

Improving Drug-Drug Interaction Alert System

Ge Liu, Matthew Ploenzke, Michael Choi,
Ruizhi Liao, Tossaporn Saengja

Motivation

- BWH recently adopted a new Clinical Decision Support (CDS) Alert system
- These alerts trigger to assist practitioners in clinical decision making and fire with 3 levels of intensity

Motivation

- BWH recently adopted a new Clinical Decision Support (CDS) Alert system
- These alerts trigger to assist practitioners in clinical decision making and fire with 3 levels of intensity
- The practitioner may choose to accept or override any given alert, any may also choose to provide a textual reason for doing so

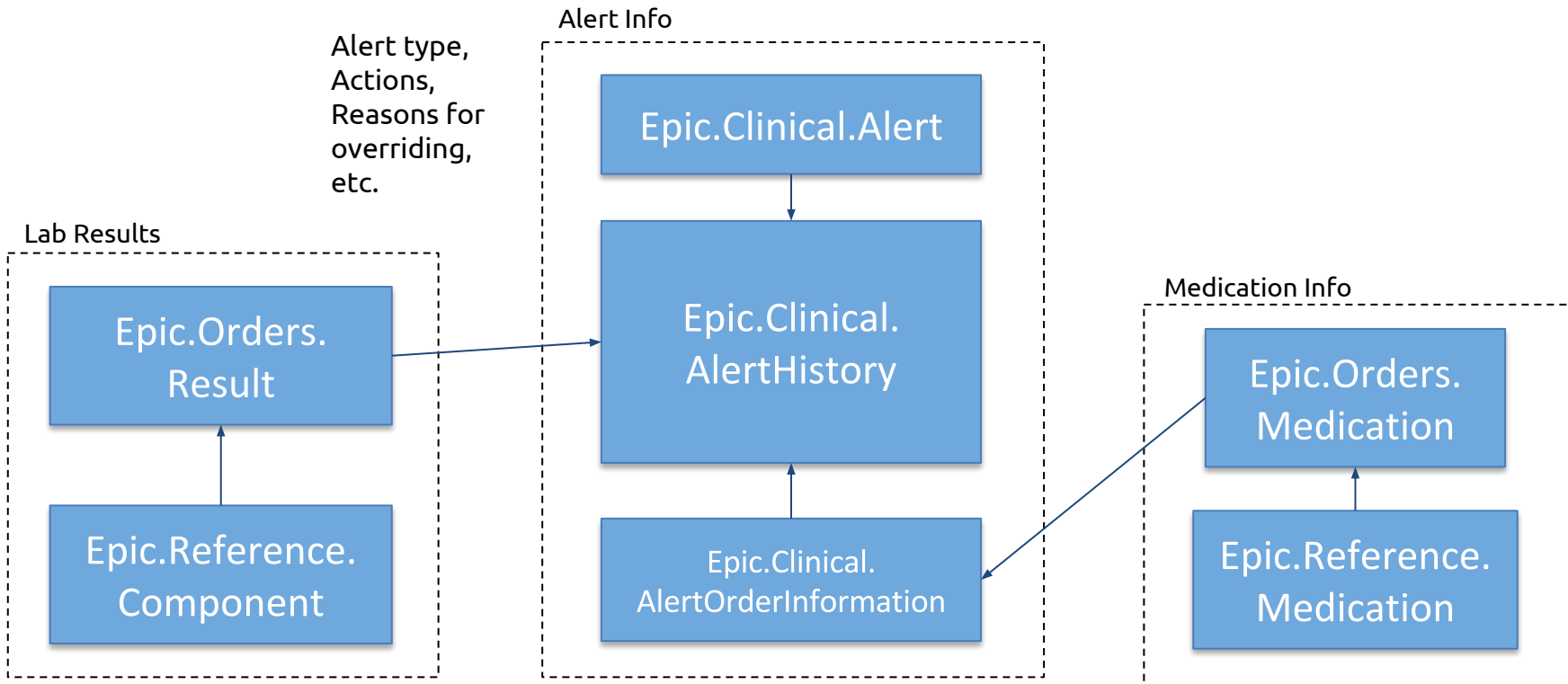
Motivation

- BWH recently adopted a new Clinical Decision Support (CDS) Alert system
- These alerts trigger to assist practitioners in clinical decision making and fire with 3 levels of intensity
- The practitioner may choose to accept or override any given alert, any may also choose to provide a textual reason for doing so
- We sought to leverage these data to investigate two questions:
 - Are we able to **predict alert dismissal**?
 - Do any underlying **causes for alert dismissal** exist?

Data

- Alert status(e.g. Actions, type of alerts, severity, etc)
- Alert information(descriptive features about the alert)
- Patient data (e.g. lab test, medication, vitals, department)
- User information (e.g. provider type, expertise)
- Notes (e.g. medical notes, comments about the reasons of dismissal)

Dataset Mapping Overview



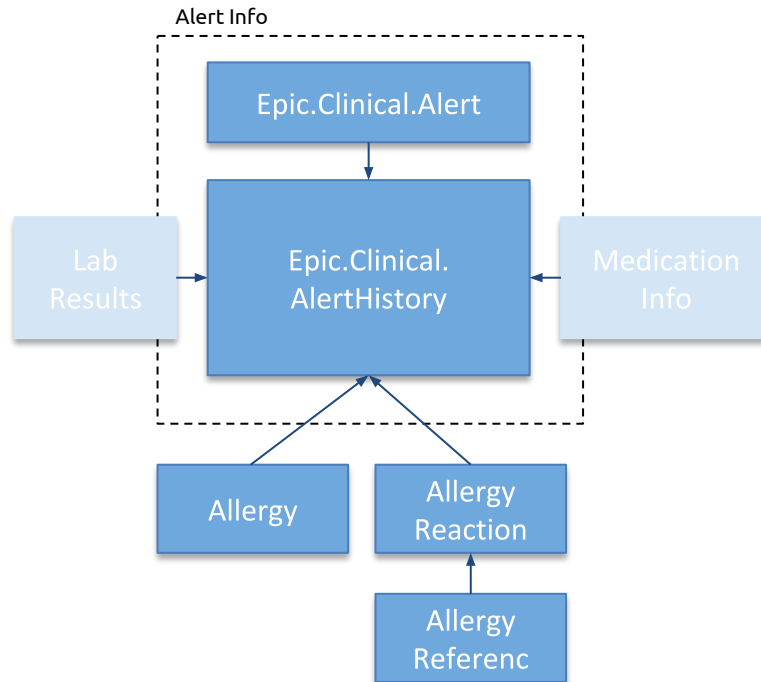
Tasks

- Predicting Alert Dismissal (supervised Learning)
 - Drug-Allergy Alerts
 - Drug-Drug Interaction Alerts
 - Drug-Dosage Alerts
- Analyzing causes for alert dismissal(unsupervised learning)
 - LDA
 - LLDA

Drug-Allergy Alerts

Alerts that are caused when a drug is prescribed that may induce allergic reactions in patients

- Used additional data relevant to patient allergy



Drug-Allergy Alerts

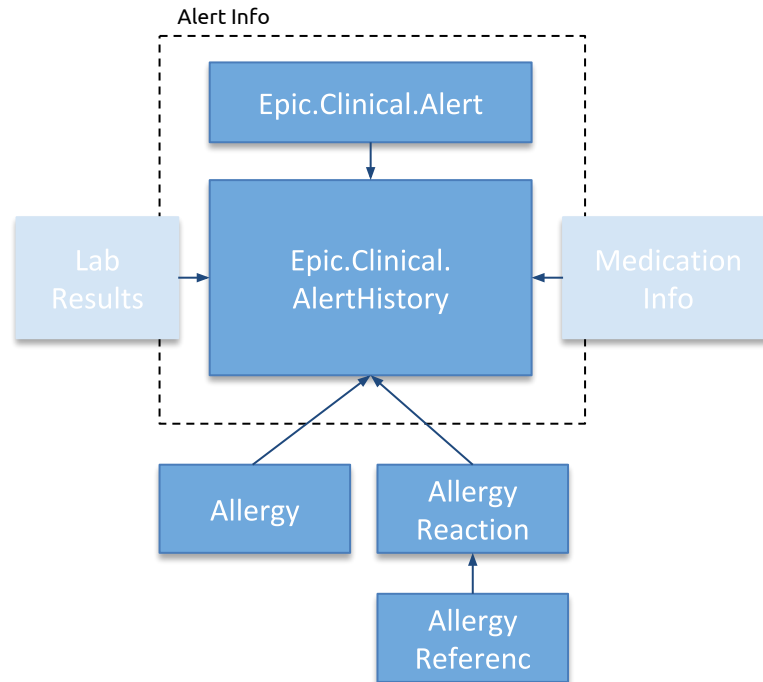
Alerts that are caused when a drug is prescribed that may induce allergic reactions in patients

- Used additional data relevant to patient allergy

Unbalanced Label distribution :

0- Accept: 15808

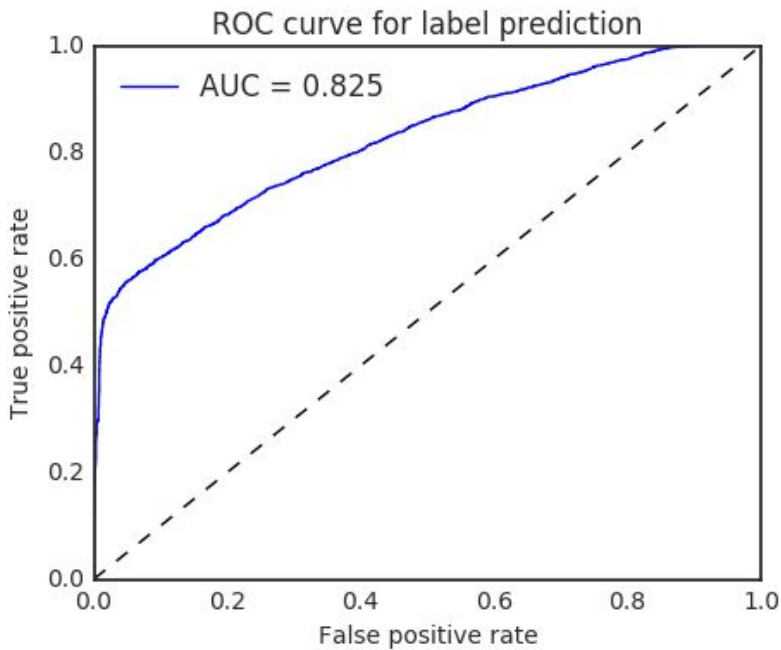
1- Overridden: 333780 -> 20000 (Down sampled)



Drug-Allergy Alerts

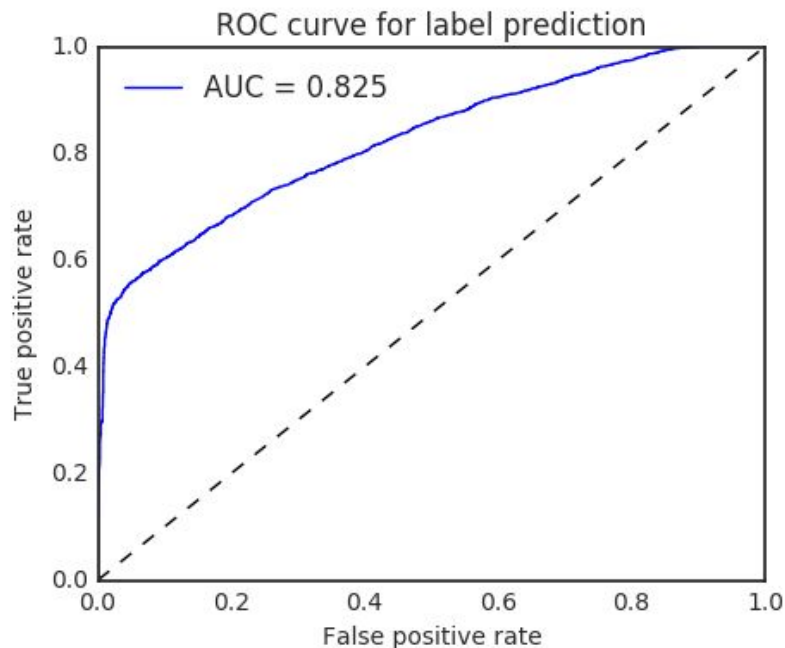
		Features			
Alerts that are caused when a drug is prescribed that may induce allergic reactions in patients		673	3	500	1212 + 989
<ul style="list-style-type: none">Used additional data relevant to patient allergy		One-hot categorical	Binary flags	Bag of words	Lab + Meds
Unbalanced Label distribution :		Alert description, Importance level, provider type, Patient department, ...	Inactive ingredient, Potential inactive ingredient, On allergen preference list	Allergy reaction Description (syndrome of allergy)	One-hot encoding on individual lab tests, binary value for medication classes
0- Accept:	15808				
1- Overridden:	333780 -> 20000 (Down sampled)				

Evaluation - L1 Regression



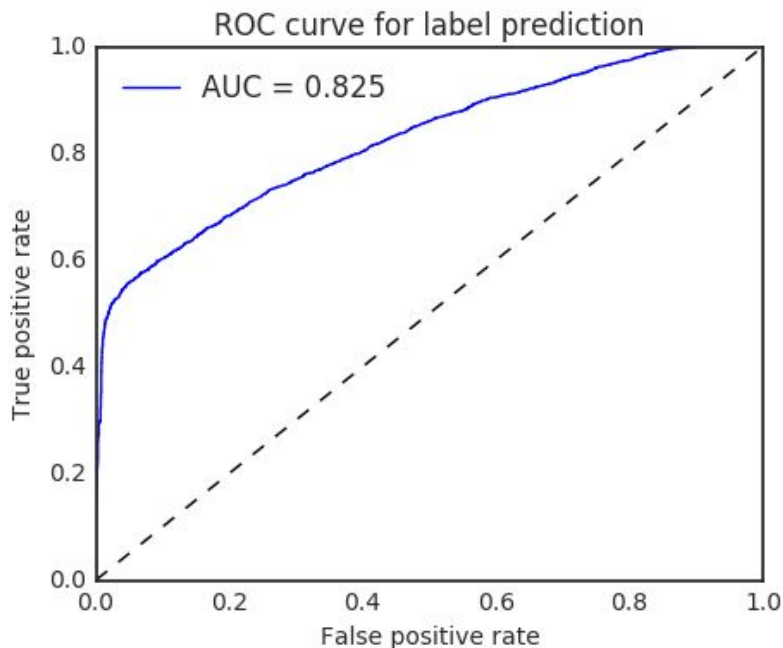
Resident	27.94717633	ProviderTypeDSC
Physician Assistant	19.33646957	ProviderTypeDSC
Physician	3.81350024	ProviderTypeDSC
Nurse Practitioner	3.288241654	ProviderTypeDSC
Anesthesiologist	3.088670328	ProviderTypeDSC
Fellow	2.673645648	ProviderTypeDSC
High	2.173958187	ImportanceLevelDSC
Very High	1.648955161	ImportanceLevelDSC
weakness	1.373103437	ReactionDSC
lipitor	1.360858185	ReactionDSC
BWH CARD CCU SH 9E	0.912523249	PatientDepartmentDSC
LACTOSE (INACTIVE INGREDIENT)	0.629088639	AlertDSC

Evaluation - L1 Regression



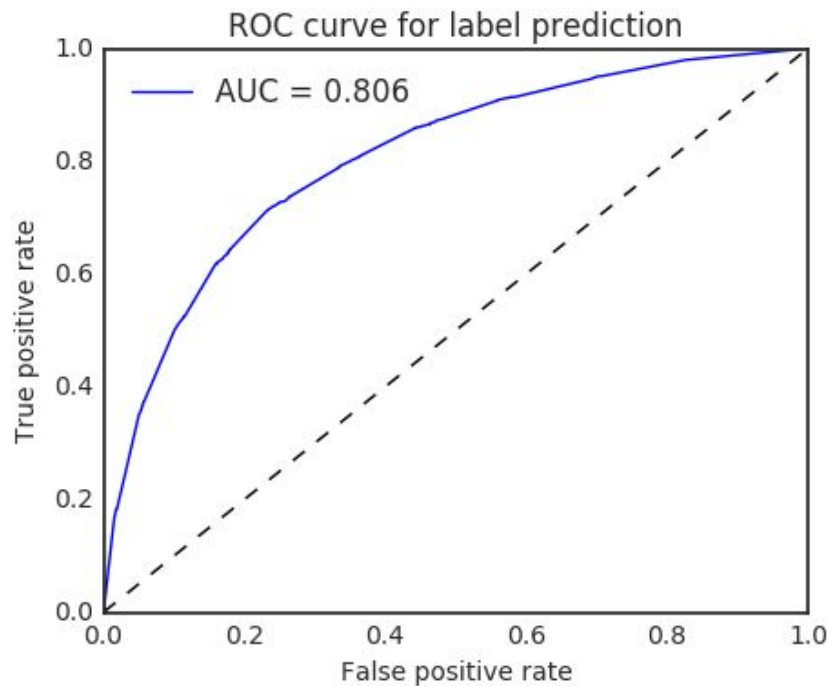
Technologist	0.586035133	ProviderTypeDSC
PharmaceuticalClassDSC_ANTIFLATULENTS	0.429036434	PharmaceuticalClassDSC
LATEX (INACTIVE INGREDIENT)	0.417904381	AlertDSC
EXACT INGREDIENT MATCH	0.314491457	AllergySeverityLevelDSC
PharmaceuticalClassDSC_URINARY PH MODIFIERS	0.21928017	PharmaceuticalClassDSC
LAB_INFD-GALACTOMANNAN AG (INDEX)_normal	0.198249733	LAB_
Pharmacist	0.162252671	ProviderTypeDSC
TherapeuticClassDSC_ANTICOAGULANTS	0.154907173	TherapeuticClassDSC
PharmaceuticalClassDSC_ANTICOAGULANTS,CO UMARIN TYPE	0.154907173	PharmaceuticalClassDSC
MGH EMERGENCY	0.143663898	PatientDepartmentDSC

Evaluation - L1 Regression



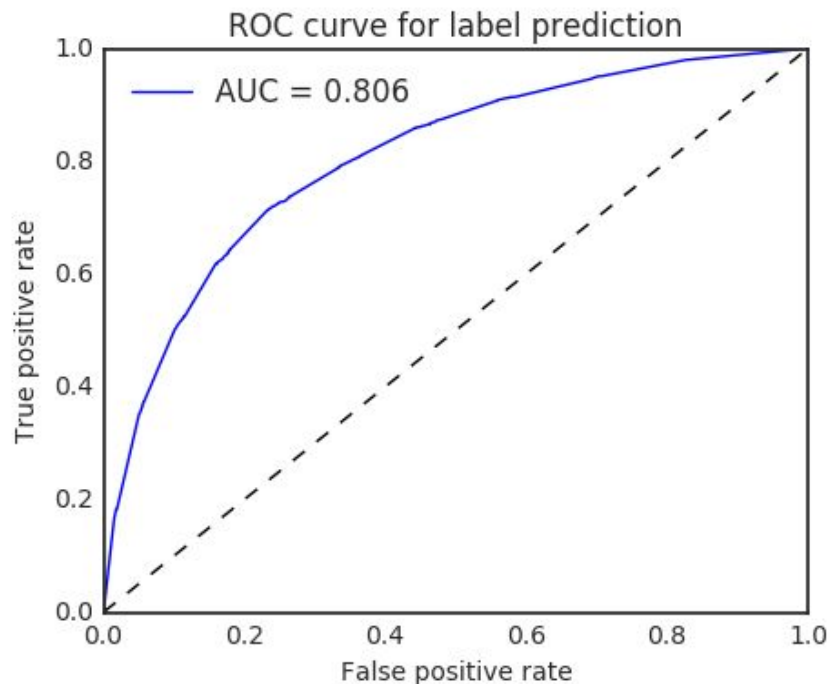
Medical Assistant	-6.137567597	ProviderTypeDSC
Outpatient	-1.234628685	OrderContextDSC
Minority	-0.660149853	PatientDepartmentDSC
Registered Nurse	-0.584951214	ProviderTypeDSC
TherapeuticClassDSC_CONTRACEPTIVES	-0.577527346	TherapeuticClassDSC
Allergies	-0.509071859	DrugAllergyContraindicationGroupDSC
PharmaceuticalClassDSC_CONDOMS	-0.372697427	PharmaceuticalClassDSC
MGH WHITE 7 GEN SURG	-0.299831847	PatientDepartmentDSC
Adverse Reactions/Drug Intolerances	-0.282035473	DrugAllergyContraindicationGroupDSC
LAB_GRANULOCYTES, IMMATURE (%)_normal	-0.280653413	LAB
NWH 6 EAST	-0.159344194	PatientDepartmentDSC

Evaluation - Random Forest



Resident	ProviderTypeDSC
Registered Nurse	ProviderTypeDSC
Pharmacist	ProviderTypeDSC
Physician	ProviderTypeDSC
Physician Assistant	ProviderTypeDSC
Nurse Practitioner	ProviderTypeDSC
High	ImportanceLevelDSC
Allergy	SeverityDSC
Medical Assistant	ProviderTypeDSC
TherapeuticClassDSC_GASTROINTESTIN AL	TherapeuticClassDSC

Evaluation - Random Forest



TherapeuticClassDSC_ANTIBIOTICS	TherapeuticClassDSC
DRUG CLASS MATCH	AllergySeverityLevelDSC
Outpatient	OrderContextDSC
rash	ReactionDSC
LAB_GLUCOSE (POC)_fail	LAB
Drug Ingredient	TypeDSC
LAB_GLUCOSE_fail	LAB
Minority	PatientDepartmentDSC
TherapeuticClassDSC_MISCELLANEOUS MEDICAL SUPPLIES, DEVICES, NON-DRUG	TherapeuticClassDSC
Fellow	ProviderTypeDSC

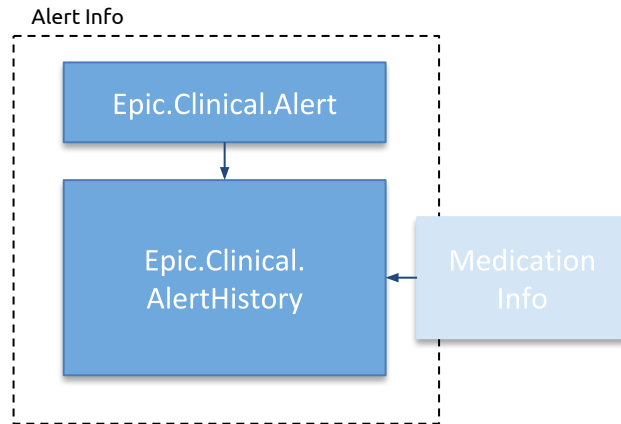
Drug-Dose Alerts

These alerts are drug-specific which are generated when overdosed orders are being made, for example.

Unbalanced Label distribution :

0- Accept: 23322

1- Overridden: 578126 -> 40000 (Down sampled)



Drug-Dose Alerts

These alerts are drug-specific which are generated when overdosed orders are being made, for example.

Unbalanced Label distribution :

0- Accept: 23322
1- Overridden: 578126 -> 40000 (Down sampled)

Features

2273

**One-hot
categorical**

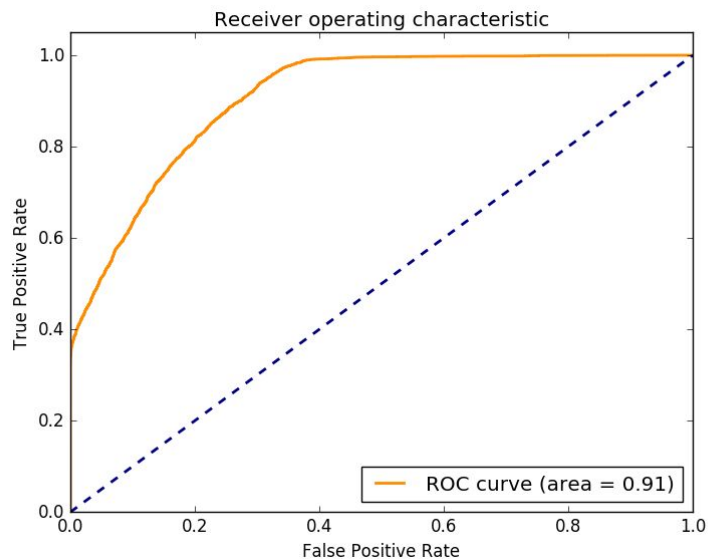
Alert description,
Importance level,
provider type,
Patient
department,
...

989

Meds

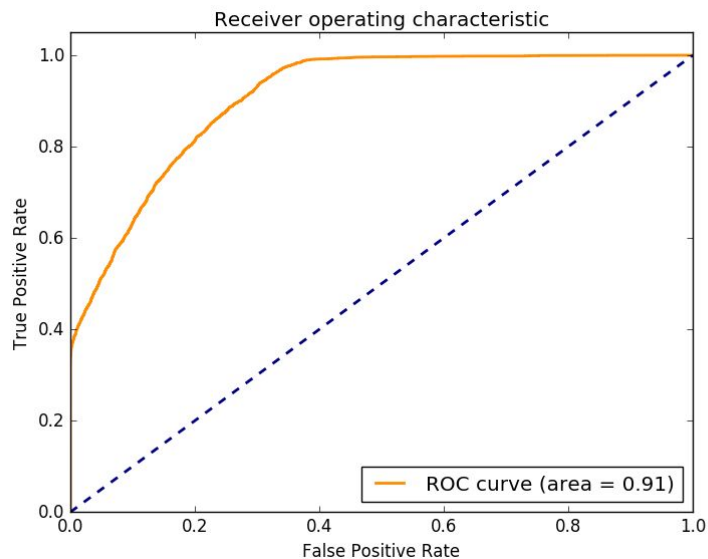
binary value for
medication
classes

Evaluation - L1 Regression



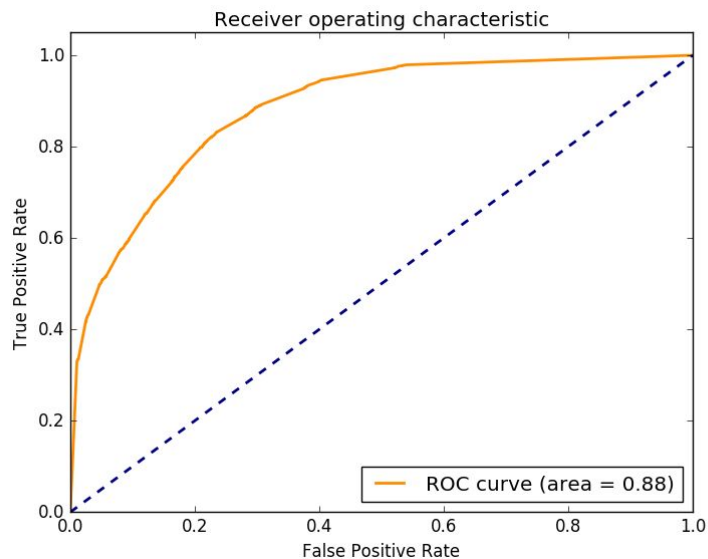
Resident	5.6508	ProviderTypeDSC
Anesthesiologist	5.0816	ProviderTypeDSC
Physician Assistant	4.5143	ProviderTypeDSC
Licensed Dietitian/Nutritionist	4.3091	ProviderTypeDSC
Nurse Practitioner	3.7346	ProviderTypeDSC
Physician	3.4881	ProviderTypeDSC
Midwife	3.0275	ProviderTypeDSC
DIAGNOSTIC	2.8221	TherapeuticClassDSC
NSC MAURA MCGRANCE	2.7637	PatientDepartmentDSC
NSP OBGYN DAN 1 HUTCH	2.6822	PatientDepartmentDSC

Evaluation - L1 Regression



NSPG HEALTH INFO MGMT	-8.6150	PatientDepartmentDSC
NWH HEALTH INFO MGMT	-8.2443	PatientDepartmentDSC
MGP PED GI NUTR SNH	-4.4202	PatientDepartmentDSC
DF EARLY DRUG DEVPMT	-4.3512	PatientDepartmentDSC
NWC ELIZ HANDEL	-4.2086	PatientDepartmentDSC
NSP RHEUM LYNN	-4.1709	PatientDepartmentDSC
MGP PED SURG WAR	-4.0011	PatientDepartmentDSC
MGH RAD ONC MC	-3.6365	PatientDepartmentDSC
MGH CC HEMMAL YAW7B	-3.6260	PatientDepartmentDSC
NSC RENIN ASSOCIATES	-3.6020	PatientDepartmentDSC

Evaluation - Random Forest

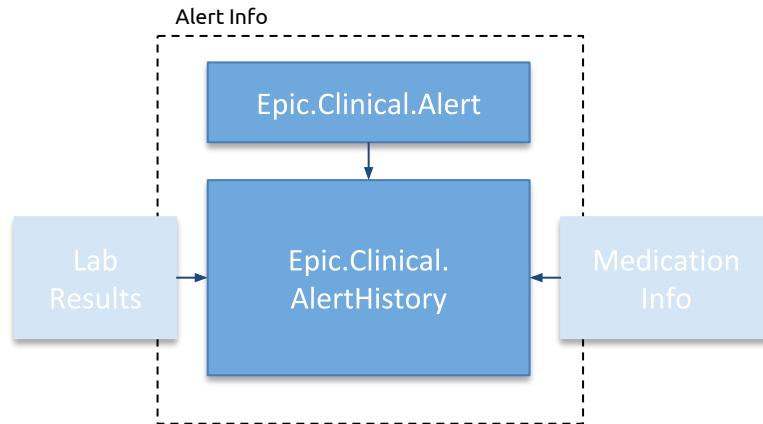


Resident	ProviderTypeDSC
Physician	ProviderTypeDSC
tab	AlertDSC
NSPG HEALTH INFO MGMT	PatientDepartmentDSC
Pharmacist	ProviderTypeDSC
NWH HEALTH INFO MGMT	PatientDepartmentDSC
Registered Nurse	ProviderTypeDSC
mg	AlertDSC
Nurse Practitioner	ProviderTypeDSC
Outpatient	OrderContextDSC

Drug-Drug Interaction (DDI) Alerts

Generated when a physician

- prescribes two interacting drugs at the same time
OR
- prescribe a drug that interacts with another drug previously documented on the patient's active medication list.



Drug-Drug Interaction (DDI) Alerts

Generated when a physician

- prescribes two interacting drugs at the same time
OR
- prescribe a drug that interacts with another drug previously documented on the patient's active medication list.

Features

883

500

2272 + 989

One-hot categorical

Bag of words

Lab + Meds

Unbalanced Label distribution :

0- Accept: 116945 -> 40000

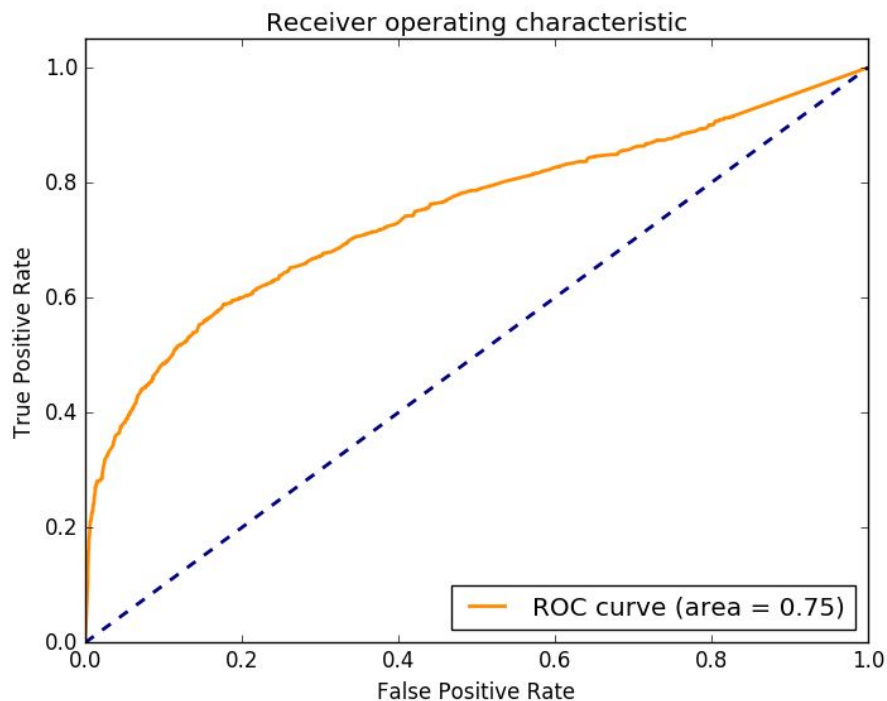
1- Overridden: 1221106 -> 40000

Alert description,
Importance level,
provider type,
Patient department,
Drug Interaction
National Drug Severity

Drug Drug
Interaction
Description
(pairs of drugs)

One-hot encoding on
individual lab tests,
binary value for
medication classes

Evaluation: L1 Regression



ANTIALLERGY	TherapeuticClassDSC
physician	ProviderTypeDSC
ANESTHETICS	TherapeuticClassDSC
number	AlertDSC
ANTIBACTERIAL AGENTS,MISCELLANEOUS	PharmaceuticalClassDSC
CHLORIDE	Lab
High	ImportanceLevelDSC
Minority	PatientDepartmentDSC
LAB_PCO2, ARTERIAL	Lab
muscle	AlertDSC

Tasks

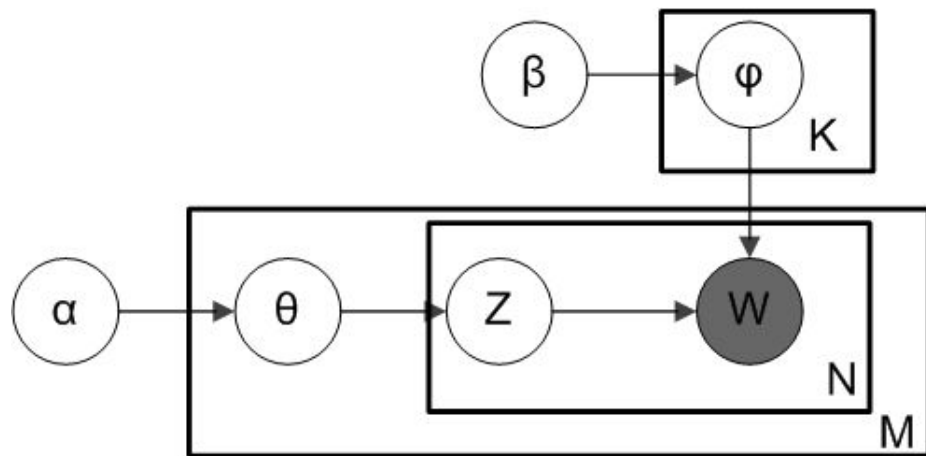
- Predicting Alert Dismissal (supervised learning)
 - Drug-Allergy Alerts
 - Drug-drug Interaction Alerts
 - Drug-dosage Alerts
- Analyzing causes for alert dismissal(unsupervised learning)
 - LDA
 - LLDA

Common Reasons for Overriding Alerts

- Providers sometimes give comments when they override the alerts.
- Some common reasons for overriding alerts can be summarized from the comments.
- Latent Dirichlet allocation (LDA) is employed to model the comments.

- LDA Setup

- α is set to be 0.1 to encourage sparsity of topics corresponding to each comment.
- Different number of topics are tested



Common Reasons for Overriding Alerts

Topics/Reasons	Key words	Sample comments
Reduced dose & Being monitored	aware patient tolerated monitor allergy team qtc reaction care desensitization	Buspar and Zoloft at these doses and frequencies are on patient's medication list from oncology clinic and renal clinic. Will order and confirm with daughter in am.
Patients taken the drug before	home dose med patient taking takes dosing meds medication regimen	High risk withdrawal, high risk sedation with known liver disease. patient subjectively endorses allergy but per chart has tolerated phenobarb for withdrawal at XXX.
“Third party overrides”	conversion team order nsu duplicate lmr aware d/c verified orders	Paged MD and spoke to MD that she is aware of the poddible DDI interactions and patient is acute and requires the haldol, benefite out weighs the risk (common practice per MD).

Conceptualizing Cause of Alert Dismissal

- Practitioners sometimes provide comments detailing the specific cause for the override
 - *High risk withdrawal*
 - *Not a duplicate order. One order was for ... and the other for ...*

Conceptualizing Cause of Alert Dismissal

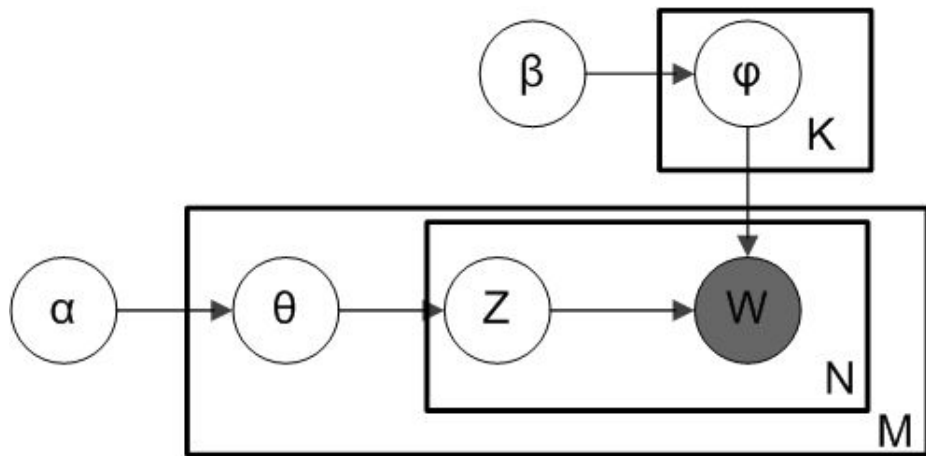
- Practitioners sometimes provide comments detailing the specific cause for the override
 - *High risk withdrawal*
 - *Not a duplicate order. One order was for ... and the other for ...*
- We hypothesize broader concepts exist for overriding alerts which may be summarized from these comments

Conceptualizing Cause of Alert Dismissal

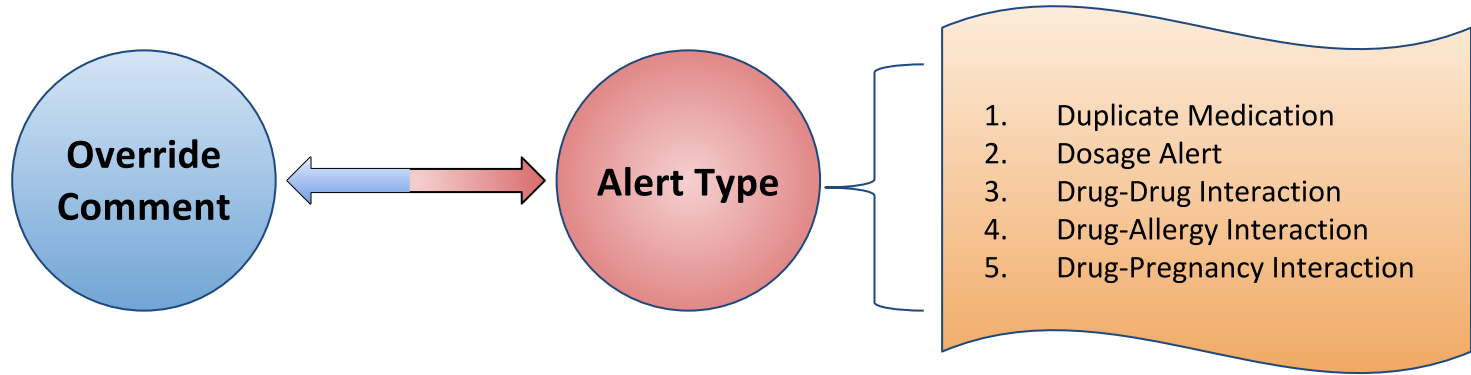
- Practitioners sometimes provide comments detailing the specific cause for the override
 - *High risk withdrawal*
 - *Not a duplicate order. One order was for ... and the other for ...*
- We hypothesize broader concepts exist for overriding alerts which may be summarized from these comments
- Medication, alert cause, as well as further textual information may also provide information

LDA

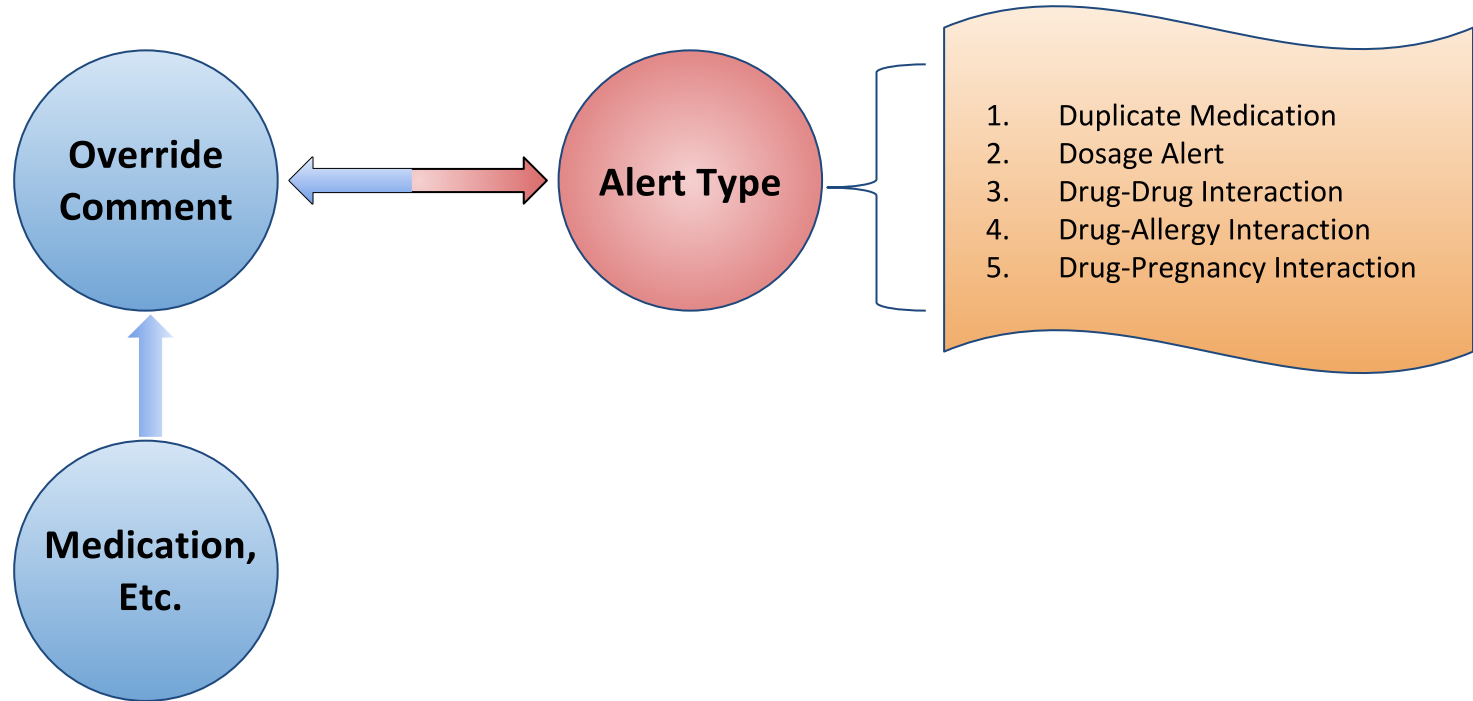
- Latent Dirichlet allocation (LDA) to investigate these concepts ($N \approx 23K$)
- Performed within *Alert_type* as well as in the aggregate
- Parameters considered:
 - Number of topics
 - Inclusion of extra variables
- $\alpha = .1$ to encourage sparsity



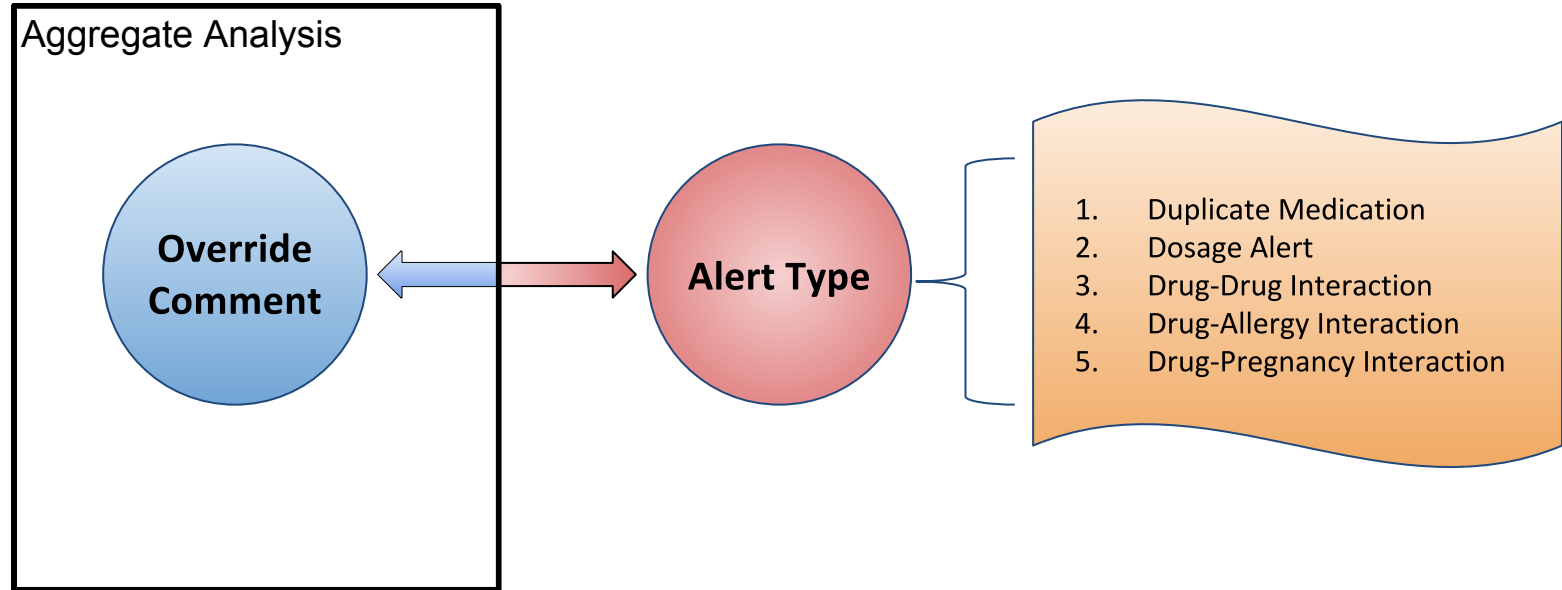
LDA



LDA

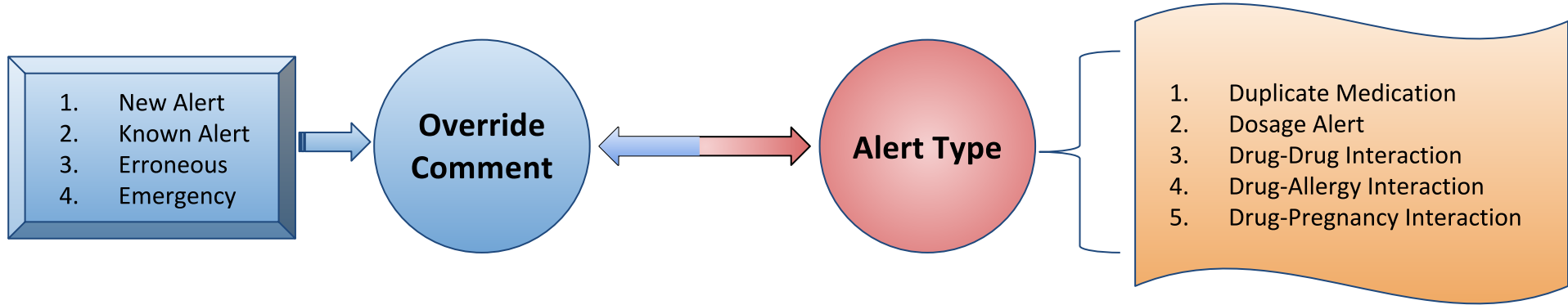


LDA



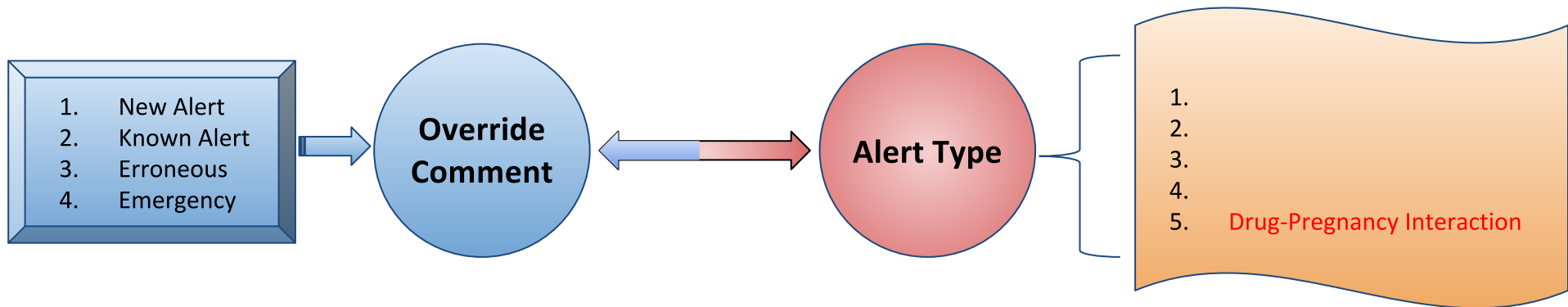
Conceptualizing Cause of Dismissal

LDA



Conceptualizing Cause of Dismissal

LDA



Topic	Inferred Concept	Example Alert Override Notes	Top Associated Words
Pregnancy Alert	New	1. per home regimen managed by outside providers 2. Uncertain which she has at home	risk limited known data conversion home oxycodone combination albuterol
	Known	1. per NSU D-KNOWN RISK 2. ok NO CLEAR RISK	risk known data limited d-known pregnant patient
	Erroneous	1. Patient is NOT pregnant (has IUD in place) 2. Pregnancy concluded - patient delivered	data limited contraindicated for ibuprofen patient postpartum not pregnant

Conceptualizing Cause of Dismissal

Topic	Subtopic	Inferred Concept	α	Example Alert Override Notes	Top Associated Words
Dose Alert	1	New	32005	1. High risk withdrawal 2. very opioid tolerant and utilizing 200mc hourly with ~150mcg delivered in last 24 hours without considerable side effect	dose daily max overdose oral exceeded single every frequency times doses/day hours intravenous once required perform checking weight prn per
	2	Emergency	17994	2. Patient w/ lupus nephritis and edema. Will monitor for ototoxicity and further renal impairment. 2. entering one time dose so a dose can be given while waiting for renal dosage adjustment	for this dosing not specific are guidelines available patient's renal level oral impairment dose the daily ordered every times intravenous
	3	Known	12174	1. x1 dose 2. okay per team	this intravenous mmol per continuous ml/hr for tprn level not dosing renal specific guidelines meq nsu phosphate daily with use
Drug-Allergy Alert	1	Erroneous	11262	1. Patient is not sure whether this is an allergy. She thinks that this is because of reported sulfa allergy 2. Not true allergy.	penicillins tolerated dose allergy patient has test with not and per amoxicillin will reaction nsads this aspirin monitor cephalosporins drug
	2	New	6827	1. Paged MD regarding allergy-med interaction. Asked MD to assess reaction history since no reaction documented. 2. FYI paged RC re: allergy alert and unknown reaction. Asked RC to assess reaction history.	ingredient inactive per latex contrast media and dye iodinated nsu rubber natural desensitization oral premedicated for aware patient will team
	3	Known	13476	1. Patient tolerated Tylenol. She reports rash to Percocet and stated she does not recall any reaction to Dilaudid. Discussed with patient that she will try half a tablet and we will monitor for reaction.	codeine morphine home per percocet oxycodone oxycodone-acetaminophen tolerated patient allergy not will monitor med aware has with hydromorphone hydrocodone-acetaminophen tolerates
Drug-Drug Alert	1	Known	6695	1. spoke with dr. wong and will monitor for QTC and he also made me aware that pt was on this combination with the previous admission 2. ARP effect on QTC is nominal. Even if serum level were to double/triple in presence of FLX	selected anticoagulants inhibitors will cyp aware per citalopram vitamin oxycodone fentanyl hydrocodone inhibit alfentanil slt team dose thrombolytics home metoclopramide
	2	New	13163	1. Paged MD and spoke to MD that she is aware of the possible DDI interactions and patient is acute and requires the haldol 2. Aware of possible DDI interactions. 3. Per nurse.	agents prolonging ondansetron aware qtc will not possible monitor haloperidol azithromycin ketorolac amiodarone taking aspirin per patient hydroxyzine for injectable
	3	Emergency	7531	1. Patient takes nitroglycerin in the event of cardiac concern. Patient has been advised not to take the avanafil with nitroglycerin. 2. patient lost ALL of the prescription so needed to electronically prescribe them and faxed the depakote er taper to walgreens in salem	and ssris snris slt simvastatin tramadol tricyclic trazodone home not tapentadol comp inhibitors conversion patient will cough taking cold opioids
Duplicate-Medication Order Alert	1	New	16984	1. Buspar and Zoloft at these doses and frequencies are on patient's medication list from oncology clinic and renal clinic. Will order and confirm with daughter in am. 2. Team changed TPN start/end time accidentally. Spoke w/ RN who is aware current bag should be taken down tonight @ 8pm and new bag to be hung at that time. Only 1 TPN bag to be run at a time.	oral order non-prn conversion frequency hcl dose subq insulin home sodium different and for doses needs med lmr duplicate prednisone
	2	New	9351	1. Pt order was accidentally d/c'd during transfer. Renewed by primary team. NSU aware.	order non-prn per team sodium heparin chloride sodium, porcine/pf potassium acetate nsu okay phos, m-basic-d-basic gluconate calcium sulfate acid with magnesium dextrose
	3	Erroneous	12818	1. Not a duplicate order. One order for arterial cath lumen dwell and second order for venous lumen cath dwell. 2. Pt provided with Rx for narcotic pre-op for pain control. Now receiving Rx for post-op pain control	order prn non-prn oral hcl eye different for one sulfate only will oxycodone duplicate not acetaminophen hcl/pf ondansetron care verified

Aggregate Analysis

Topics/Reasons	Key words	Sample comments
Reduced dose & Being monitored (New)	aware patient tolerated monitor allergy team qtc reaction care desensitization	Buspar and Zoloft at these doses and frequencies are on patient's medication list from oncology clinic and renal clinic. Will order and confirm with daughter in am.
Patients taken the drug before (Known)	home dose med patient taking takes dosing meds medication regimen	High risk withdrawal, high risk sedation with known liver disease. patient subjectively endorses allergy but per chart has tolerated phenobarb for withdrawal at XXX.
“Third party overrides” (Emergency)	conversion team order nsu duplicate lmr aware d/c verified orders	Paged MD and spoke to MD that she is aware of the poddible DDI interactions and patient is acute and requires the haldol, benefite out weighs the risk (common practice per MD).

[Things that can be improved in the future]

- Better data cleaning strategy (e.g. filter out lab tests using time stamps)
- Interpretation of nonlinear models
- Make use of the left-out data (because of the unbalance of pos/neg set)
- Deeper analysis in dismissal reasons (Including more relevant information as labels/features)
- Consider more variables for the topic model
 - E.g. hospital stay is very indicative of override/accept