

Alert Fatigue with DDI Software: Potential Solutions

John R. Horn, PharmD, FCCP

Professor of Pharmacy

School of Pharmacy and

Associate Director of University of Washington

Medical Center Pharmacy Department

University of Washington

Seattle, Washington

What is the Purpose of a Drug Interaction Screening Program?

To identify potential interactions and initiate steps to prevent possible patient harm

Prediction

“Prediction is very difficult. Especially if it’s about the future.”

Niels Bohr

Physicians and Computerized Drug Interaction Alerts

- 4751 First Data Bank DI alerts
- MDs tried to reenter same drug pair 26% of the time
- 3129 separate pairs: Override rate:
 - » Level 1 (Serious / substantial evidence) 89.4%
 - » Level 2 (Less serious) 96.3%
 - » Level 3 (Serious / some evidence) 85.4%

Drug Interaction Severity: What is Severe?

- Evaluated alerts rated as contraindicated by CDS software
- Found that 50% of the alerts were not contraindicated in labeling
- Many contraindicated in label could be administered under appropriate monitoring

Drug Interaction Severity: What is Severe?

- Common contraindicated alerts:
 - » Ibuprofen – Ketorolac
 - » Glycopyrrolate etc – KCL
 - » Linezolid – NE, Epi
- Common contraindicated alerts that are not:
 - » Amiodarone – Haloperidol
 - » Linezolid – Morphine, Fentanyl, Dextromethorphan
 - » Amiodarone - Azithromycin

Pennsylvania Patient Safety Advisory

- A 30-yr old patient was ordered Percocet (325 APAP and 5 mg oxycodone). The patient also was ordered Darvocet N-100 (650 mg APAP and 100 mg propoxyphene). APAP intake was 4550 mg and 5200 mg on the first 2 days. Safety comment: Computer did not notice excessive APAP dose.
- But, no mention of propoxyphene (3A4 and 2D6 inhibitor) PK and PD interaction with oxycodone (3A4 and 2D6 substrate) that computer did not note.

Drug Interactions in Croatia

- Patients taking 2 or more drugs during 2 days screened with computerized database (n=380)
- 46% of prescriptions involved at least one drug-drug interaction
- 6.2 drugs/pt and 2.8 DDIs/pt
- 33% Rated Severe; 56% Rated Moderate
- 45% Pharmacodynamic mechanism

Drug Interactions in Croatia

Drug 1	Drug 2	% of INXs	Severity
Furosemide	ACEI	6.3	Moderate
Furosemide	Corticosteroids	5.4	Moderate
Theophylline	Diuretic	4.2	Minor
Digoxin	Diuretic	4.2	Moderate
ACEI	KCL	4.0	Major
LMWH	Aspirin	3.3	Moderate
Corticosteroids	Fluconazole	2.9	Major
LMWH	NSAID	2.9	Moderate
Theophylline	H2-RA	2.7	Minor

Clinical Decision Support: Properties of an Ideal DDI Alerting System

- Sensitive and specific
- Clearly identified criteria for severity rating
- Customizable
- Summary of clinical data
- Management options provided
- Ignores discontinued meds / non-interacting formulations

Causes of Alert Fatigue

- Refills
- Discontinued prescriptions
- Low specificity for clinical significance
- Based on non-clinical data
- Desire to have “complete” listing
- Legal concerns

What To Do About Too Many DDI Alerts

- Turn off selected categories or remove “really irritating” alerts
- Do in-house review of DI database to revise existing alerts
- Outsource review of DI database to revise existing alerts

Alert Major-Contraindicated Only: What You Will NOT See

- Amiodarone – Amitriptyline, Desipramine, Haloperidol
- Haloperidol – Quinidine
- Conivaptan – Ergots, Simvastatin, Lovastatin
- Ramelteon – Fluvoxamine (190x inc AUC)
- Sirolimus – Itra-, Ketoconazole, Clarithromycin, Ritonavir
- Ketoconazole – Simvastatin, Lovastatin
- Dalfo-/Quinupristin – Bepridil, Cisapride, Quinidine

Alert Level 1 Only: What You Will NOT See

- Saverno evaluated 64 DDI screening programs using 13 positive and 6 negative DDI pairs in patient profile of 18 drugs. (> 30 pDDIs)
- Median of correct responses = 89% (47 – 100%)
- Informatics listservers tested list. Missed these:
 - » CBZ – Clarithromycin
 - » Digoxin – Amiodarone, clarithromycin, itraconazole
 - » Warfarin – Amiodarone, gemfibrozil, naproxen

What To Do About Too Many DDI Alerts

- Do in-house review of DI database
 - » Advantage: Resources already there; can do by committee
 - » Disadvantage: Resources; done by committee; available expertise?
- Outsource review of DI database
 - » Advantage: Expertise, Resources
 - » Disadvantage: Resources; Updating

In House Customized Computerized DDI Screening: Critical Interactions

- Theophylline – Allopurinol, Febuxostat
- Gemfibrozil – Simva, Lova, Atorvastatin
- Selegiline – TCAs
- Atorvastatin, Lovastatin – Telithromycin
- Irinotecan – Ketoconazole (Fluconazole ok)

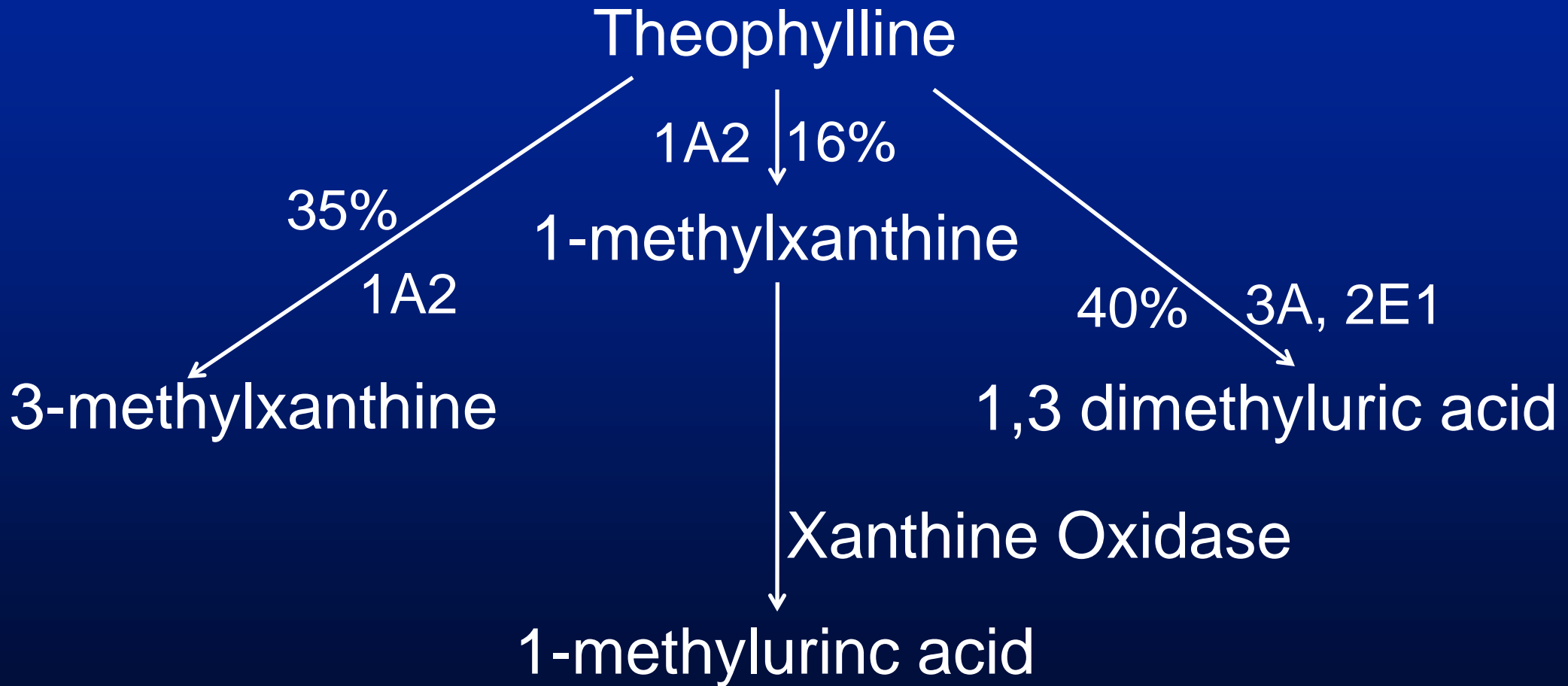
In House Customized Computerized DDI Screening: Critical Interactions

- CCBs (all) – BBs (all) [due to AV block]
- Digoxin - Amiodarone, Macrolides (all), Quinidine, Verapamil, Tetracycline (But not azoles)
- Quinidine – Amiodarone, Verapamil
- Warfarin – Macrolides (all)
- Theophylline – Allopurinol

Theophylline – Allopurinol: A Major Drug Interaction

- Listed as major in several CDS databases, including institutionally customized
- Two studies found no change in theo PK with allopurinol 300 mg daily x 7 days.
- One study found approx 25% incr in AUC and half-life after 2 weeks of allopurinol 300 mg BID compared to the first dose of theophylline.

Theophylline – Allopurinol: A Major Drug Interaction?



What To Do About Too Many DDI Alerts

- Do in-house review of DI database
 - » Advantage: Resources already there; can do by committee
 - » Disadvantage: Resources; done by committee; available expertise?
- Outsource review of DI database
 - » Advantage: Expertise, Resources
 - » Disadvantage: Resources; Updating

Simplified CDS DDI Categories: Action Based on Risk

- Intervention Required
 - » This drug combination is contraindicated.
- Review Required
 - » A serious adverse outcome may occur.
Interventions are necessary to reduce patient risk.
- Potential Interaction Identified
 - » This interaction has been documented; however, the risk is modest or unclear.

Customized DI Screening

- In preparation for CPOE, customize DI database
- Start with DIs labeled as MAJOR
- About 8000 unique pairs in UWMC's database (2007)
- Each pair evaluated for appropriate classification in database (Major – Moderate – Minor)

Customized DDI Screening

- Evaluation criteria was probability of patient harm
- MAJOR should only include DDIs where risk likely to exceed benefit in most patients
- MAJOR DDIs should require thought and action

Customized DDI Screening

Hospital	Total MAJORs in Database	DIs Reduced in Severity (%)
UWMC	7970	57
Hospital 2	8404	59
Hospital 3	11727	65
Hospital 4	12268	77
Hospital 5	15271	67

Customized CDS – DDI Alerts

- Reviewed all DDI alerts over 24 hours (9/15/09) at HMC / UWMC
- 410 / 395 beds – 400 / 336 occupied
- 25,697 / 29,671 alerts = 64 / 88 pt/day
- 505 / 617 were Major under our customized classification system

Computerized DDI Screening: Future Directions

- Improve the computer drug interaction screening systems – knowledge base systems
- Consistent classification system for drug interactions – probably will never happen
- Obtain additional epidemiological data
- User selectable choice in severity ratings

Drug Interaction to Avoid

“Never, under any circumstances, take a sleeping pill and a laxative on the same night.”



BRIGHAM AND WOMEN'S HOSPITAL



Member of **PARTNERS**[™] HealthCare



BRIGHAM AND
WOMEN'S HOSPITAL



Alert Fatigue with Drug-Drug Interaction Software: The Way Forward

Andrew C. Seger, PharmD

Senior Research Pharmacist

Division of General Internal Medicine and Primary Care

Clinical and Quality Analysis, Information Systems

Partners HealthCare System

June 22, 2011

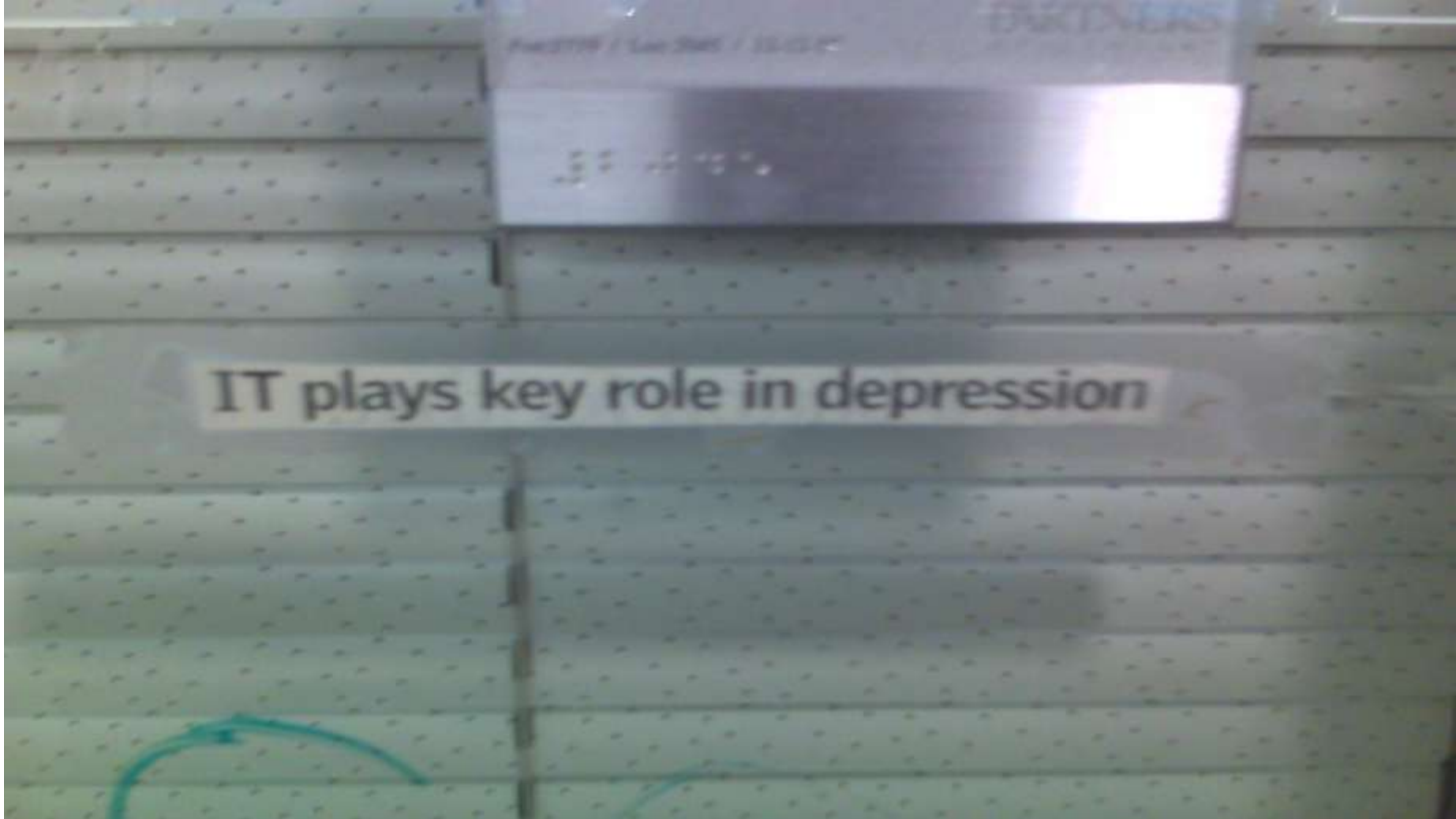
Goals

- Develop understanding of how DDI alerting fails patients
- Think about how DDI alerting can be improved

Objectives

- Describe how DDIs work from an informatics perspective
- Understand potential DDI improvement strategies

What role does IT play?



IT plays key role in depression

“ To make no mistakes in not in
the power of man; but to learn
from their error and mistakes the
wise and the good learn wisdom
for the future.”

Plutarch (AD 46-120 AD)

Every day I write the book

- Clinical Providers
- Pharmacists
- Nurses
- Physicians
- Respiratory Therapists



www.123rf.com

IV Bag Label 1: Yellow label with illegible text.

IV Bag Label 2: White label with 'A' logo and illegible text.

IV Bag Label 3: Yellow label with illegible text.

IV Bag Label 4: Clear label with illegible text.

IV Bag Label 5: Yellow label with illegible text.

IV Bag Label 6: Yellow label with illegible text.

IV Bag Label 7: Clear label with illegible text.

IV Bag Label 8: Yellow label with illegible text.

FFP
Inmed
500ml
300ml
NS

Fencal
Inmed
200ml
100ml
NS

FENT
Inmed
100ml
100ml
LACROSOLO

From Singapore



Drug-Drug Interactions

- Clinical Decision Support (CDS)
- Why, they stink!
- Epidemiology
- Informatics

DDI: Informatics

- How they work
- CPOE perspective
- Similar in pharmacy systems, but different nomenclature
- ? EMAR

DDI: Informatics

- 1 very large table (all meds)
- Behind it are other tables
- IF active drug a AND order for drug b, THEN show this alert

DDI: Informatics

- How many?
- Around 1.25 million pairs
- How to reduce?
- Expert committee
- Re-invents the DDI wheel

DDI: Informatics

- Other reduction strategies
- Tiering?
- Once again, committee
- Once again, re-invents DDI wheel

DDI: Informatics

- Other reduction strategies
- Patient's clinical state?
- How does this work?
- Aspirin-Warfarin example

DDI: Informatics

- Problems?
- Re-working all 1.25 million DDIs
- Shoveling out the stables
- Insert IS joke here
- More patient specific

DDI: Epidemiology

- Does not exist
- Currently all reports are anecdotal
- No rates
- There never will be!

DDI: Epidemiology

- Why Not?
- This is REALLY important for us to improve DDI functionality
- Ethics

DDI: Epidemiology

- No current surveillance
- Why not?
- MONEY, MONEY, MONEY
- Not just the mother's milk of politics

DDI: Epidemiology

- Back to square 1
- Improvement of current alerting
- Is it possible?
- Example

DDI: Example

- Moxifloxacin
- Calcium Carbonate
- Magnesium Oxide
- Same Time (DDI)
- 2 hours later (Ø DDI)

DDI: Future Thoughts

- How to improve?
- Where should they alert?
- CPOE?
- Pharmacy OE?
- EMAR?

“ The true goal of patient safety efforts is to reduce the harm we do to our patients while providing them with the care they need” “recognizing the nature and sources of harm is critical to this endeavor”

Kilbridge PM, Classen DC Quality and Safety in Healthcare Vol 15 (3) June 2006