergy alerts should occur when a drug is contraindicated based on a patient’s documented allergy. For example, a Drug-Allergy alert occur when the patient has a documented allergy to Penicillin (particularly when the reaction is Anaphylaxis) and is ordered a medication that has the potential to cause a severe reaction. Penicillin Drug-Allergy alerts should occur if a 1st generation cephalosporin is being ordered for a patient with a documented Anaphylaxis reaction to Penicillin. We would not expect prescribers to receive penicillin drug-allergy alerts for the later generation cephalosporins. For hospitals focused on improving their antibiotic stewardship practices, it is recommended that patients, who report a penicillin allergy with a documented anaphylaxis reaction, be sent for skin testing to determine if they have a true allergic reaction.
REFERENCES


