

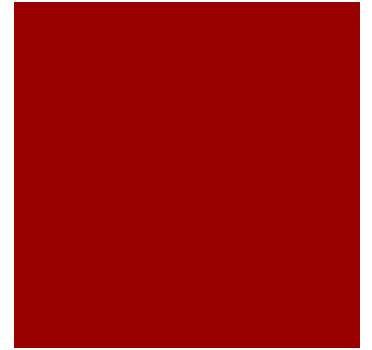
Ability of Clinical Decision Support Systems to Alert Pharmacists of Clinically Important Drug-Drug Interactions

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Collaborators: Dan Malone, PhD, RPh, Lisa Hines, PharmD, and Amy Grizzle, PharmD

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Outline

- Background
- Purpose
- Methods
- Results
- Discussion/Limitations
- Future Research
- Conclusions



Drug Interactions

- Unwanted and unintended consequence of combining two or more therapeutic agents
- Preventable medical errors
- Can cause patient harm, including hospitalizations and death
- Pharmacist reliance on computer software for DDI screening is commonplace and warranted



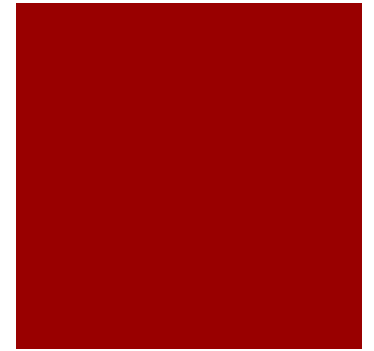
Possible drug interactions as a function of number of medications

Medications	Possible Interactions
2	1
4	6
8	28
16	120

Karas S. Ann Emerg Med 1981; 10: 627-630.

Purpose of Study

- Assess the performance of drug-drug interaction (DDI) software programs currently used in pharmacies throughout Arizona
- Recommend changes for improvement
- Re-evaluate the same programs after changes are implemented to maximize the efficiency of software support in pharmaceutical care.



Methods

- Sample
 - Conducted between December 2008 and November 2009
 - Pharmacies were eligible to participate in the study if they were either University of Arizona College of Pharmacy rotation sites or Area Health Education Centers (AHEC)
 - Approximately 100 pharmacies were invited to participate
 - To prevent over-sampling of retail chain pharmacies, we initially limited our study to two urban sites and one rural site within the same pharmacy chain



Methods

- For those pharmacies that agreed to participate:
 - Researcher made on-site visit to pharmacy
 - Direct analysis of the DDI software was conducted by analyzing DDI alerts arising from a standardized fictitious patient profile
 - Researcher conducted brief interview with pharmacy staff member regarding functionalities of software system



Fictitious Patient Profile



- Consisted of 18 different medications
- Nineteen drug pairs were assessed
 - Thirteen drug pairs were clinically significant DDIs
 - Six were non-interacting drug combinations
- One clinically significant allergy-interaction was assessed

Patient: John Doe

Gender: Male

Date of Birth: 3/28/1950

Allergies: Penicillin

Definitions

- Sensitivity is the probability of a DDI alert given that a clinically significant DDI is present. Sensitivity is calculated as follows: (number of true positive DDI alerts)/(number of clinically significant DDI pairs).
- Specificity is the probability of the absence of an alert given that a DDI is not present. Specificity is calculated as follows: (number of true negative non-alerts)/(number of non-DDI pairs).
- Positive predictive value (PPV) is a measure of the usefulness of the alert in that it is the probability that a DDI alert represents a true DDI: $PPV = (\text{number of true positives}) / (\text{number of true positives} + \text{number of false positives})$.
- Negative predictive value (NPV) is the probability that the absence of a DDI alert represents a true absence of a DDI: $NPV = (\text{number of true negatives}) / (\text{number of true negatives} + \text{number of false negatives})$.

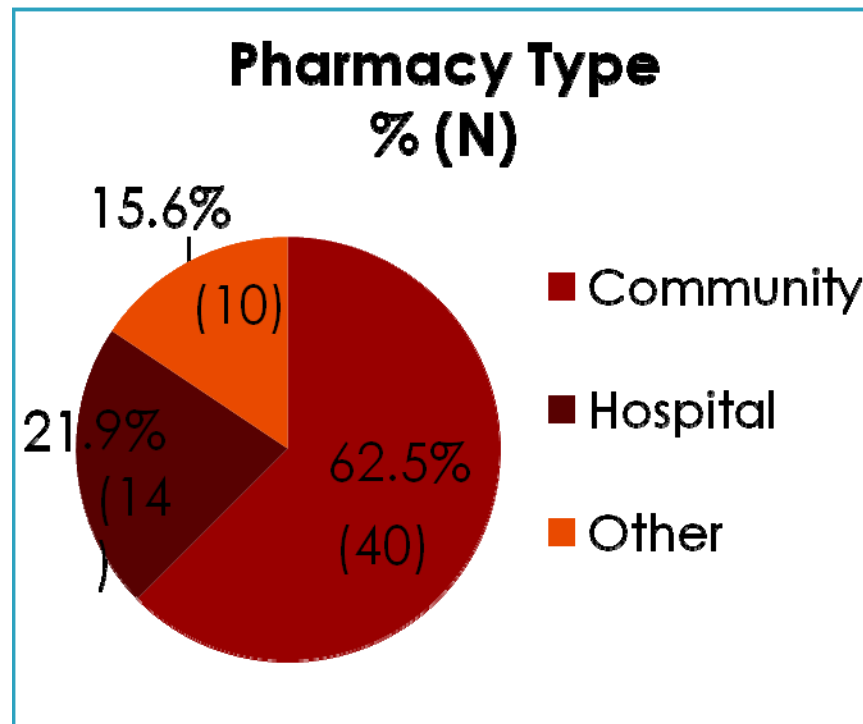
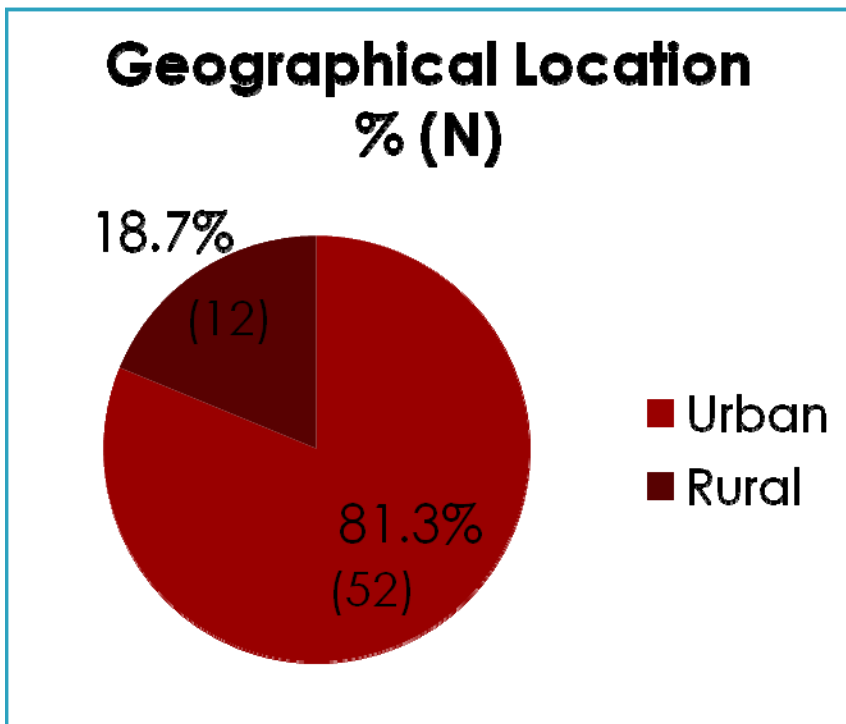
Methods

- All data analyzed using Microsoft Excel® 2007.
- The number of correct responses, sensitivity, specificity, PPV and NPV were calculated for each pharmacy.
- The median number of correct responses, median sensitivity, median specificity, median PPV and median NPV were calculated for all study participants combined.
- Interview responses pertaining to participating pharmacies' DDI software capabilities were also summarized.
- This study was deemed exempt by the IRB process.



Results

- ▶ Sixty-four pharmacies throughout Arizona participated in our survey.

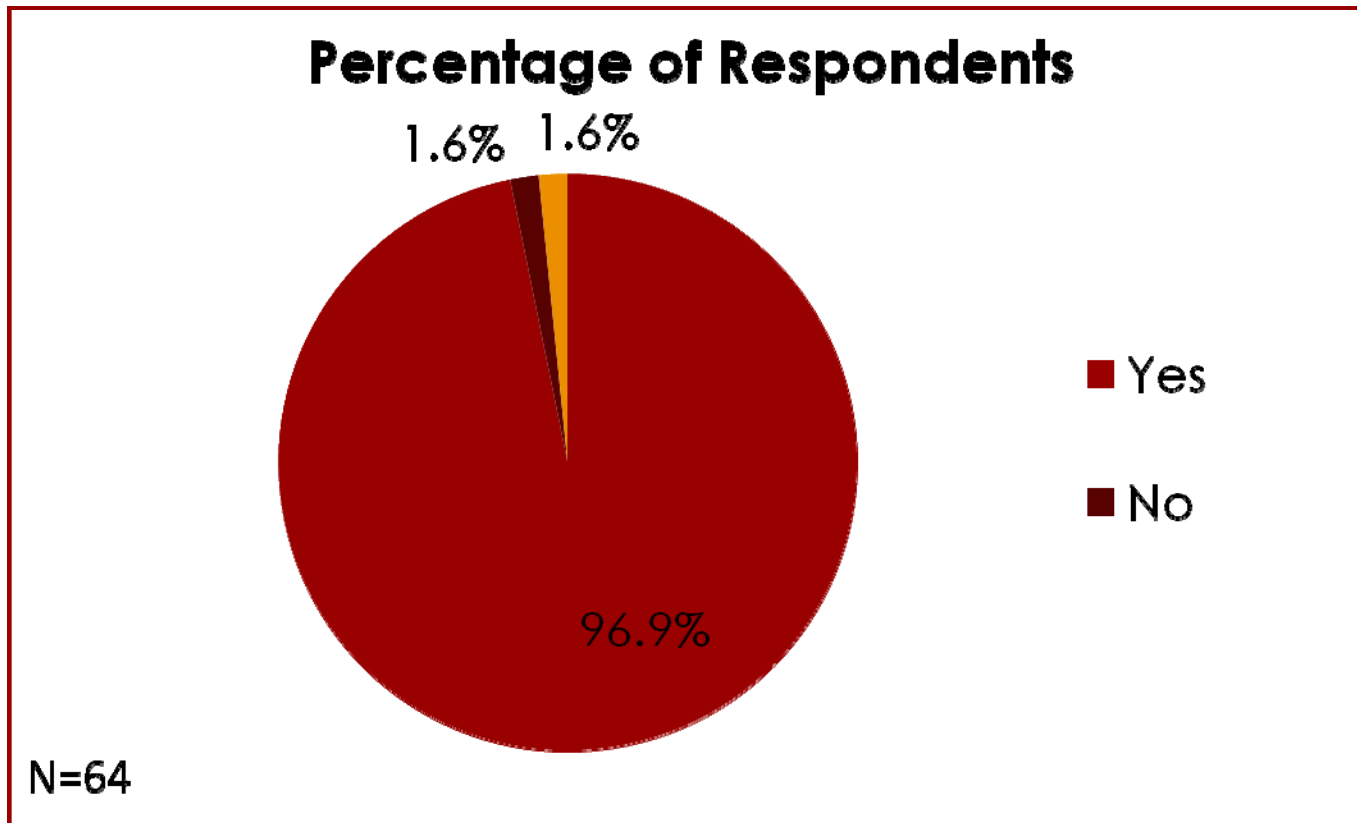


DDI Results

	<u>Sensitivity</u>	<u>Specificity</u>	<u>PPV</u>	<u>NPV</u>
Median	0.85	1.00	1.00	0.75
Best	1.00	1.00	1.00	1.00
Worst	0.23	0.83	0.75	0.33

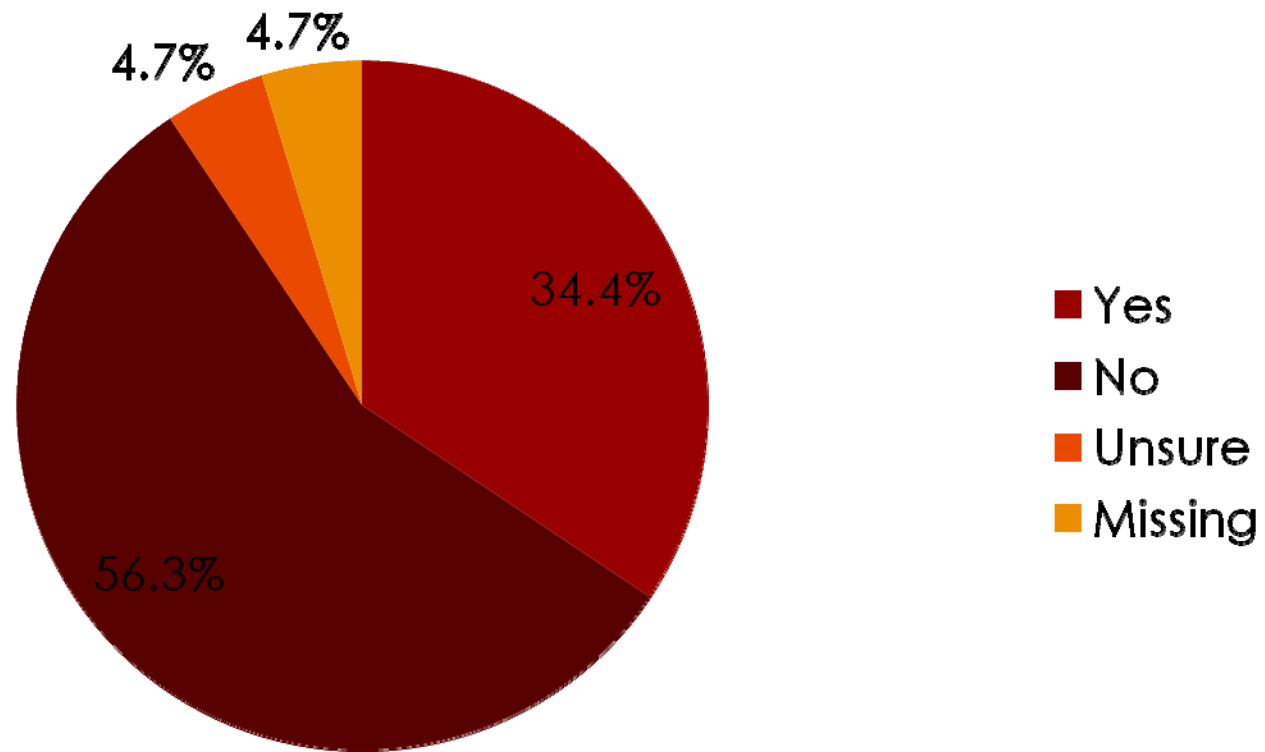
- Mean (SD) percentage of correct DDI responses: 85% (16%)
- Sixty (93.7%) of pharmacy software systems correctly detected the drug-allergy interaction

Are alerts categorized?



Does the software provide documentation of what the DDI categories mean?

Percentage of Respondents

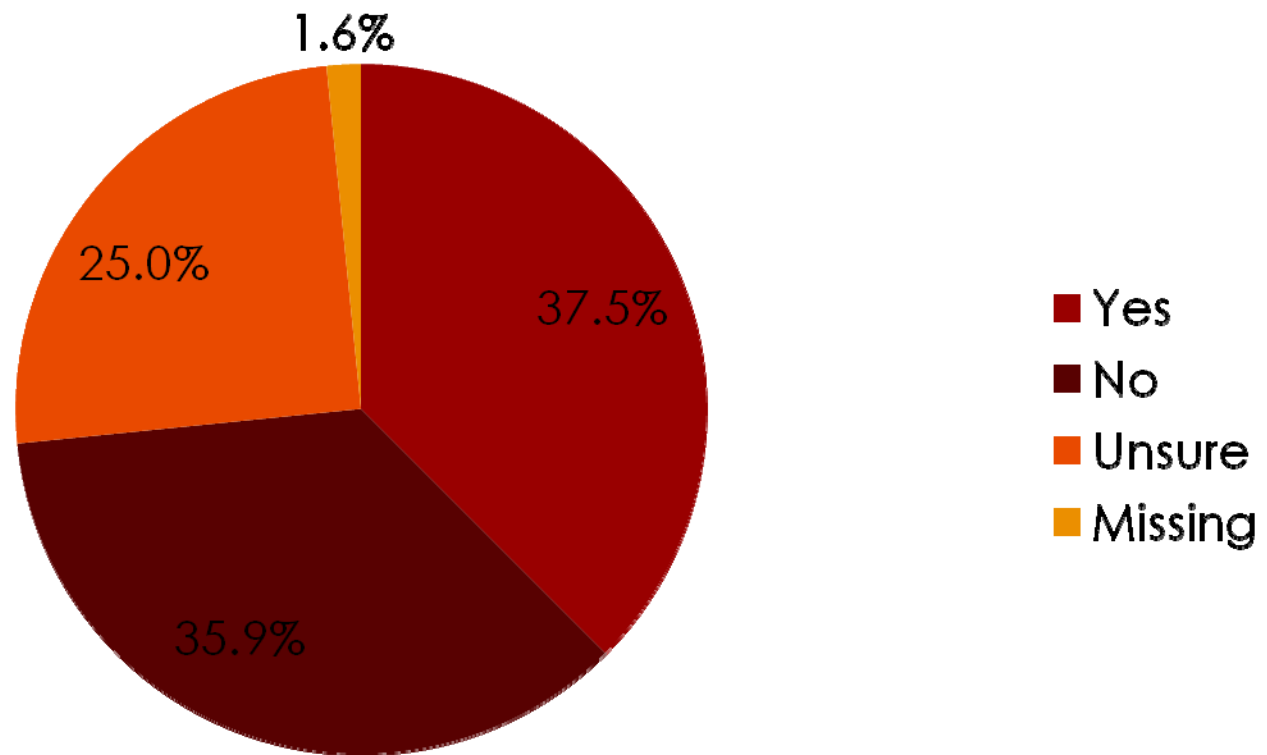


N=64

Are certain categories or levels of interactions suppressed?



Percentage of Respondents

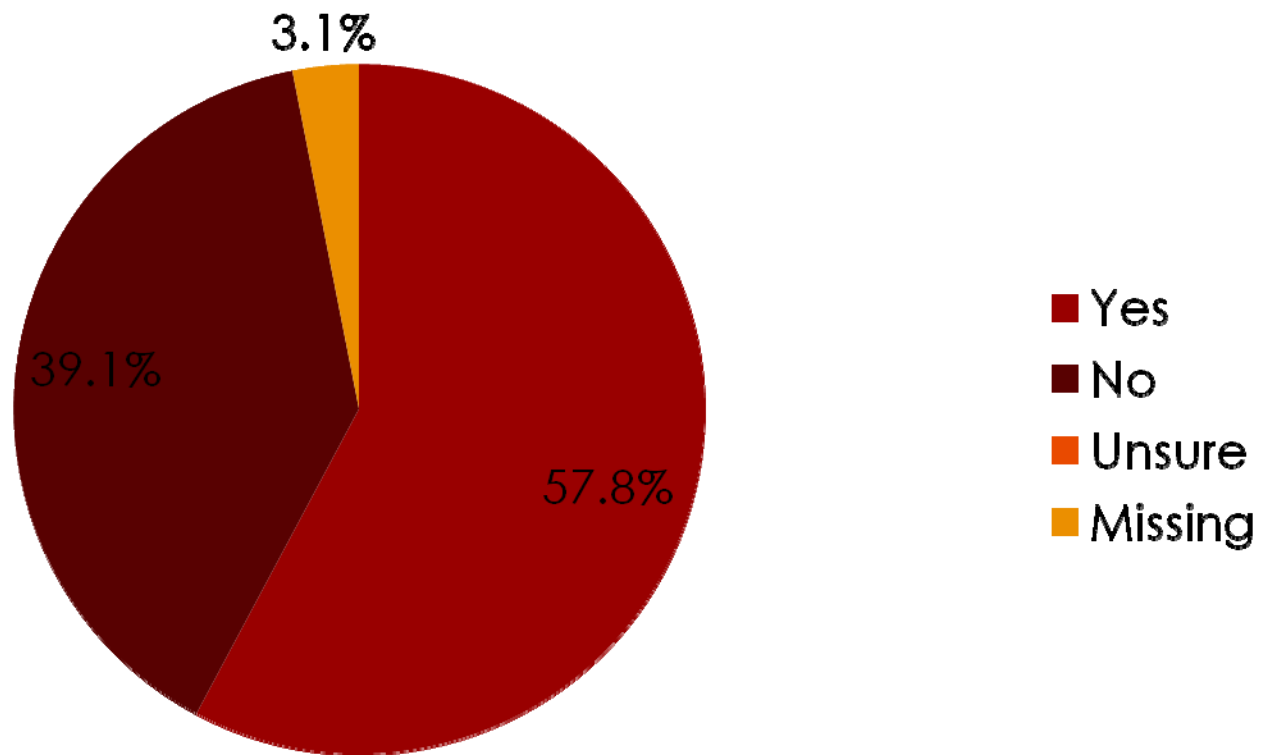


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Are interaction management strategies provided with DDI alerts?



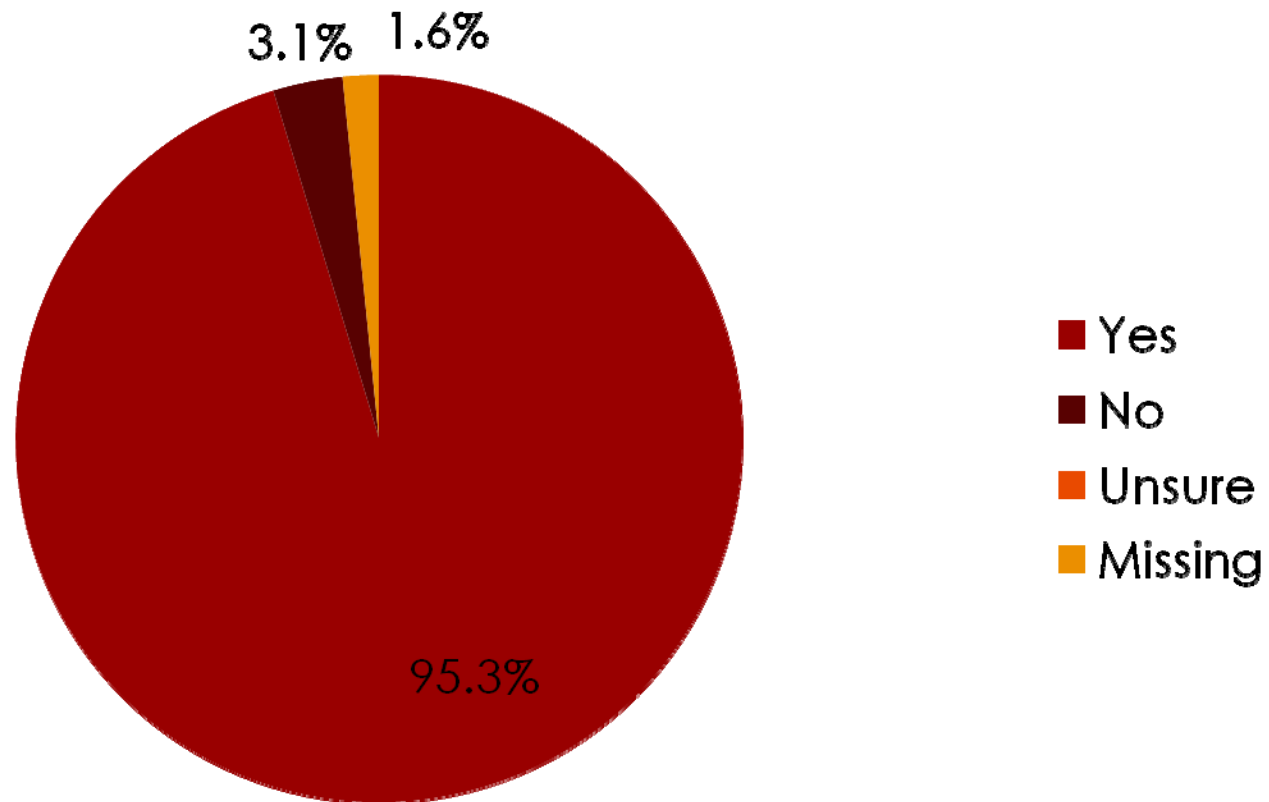
Percentage of Respondents



N=64

Is a pharmacist required to review DDI alerts?

Percentage of Respondents

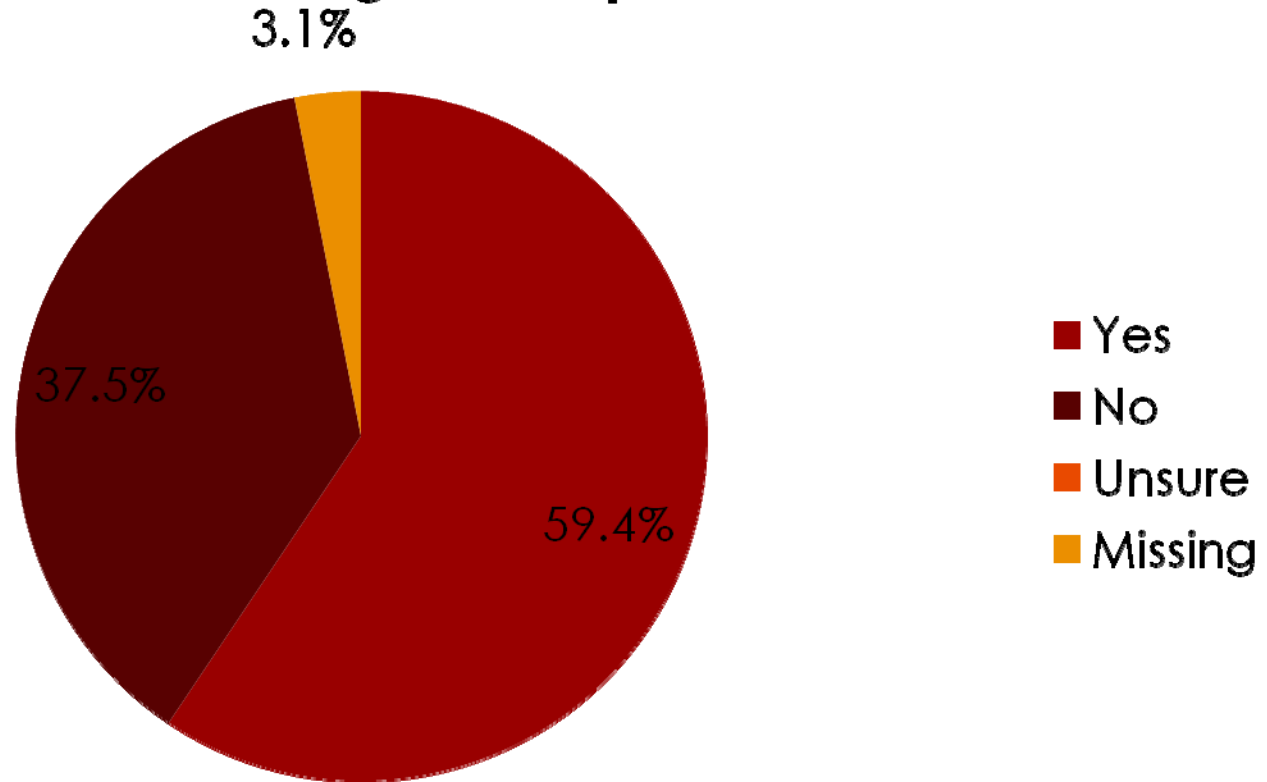


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Are references or supporting documents provided?



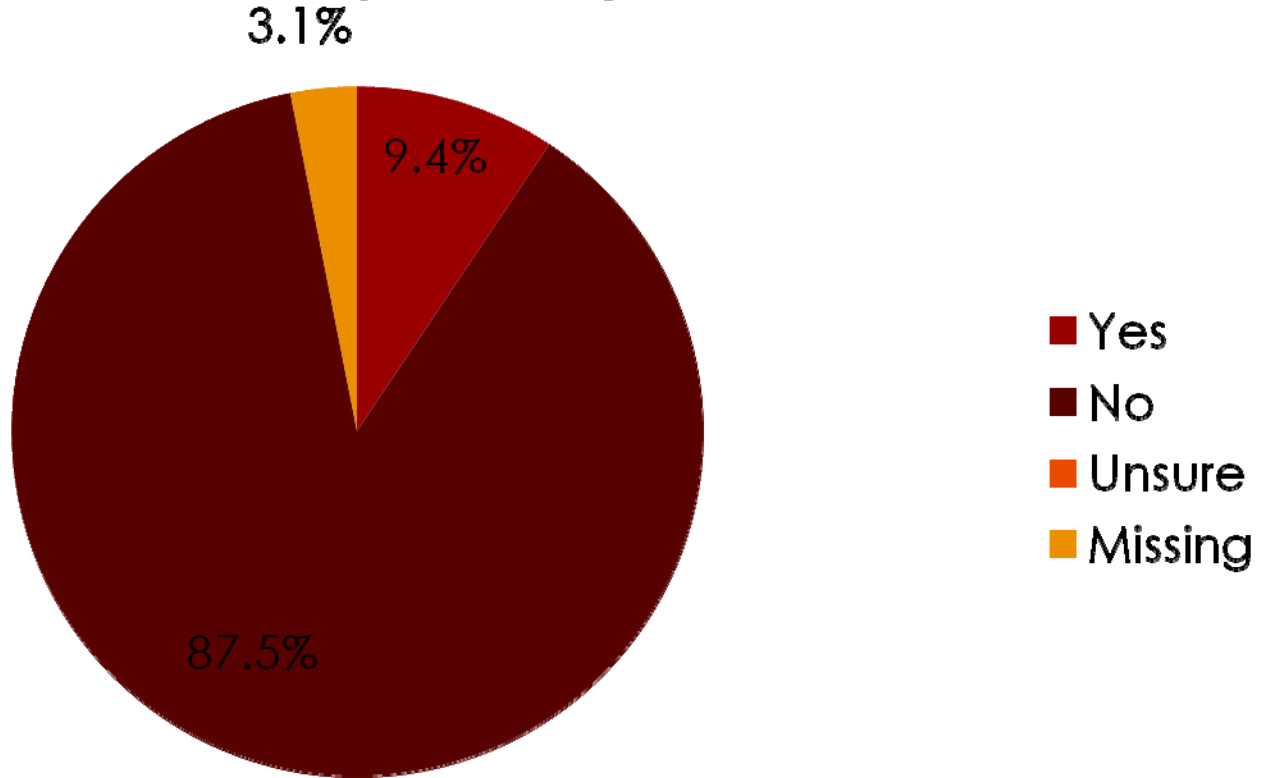
Percentage of Respondents



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Is a link provided for additional information?

Percentage of Respondents

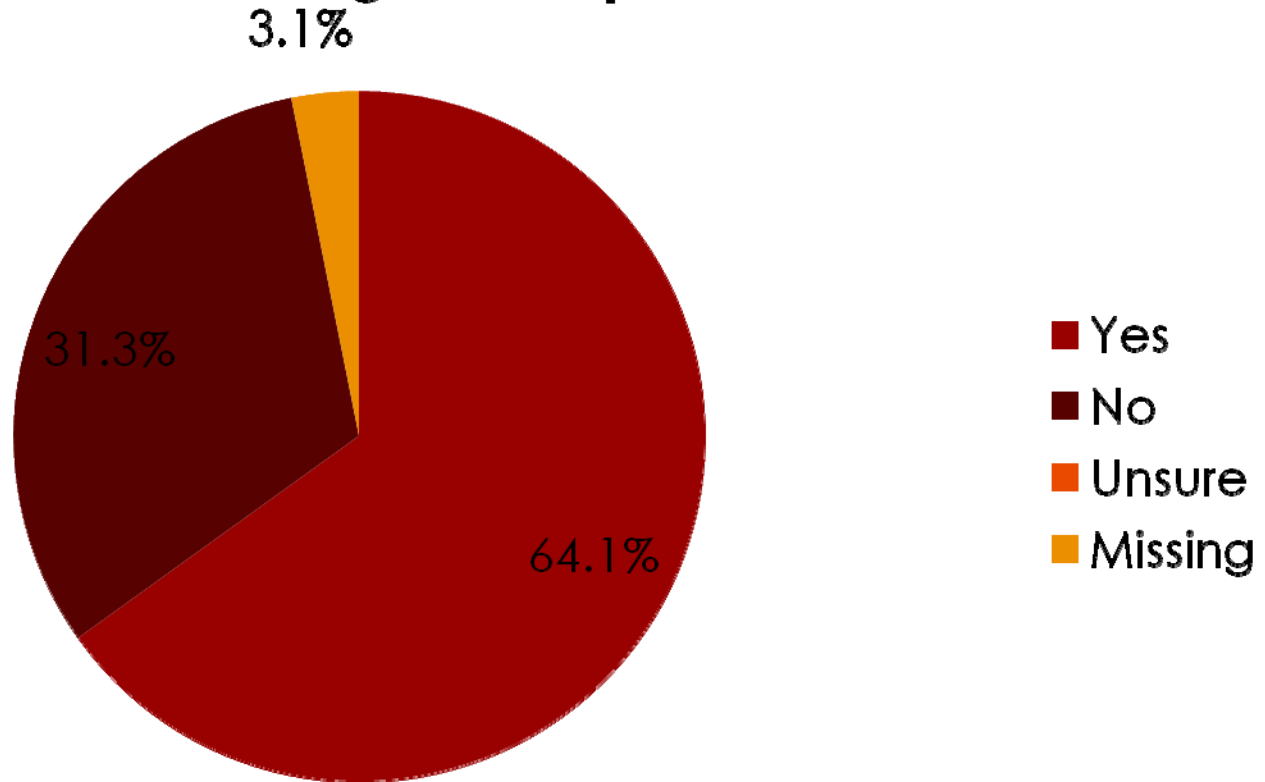


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Is it possible to add current medications from other pharmacies and/or OTCs?



Percentage of Respondents

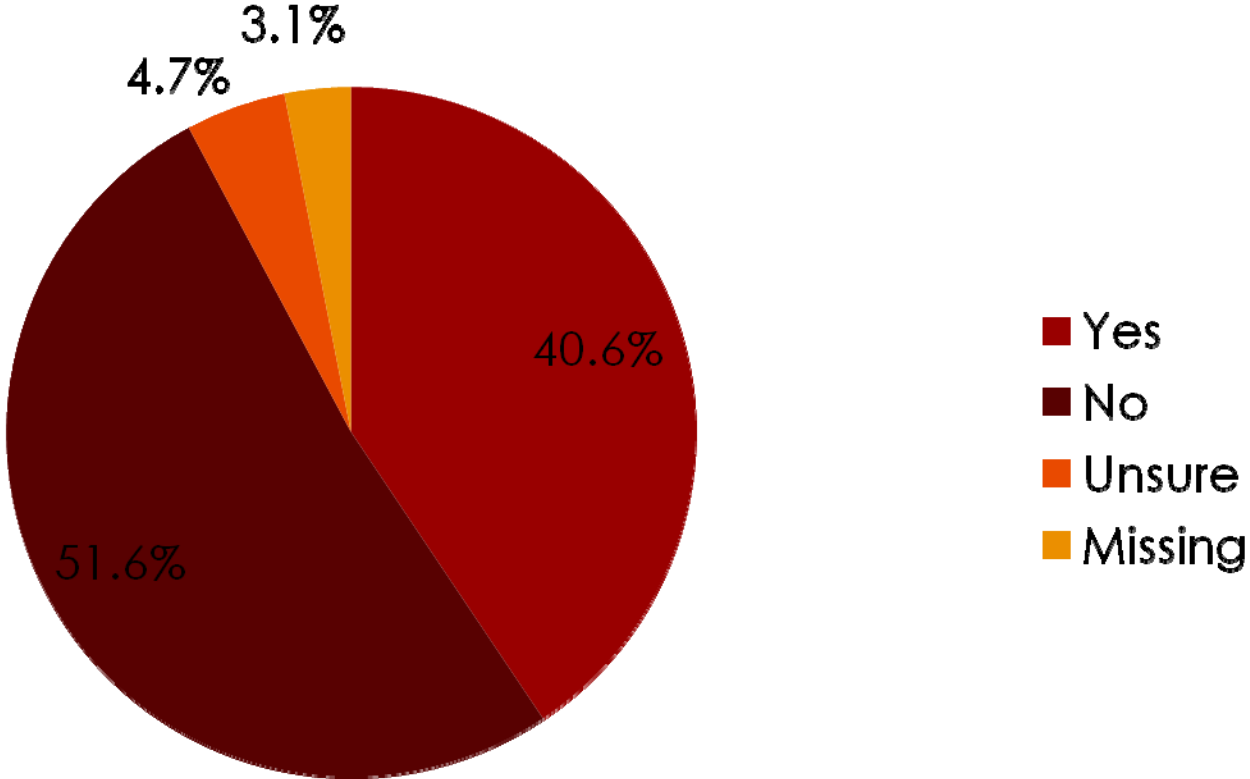


N=63

Are drugs entered into the computer system that are not linked to the DDI software?



Percentage of Respondents

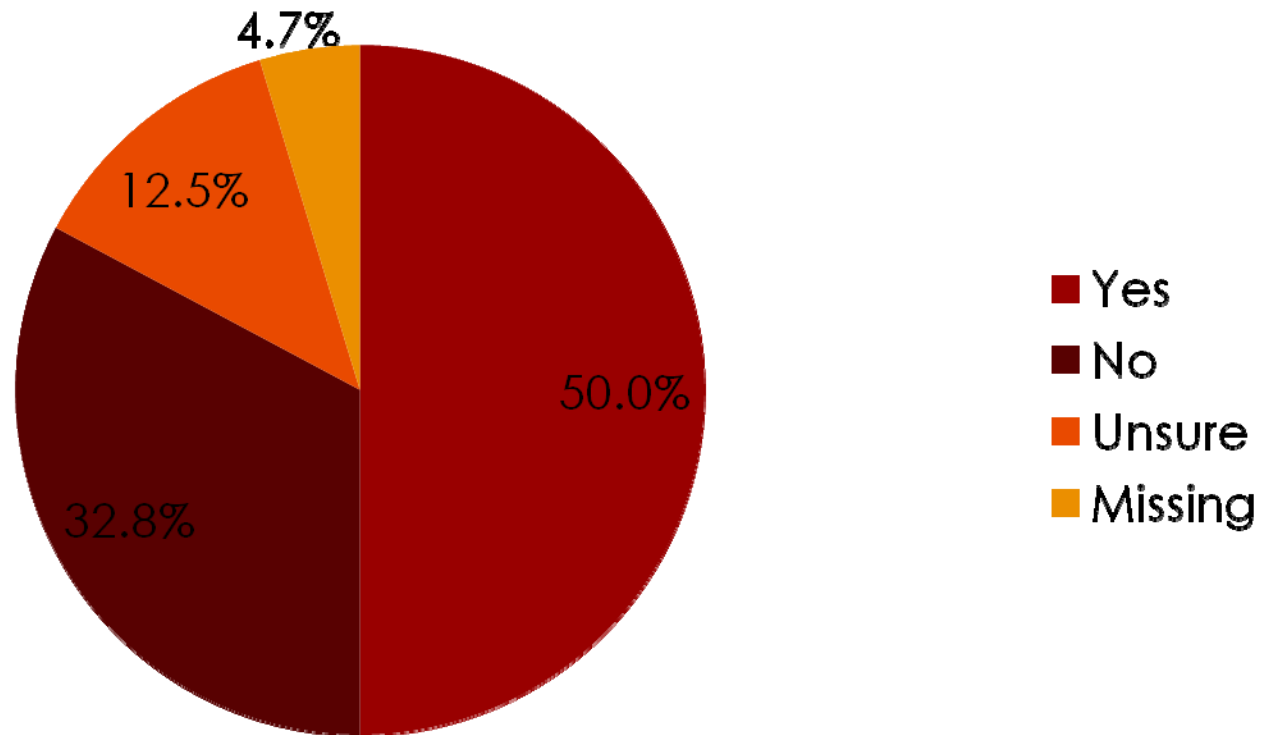


N=64

Is duration of therapy factored into DDI alerts?



Percentage of Respondents



N=64

Results: Pharmacy Computer Software Programs



- The pharmacies surveyed utilized a total of 24 different software vendors, representing both commercial and proprietary sources
- Frequency of software updates:
 - X% Quarterly
 - X% Monthly
 - X% Unknown

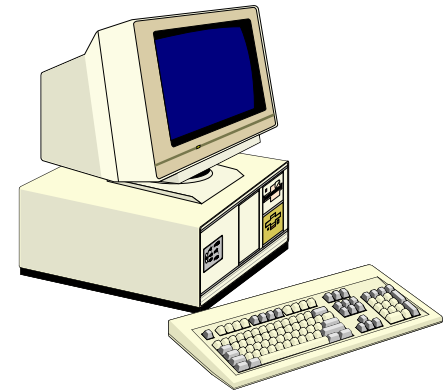
Discussion

- Prior research investigating the accuracy and reliability of pharmacy software programs has revealed inconsistencies in pharmacy software's ability to warn pharmacists of potentially clinically significant DDIs



In-store Pharmacy Software to Detect Drug-Drug Interactions

- 9 different drug-drug interaction software programs used by 516 community pharmacies in Washington State
- Patient specific profiles constructed for 16 “well-established” interactions



In-store Pharmacy Software to Detect Drug-Drug Interactions

	<u>Sensitivity</u>	<u>Specificity</u>	<u>PPV</u>	<u>NPV</u>
Mean	0.71	0.89	0.83	0.80
Best	0.88	1.00	1.00	0.90
Median	0.69	0.90	0.83	0.79
Worst	0.44	0.71	0.67	0.69

In-store Community Pharmacy Software to Detect Drug-Drug Interactions – An Update

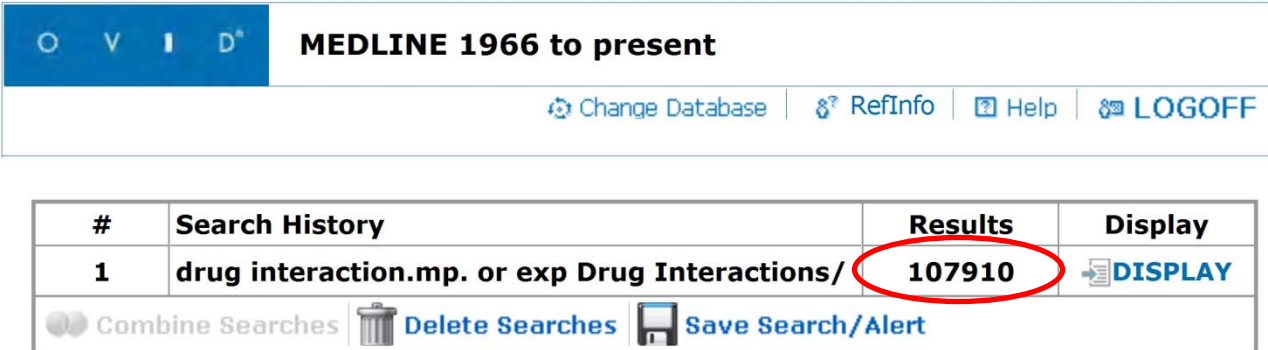
	<u>Sensitivity</u>	<u>Specificity</u>	<u>PPV</u>	<u>NPV</u>
Median	0.88	0.91	0.88	0.91
Best	0.94	1.00	1.00	0.95
Worst	0.81	0.67	0.68	0.86

Hospital Pharmacy Software to Detect Drug-Drug Interactions – “Warning”

	<u>Sensitivity</u>	<u>Specificity</u>	<u>PPV</u>	<u>NPV</u>
Median	0.38	0.95	0.83	0.67
Best	0.94	0.95	0.94	0.95
Worst	0.15	0.81	0.67	0.65

Some realities about DDIs

- Thousands of known drug-drug interactions



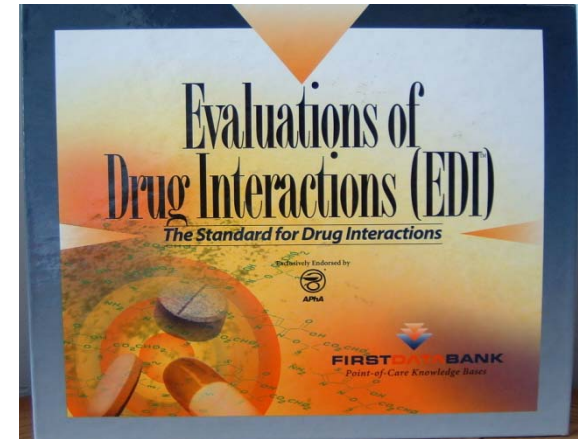
The screenshot shows a search interface for MEDLINE from 1966 to the present. The search history includes 'drug interaction.mp. or exp Drug Interactions/'. The results count is 107910, which is circled in red. Below the table are buttons for 'Combine Searches', 'Delete Searches', and 'Save Search/Alert'.

#	Search History	Results	Display
1	drug interaction.mp. or exp Drug Interactions/	107910	DISPLAY

Combine Searches Delete Searches Save Search/Alert

- Are they all relevant?

Tertiary References for DDIs



DRUG-REAX[®] System

from MICROMEDEX

Rating Systems for Drug-Drug Interactions



Reference	Levels
Evaluation of Drug Interactions	1: highly clinically significant; 2: moderate; 3: minimally; 4: not
Drug Interaction Facts	Severity: Major; moderate; minor Documentation: Established, probable, suspected, possible, unlikely
Drug Interactions: Analysis and Management	1: contraindicated; 2: usually avoid; 3: conditional; 4: minimal risk; 5: no interaction
DRUG-REAX®	Major; moderate; minor

Problems with Identifying Drug-Drug Interactions



“Major” Drug Interactions (at ***Medication Class Level***) by Compendium

Compendium	No.
MicroMedex <i>DRUG-REAX</i> ®	275
<i>Evaluation of Drug Interactions</i>	64
<i>Drug Interactions: Analysis and Management</i>	94
<i>Drug Interaction Facts</i>	141
Total	406*

* Sum of column exceeds total due to duplicate interactions.

Concordance of "Major" Drug Interaction Classifications by Compendia



Number of compendia listing interaction	Micro-Medex	Evaluation of Drug Interactions	Drug Interactions: Analysis and Management	Drug Interaction Facts	Total Cumulative Total
Four	9	9	9	9	9 (2.2%)
Three	3	3	3		
	7	7		7	
	20		20	20	
		5	5	5	35 (8.6%)

Why the “poor” performance of pharmacy systems to “catch” interactions



- Poor definitions of what “significant” means
 - The risk/benefit formula is determined in subjective manner
 - Few studies to support interactions
 - Those studies are evaluated by a few persons operating in different environments than the end users
- Ability to enter new drug products into the pharmacy system – not linked to the underlying databases
 - Most clinical support systems use NDC codes - opportunity for error or work a rounds.

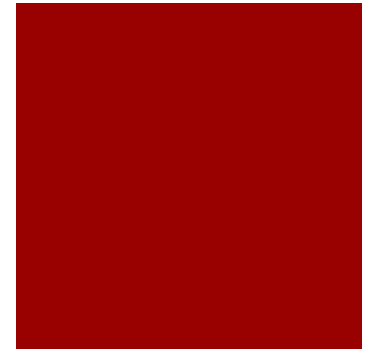
Characteristics for an “Ideal” Computer-System to Identify Drug-Drug Interactions



- Sensitive
- Specific
- Level of severity stated
- Detailed information about the interaction is readily available
- Documentation supporting the interaction is available, accurate, and regularly updated
- Provides management strategies for interaction
- Ignores refills for the same patient, interaction pair
- Time sensitive – ignores inactive or discontinued medications
- Permits users to “check” for an interaction

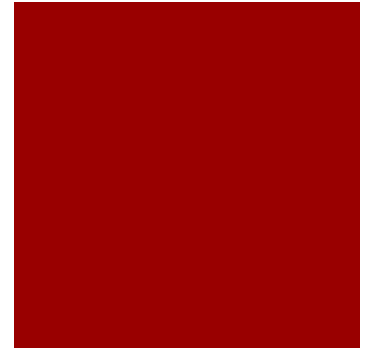
Limitations

- Patient profile reflected a limited set of available medications
- Alerts for non-targeted drug combinations were not documented or analyzed
- No effort was made to quantify the total number of alerts generated by pharmacy software systems



Limitations

- Not all of the pharmacies were able to enter all of the medications in the fictitious patient profile
- No attempt was made to correlate patient outcomes with the performance of the pharmacy's DDI software program
- Generalizability of these results may be somewhat limited



Future Research Considerations

- After providing recommendations for system improvements and feedback on the performance of DDI screening software, re-evaluate the same pharmacies to try to detect improvement



Conclusion

- The results of this survey indicate a need for comprehensive system improvements in the manner in which pharmacy software systems screen for and present DDIs to pharmacists, as well as the level of education pharmacists possess regarding the capabilities and limitations of their software systems.



Acknowledgements

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Questions?

